UNIVERSIDADE ESTADUAL PAULISTA
FACULDADE DE MEDICINA VETERINÁRIA E ZOOTECNIA

ESTUDO PROTEÔMICO DO DESENVOLVIMENTO FOLICULAR DE VACAS ZEBUINAS NÃO GESTANTES

Tarcísio Torre Lourenço

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DEDICATÓRIA

Dedico à minha noiva Fernanda, aos meus pais Francisco e Michelina, às minhas irmãs Tatiane e Taciane, aos meus cunhados Márcio e Tiago, e à minha sobrinha Lenise por sempre me apoiarem em todos os passos.

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EPÍGRAFE

Fazer o que você gosta é liberdade.

Gostar do que você faz é felicidade.

Frank Tyger

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RESUMO

LOURENÇO, T.T. ESTUDO PROTEÔMICO DO DESENVOLVIMENTO FOLICULAR DE VACAS ZEBUINAS NÃO GESTANTES. Botucatu – SP. 2015.42 Dissertação (Mestrado) – Faculdade de Medicina Veterinária e Zootecnia, Campus Botucatu, Universidade Estadual Paulista.

O ciclo estral da vaca é composto por 2-3 ondas de crescimento folicular, no qual vários folículos são recrutados e iniciam um novo crescimento. Durante o período denominado desvio folicular, um folículo se torna dominante e os outros entram em atresia. Este processo envolve um mecanismo ainda não completamente compreendido, incluindo proteínas específico, como já estabelecido pela expressão gênica. O objetivo do presente estudo foi caracterizar as proteínas do fluído folicular a fim de identificar macromoléculas relacionadas ao desenvolvimento dos folículos de vacas zebuínas nã-gestantes. Foram colhidos os ovários de 25 vacas mestiças não-gestantes em um abatedouro. A presença do corpo lúteo foi anotada para cada ovário. O líquido folicular foi colhido utilizando-se a imersão do ovário em meio líquido e ultrassonografia. De acordo com a mensuração do diâmetro folicular, foram formados 3grupos, folículos pequenos (≤6,5mm, n=25), médios (>6,5mm a ≤9mm, n=9) e grandes (>9,0mm, n=11). Após 2 centrifugações (600xg/10 minutos e 15.000xg/30 minutos, 4ºC) o sobrenadante foi separado e utilizado para determinação da concentração de proteína total (método de Bradford). A eletroforese foi conduzida sob condições desnaturantes e redutoras, em gel de separação de poliacrilamidaà 12%. A concentração de progesterona e estradiol do líquido folicular foi determinada a fim de identificar os folículos saudáveis. As proteínas diferenciais identificadas pela eletroforese foram submetidas à espectrometria de massas e a ontologia gênica foi investigada nos bancos de dados disponíveis. Foram encontradas 45 bandas proteicas em 45 amostras de líquido folicular. A média da concentração ± desvio padrão da progesterona foi de 129,91 ± 186,43, considerando todos os folículos. Os resultados mostram que houve uma expressão diferenciada de proteínas nas diferentes categorias de folículos.

Palavras chave: eletroforese, folículo, MALDI-TOF, vacas

ABSTRACT

LOURENÇO, T.T. PROTEOMIC STUDY OF FOLLICULAR DEVELOPMENT ZEBU COWS NOT PREGNANT. Botucatu – SP. 2015. 42 Dissertação (Mestrado) – Faculdade de Medicina Veterinária e Zootecnia, Campus Botucatu, Universidade Estadual Paulista.

The estrous cycle of the cow consists of 2-3 follicular waves, in which several follicles are recruited and initiate growth. During the period called follicular deviation, one follicle becomes dominant and the other come into atresia.This process involves mechanisms not yet fully understood, including specific proteins as already determined by gene expression. As a result, the objective of this study was to characterize the proteins of the follicular fluid to identify macromolecules related to the development of follicles from Zebu cow. The ovaries of non-pregnant cows 25 were harvested. The presence of luteum body was noted for each ovary. Follicular fluid was collected using ultrasound. According to the measurement of follicular diameter was 3 separate groups, small follicles (≤6,5mm, n = 28), medium (> 6.5mm to ≤9mm, n = 7) and large (> 9,0mm, n = 11). After 2 centrifugations (600xg / 10 minutes, 15.000xg / 30 minutes, 4 ° C) the supernatant was separated and used for determination of total protein concentration (Bradford method). Electrophoresis was conducted under denaturing and reducing conditions on polyacrylamide separating gel at 12%. The concentration of progesterone and follicular fluid estradiol was determined to identify healthy follicles. The differential proteins identified by electrophoresis will be submitted for MALDI TOF MS / MS approach and gene ontology will be investigated in the databases available. They found 45 protein bands in electrophoresis in 45 follicular fluid samples. The mean ± standard deviation of progesterone concentration was 129.91 ± 186.43 considering all follicles. The results show that there was a differential expression of proteins in different categories of follicles

Key-words: cows, electrophoresis folicule, MALDI-TOF

CAPÍTULO 1

1. INTRODUÇÃO E JUSTIFICATIVA

Atualmente a pecuária de corte e de leite é a principal atividade do agronegócio brasileiro. Para o desenvolvimento deste setor do mercado, é necessário um aprimoramento do melhoramento genético do rebanho nacional, o qual está diretamente associado ao manejo reprodutivo, a mão de obra, as instalações, aos tipos de forragem e a eficiência no manejo sanitário, tornando a pecuária uma área especializada.

Com o crescimento da bovinocultura, o Brasil se tornou o maior exportador de carne do mundo, alcançando quase 7,68 milhões de toneladas por ano. O rebanho esta estimado em 200 milhões de animais tendo um crescimento mais elevado em 2014 em relação aos outros anos (MAPA, 2015).

A produção de embriões *in vitro* (PIV) tem contribuído para a elevação da produção na pecuária e está sendo incorporada aos projetos de reprodução. Com o desenvolvimento do método de punção folicular, tornou-se possível à recuperação de oócitos de fêmeas para fecundação *in vitro* (FIV). Dessa forma, abrindo novos caminhos para a multiplicação de animais de interesse econômico, superando os atuais índices da transferência de embriões clássica no que diz respeito ao número de bezerros/vaca/ano. Essa técnica pode ser utilizada em animais jovens, senis, gestantes ou lactantes e animais com problemas adquiridos de fertilidade. (TERVIT, 1996; GOODHAND et al., 1999; MALARD et al., 1999; TANEJA et al., 2000).

Apesar de todo avanço na FIV, pouco se conhece a respeito da composição química do líquido folicular, especialmente no que diz respeito à proteômica. O líquido folicular é formado a partir de produtos de secreção das células da granulosa e da teca e difusão dos capilares que irrigam o tecido ovariano (HESS et al., 1998). Os oócitos estão contidos no líquido folicular, no qual sofrerão o processo de maturação e desenvolvimento. A composição bioquímica do líquido folicular influencia a qualidade dos oócitos, competência oocitária, capacidade de desenvolvimento e qualidade embrionária (ALI et al., 2004, IWATA et al., 2005; KIM et al., 2006; BIANCHI et al., 2013). Também está relacionada à condição fisiológica da fêmea, estágio de desenvolvimento e *status* funcional do folículo (IWATA et al., 2006; KIM et al., 2006; BIANCHI et al., 2013).

O líquido folicular contém moléculas ativas e proteínas que estão

relacionadas ao crescimento folicular, fertilização dos oócitos e ao desenvolvimento embrionário. A caracterização proteômica do líquido folicular pode determinar biomarcadores para identificar a competência/qualidade dos oócitos e aumentar a taxa de sucesso na fertilização *in vitro* (WALLACE et al., 2012; BIANCHI et al., 2013). Em humanos, a análise proteômica do fluído folicular é indicada para identificar a resposta do paciente, frente à fertilização *in vitro* (SALERNO et al., 2011).

Após a transcrição e tradução, as proteínas podem sofrer modificações pós-traducionais (GOBBETTI et al., 2002). Dessa forma, resultados da expressão gênica podem ser complementados com a caracterização das proteínas e dos peptídeos do líquido folicular, a fim de permitir a identificação do seu papel na fisiologia folicular e maturação oocitária (DUCOLOMB et al., 2013).

Em vista disso, o objetivo deste estudo foi determinar a composição proteica do líquido folicular de diferentes classes de folículos de vacas vazias, por eletroforese e espectrometria de massas.

2. REVISÃO DA LITERATURA

2.1. Fisiologia do ciclo estral das vacas

O sistema reprodutor dos bovinos é formado pelos ovários, tubas uterinas, cornos uterinos, corpo do útero, cérvix, vagina e vulva (SISSON, 1986). Os ovários são a fonte dos gametas femininos, sendo composto por duas porções, medula e córtex, no qual estão localizados os folículos em diferentes estágios de desenvolvimento. As fêmeas dessa espécie nascem com *pool* de folículos, os quais são perdidos durante a vida, em vista da atresia folicular, e raros, durante a ovulação (SENGER, 2003).

Os bovinos são animais poliéstricos anuais, com ciclo estral com intervalos de 17 a 24 dias, composto de 2 a 4 ondas de crescimento folicular. O número de ondas de crescimento folicular pode variar de acordo com a subespécie/raça, sendo que nos taurinos há predominância de 2 a 3 ondas e nos zebuínos 3 a 4/ciclo estral (SAVIO et al., 1988; SIROIS; FORTUNE, 1988; GINTHER et al., 1989; RHODES et al., 1995; FIGUEIREDO et al., 1997; VIANA et al., 2008; WOLFENSON et al., 2004).

Em muitos estudos as diferenças do ciclo estral e crescimento folicular entre

as subespécies de *Bos taurus* foram demonstradas. Fêmeas *Bos taurus indicus* são caracterizadas por ter ciclos mais curtos, quando comparada as *Bos taurus taurus* (BARR, 1975). O intervalo entre as ovulações é correlacionado positivamente ao número de ondas foliculares e o dia da emergência da segunda onda folicular, diminui com o aumento do número de ondas/ciclo (RHODES et al., 1995; BÓ et al., 2003), com a emergência da 3ª onda mais precocemente nas vacas *B. indicus* (BÓ et al., 2003). A estação do ano pode influenciar na taxa de crescimento do folículo dominante da terceira onda, sendo que nas vacas *B. indicus* é mais lenta e nas *B. taurus* é rápido na estação das chuvas (BÓ et al., 2003).

Uma fase do ciclo estral é marcada pelas altas concentrações plasmáticas de estradiol (E2, fase estrogênica) e outra de progesterona (P4, fase lútea). O cilco também pode ser dividido em quatro períodos (proestro, estro, metaestro e diestro) (IRELAND; ROCHE, 1983; FORTUNE et al, 1988; GINTHER et al., 1989; SENGER, 2003).

A fase folicular ocorre do dia 19 do ciclo estral até o início do estro (STEVENSON, 2007). Ela é caracterizada pelo recrutamento (emergência folicular) de um grupo de pequenos folículos influenciado pelas secreções de FSH pela glândula pituitária (IRELAND; ROCHE, 1983; FORTUNE et al, 1988; GINTHER et al., 1989; SENGER, 2003). Esses por sua vez produzem concentrações crescentes de E2 (SENGER, 2003).

Nessa espécie, após o recrutamento, os folículos iniciam o seu desenvolvimento; essa fase tem duração média de três dias (GINTHER et al., 2003). Durante esse período, o estradiol, secretado pelos folículos em desenvolvimento, estimula a produção de IGF-1 e o LH a produção de esteroides intra-foliculares, os quais estão envolvidos na seleção folicular (GINTHER et al., 2003). Entre esses folículos, apenas um será selecionado (fase de seleção do folículo dominante), enquanto os outros apresentam um decréscimo no seu desenvolvimento (folículos subordinados) (LUCY et al., 1992), fenômeno denominado divergência folicular.

O crescimento folicular é regulado por comunicação entre oócito, células epiteliais e fatores advindos da circulação (BRITT, 2008). Durante esse período, parece que o LH estimula a produção de esteroides intra-foliculares e fatores de crescimento que estão envolvidos na seleção (GINTHER et al., 2003a) e a taxa de crescimento do folículo dominante é superior a dos subordinados. Nos zebuínos

(*Bos taurus indicus*) esse período ocorre em torno de 2,5 a 2,7 dias, após a emergência folicular, quando o folículo dominante possui 5,4 a 6,2 mm (GIMENES et al., 2005; SARTORELLI et al., 2005; CASTILHO et al.2006).

A ovulação ocorre quando o folículo atinge em torno de 7 a 10 mm de diâmetro e está associada à aquisição de receptores de LH nas células da granulosa, e quando os níveis de progesterona decaem. Folículos com diâmetro maior que 10 mm requerem concentrações mais elevadas de LH (SARTORI et al, 2001). Caso a luteólise não ocorra, o folículo dominante entra em atresia, assim como os subordinados, iniciando uma nova onda de crescimento folicular (GINTHER et al., 1989; WEBB et al.,1999).Quando o folículo dominante está presente e a luteólise é iminente, a ovulação ocorre (FORTUNE et al., 2004).

Na fase folicular ocorre o estro, período no qual a fêmea está receptiva ao macho e tem duração de 2 a 50 horas, com média de 12 a 18 horas (STEVENSON, 2007), sendo mais curto nas fêmeas *B. indicus* (entre 10 e 12 horas), o que pode dificultar sua detecção. Apesar disso, o intervalo entre o estro e a ovulação é semelhante entre as subespécies (WILTBANK et al., 2006). A maioria das vacas desta subespécie apresentam sinais de cios noturnos, o que compromete mais ainda o manejo reprodutivo (PINHEIRO et al., 1998; MEMBRIVE, 2000).

O número de folículos recrutados por onda de crescimento folicular nas fêmeas da subespécie *B. indicus* é maior quando comparadas as *B. taurus* (CARVALHO et al., 2005). Esta característica pode estar relacionada com a maior secreção de fatores de crescimento (IGF) (SIMPSON et al., 1994; BONI et al., 1997; ALVAREZ et al., 2000) apesar das menores concentrações de FSH.

Diferenças entre as subespécies ainda podem ser verificadas no diâmetro dos folículos dominantes, sendo que 33% das fêmeas *B. indicus* ovulam com folículos medindo 7,0 a 8,4 mm, 80% com 8,5 a 10 mm e 90% com diâmetro superior a 10 mm (GIMENES et al., 2005a), com diâmetros máximos entre 9,4 a 12,1 mm (FIGUEIREDO et al., 1997), o que é menor quando comparado com as fêmeas *B. taurus*. O tamanho do corpo lúteo também apresenta os mesmos resultados, com diâmetros entre 17 a 21 mm (RHODES et al., 1995; FIGUEIREDO et al., 1997) e com menor produção de progesterona (RANDEL, 1976).

A Figura 1 representa a relação entre as secreções de gonadotrofinas

hipofisárias (FSH e LH), inibina (I) e estradiol (E2) durante o proestro de vacas. Durante o recrutamento o FSH aumenta e promove o desenvolvimento do antro nos folículos em crescimento e neste período o papel do FSH é mais importante do que do LH. Os folículos secretam pequena quantidade de E2, mas isto estimula o aumento da produção de FSH. Quando os folículos entram na fase de seleção, a secreção de estradiol aumenta e a inibina também é produzida pelos folículos. A inibina tem ação inibitória sobre a secreção de FSH no lobo anterior da pituitária. A relação entre FSH e LH se inverte. Já na fase de dominância os grandes folículos produzem mais estradiol e isto estimula a onda pré-ovulatória de LH. A secreção de FSH permanece baixa porque a inibina continua a ser secretada em altas concetrações pelo folículo dominante. A queda nas concentrações de FSH faz com que os folículos antrais entrem em atresia (SENGER, 2003).

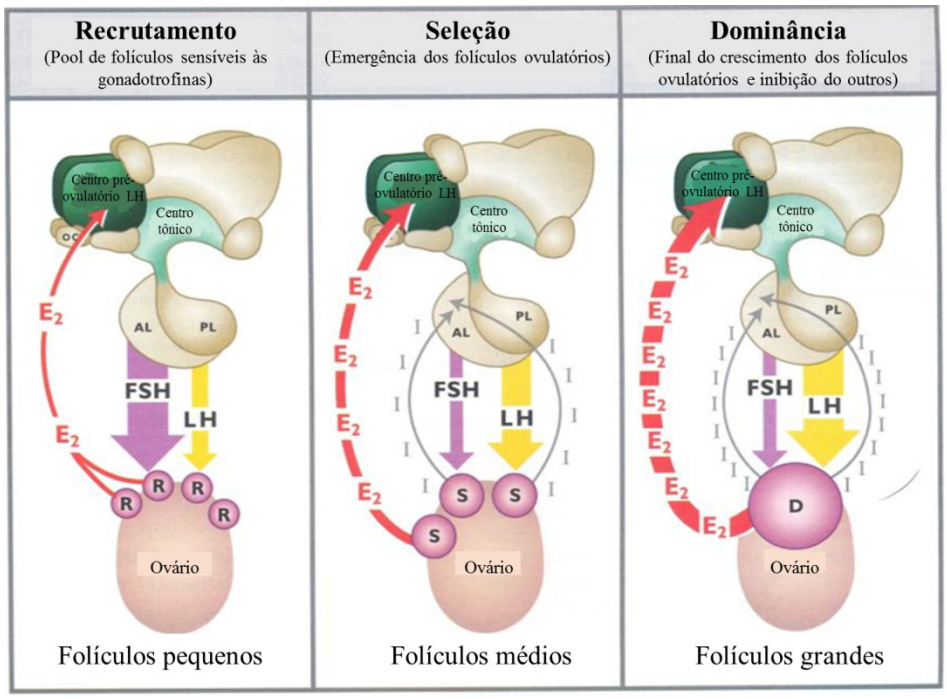

Figura 1. Relação entre as secreções de gonadotrofinas hipofisárias (FSH e LH), inibina (I) e estradiol (E2) durante o proestro de vacas. Fonte: SENGER, 2003.

A fase lútea (dias 4 a 18 do ciclo) ocorre entre a ovulação e a luteólise. Inicia-se quando o corpo lúteo secreta concentrações de P4 acima de 1 ng/mL (dia 4 e 5 do ciclo). Os padrões de liberação de LH são mais baixos e as concentrações de P4 são máximas em torno de 8 a 10 dias. Por volta de 14 dias há secreção de altas concentrações de progesterona e, na ausência de um embrião viável, a

prostaglandina F2α (PGF2α) é secretada pelo endométrio, sob influência das secreções de E2 e ocitocina, causando regressão funcional e estrutural do corpo lúteo (CL). A luteólise funcional é caracterizada pelo rápido declínio das concentrações de P4 nas primeiras 8 a 12 horas, após a secreção de PGF2α. A luteólise estrutural é identificada pela diminuição de tamanho e peso do CL em consequência da apoptose das células luteínicas (NEUVIANS et al., 2003; STEVENSON, 2007). A ocitocina lútea também está envolvida na luteólise (STEVENSON, 2007).

As ondas de crescimento folicular e ovulação na vaca estão representadas na Figura 2. As concentrações máximas de FSH são detectadas de 1 a 2 dias, antes do início de cada onda folicular e próximo da última ovulação. Durante o diestro, quando as concentrações de progesterona estão elevadas, pulsos de LH são suficientes para permitir a seleção de folículos dominantes, mas insuficientes para permitir a maturação de um folículo dominante até a progesterona retornar as concentrações basais, após a luteólise. Após a luteólise, durante o proestro, frequentes pulsos de LH e estradiol são suficientes para induzir o estro comportamental. O metaestro (dias 1 a 3) é caracterizado por concentrações baixas de LH, estradiol e progesterona. Aumento secundário de FSH de menor grandeza é observado antes da ovulação, ou 24 a 30 horas após o início do pico pré-ovulatório de LH. Esse aumento secundário pode ser uma consequência ausência de produção de inibina, derivada do folículo, durante a ovulação. Esse aumento de FSH é fundamental para o recrutamento da primeira onda folicular (STEVENSON, 2007).

2.2. Composição do líquido folicular

O maior elemento constituinte do folículo pré-ovulatório é o líquido folicular (RODGERS et al., 2001), que é composto por moléculas com baixa massa molecular advindas do soro sanguíneo (SHALGI, 1973).

O líquido folicular é formado a partir de produtos de secreção das células da granulosa e da teca e difusão dos capilares que irrigam o tecido ovariano, sendo permeável às proteínas com massa molecular <500 kDa (HESS et al., 1998). Os oócitos estão embebidos no líquido folicular, onde sofrerão seu desenvolvimento e maturação. A composição bioquímica desse fluído influencia a qualidade dos oócitos e está relacionada ao *status* fisiológico da fêmea e estágio de

desenvolvimento funcional do folículo (IWATA et al., 2006; KIM et al., 2006; BIANCHI et al., 2013).

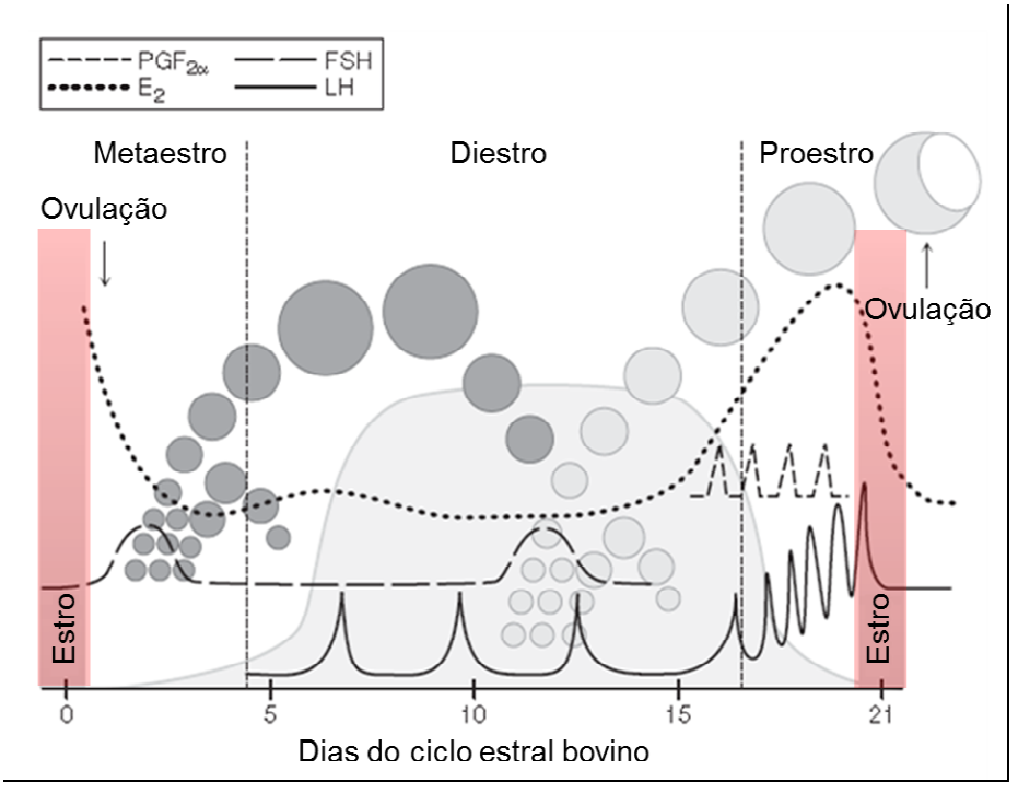

Figura 2. Esquema representando duas ondas de crescimento folicular nos bovinos. Fonte: STEVENSON, 2007

O líquido folicular contém moléculas ativas e proteínas que estão relacionadas ao crescimento folicular, à fertilização dos oócitos e ao desenvolvimento embrionário. A caracterização proteômica do líquido folicular pode revelar biomarcadores para identificar a competência/qualidade dos oócitos e aumentar a taxa de sucesso na fertilização *in vitro* (WALLACE et al.,2012; BIANCHI et al., 2013).

Apesar de muitos estudos a respeito da maturação e fertilização *in vitro* em bovinos, a análise proteômica do fluído folicular nessa espécie é mencionada em raros trabalhos e muitos desses estudos foram pontuais, a respeito de proteínas específicas, porém nenhum estudo global foi descrito.

A concentração de proteína total, sódio e potássio no líquido folicular de bovinos foi relacionado à cor (amarelo a marrom), predominando frações de albumina, quando separadas por eletroforese em acetato de celulose. As

concentrações dos componentes químicos variaram de acordo com o tamanho do folículo e a concentração de albumina, sódio, potássio e progesterona, sendo mais elevadas no líquido folicular do que no soro. Contrariamente, a concentração de proteína total, gama globulina, colesterol total, colesterol livre, colesterol ester e glicose foram mais baixos no fluído folicular. Os autores concluíram que os principais componentes químicos do fluído folicular são transferidos do plasma sanguíneo (MURANAKA et al., 1986).

Nas fêmeas pré-púberes foi sugerido que a competência do desenvolvimento reduzido dos oócitos pode ser atribuída a uma deficiência na tradução de proteínas (OROPEZA et al., 2004). A composição bioquímica do fluído folicular pode revelar não apenas a fase de desenvolvimento folicular, mas também o estado funcional geral do próprio folículo e do organismo (KIM et al., 2006; VON et al., 2010), por uma variedade de proteínas (SPITZER et al., 1996; KIM et al., 2006; SCHWEIGENRT et al., 2006; TWIGT et al., 2012). Assim, a menor concentração sérica e no fluído folicular do peptídeo fator de crescimento endotelial vascular (VEGF) e concentrações mais elevadas de inibina A e B no fluído folicular estão associadas a melhor resposta ovariana e altas taxas de gestação em mulheres submetidas à fertilização *in vitro* (OCAL et al., 2004).

O sistema IGF está envolvido no crescimento e diferenciação celular. Este sistema é formado de IGF-1, IGF-2, receptores de IGF, uma família de proteínas ligantes (IGFBPs) e proteases de IGFBP (FORTUNE et al., 2004). As proteases degradam as proteínas IGFBPs, liberando-o do complexo IGFBP–IGF. As concentrações intra-foliculares de IGFBP-2 e IGF-1 livre são baixas e altas, respectivamente no folículo maior, quando comparado ao segundo folículo maior em novilhas (BEG et al., 2006).

O potencial de desenvolvimento dos oócitos pode ser afetado pela apoptose das células da granulosa, tamanho dos folículos e densidade das células do *cumulus* (FENG et al., 2007). A taxa de apoptose nas células do *cumulus* antes (ZEUNER et al., 2003; FENG et al., 2007) ou durante (IKEDA et al., 2003) a fertilização *in vitro* é negativamente correlacionada a qualidade do oócito. O ooócito é capaz de regular os processos de proliferação, diferenciação e metabolismo das células somáticas foliculares, envolvidos no crescimento folicular final, funcionando como uma competência intrínseca (MERMILLOD et al., 2008). Neste processo estão envolvidos vários fatores de crescimento, sendo o

bone morphogenetic proteins (BMP) modulado pelo oócito (MERMILLOD et al., 2008). O BMP participa da seleção do folículo dominante (KNIGHT; GLISTER, 2006) e os oócitos bovinos que secretam BMP-6 e BMP-15 possuem células do *cumulus* protegidas contra apoptose, durante o cultivo do complexo *cumulus*-oócito (HUSSEIN et al., 2005).

O aumento induzido pelo FSH na proteína plasmática A, associada à gestação (PAPP-A) é a modificação mais precocemente detectada no futuro folículo dominante. A proteína PAPP-A é a protease que degrada IGFBP-4 e IGFBP-5, aumentando a concentração intra-folicular de IGF-I (FORTUNE et al., 2004).

Nas mulheres, a maior expressão das proteínas haptoglobulina-α (predominantemente expressando domínio T1), apolipoproteína H (β-2-glicoproteína I), transferrina, lisozima C, fibrinogênio de cadeia α e imunoglobulina de cadeia pesada V-III (região BRO) foram encontradas no fluído folicular de oócitos, que geraram produtos viáveis. Enquanto o fibrinogênio de cadeia γ e β, anti-trombina, proteína ligadora de vitamina D e complemento 3 e 4 foram menos expressas nesses produtos (ESTES et al., 2009; SALERNO et al., 2011).

Em bovinos, Muranaka et al. (1986) encontraram menor concentração de proteínas totais do fluído folicular de cistos comparada com a concentração em folículos normais. Observaram um padrão de albumina específico no líquido folicular, diferentemente daquele do soro sanguíneo. As concentrações dos componentes químicos do fluido folicular de cistos foram maiores do que as dos folículos normais, indicando o controle local das características químicas do fluido folicular cístico. As concentrações do fluído folicular de albumina, sódio, potássio, ions e progesterona foram provenientes do soro sanguíneo periférico. Ao contrário as concentrações de proteína total, de gama-globulina, colesterol total, colesterol livre e glicose do fluido folicular foram mais baixos do que no soro. Esse estudo concluiu que os principais componentes químicos do fluido folicular são transferidos a partir do sangue por capilares da parede folicular através de um mecanismo seletivo.

Posteriormente, Mortarino et al. (1999) encontraram 200 *spots* no líquido de cistos foliculares de bovinos comparados aos de folículos em diferentes estágios de desenvolvimento. Nove *spots* diferenciais foram identificados pelo

sequenciamento do N-terminal, sendo encontradas a α-1-antitripsina, albumina, sorotransferrina e apolipoproteína A-I e A-IV. Determinaram predominância de albumina e imunoglobulina G no fluído folicular colhido dos cistos ovarianos. Esses autores observaram diferentes padrões de proteínas entre os diferentes diâmetros foliculares e os cistos.

Mais recentemente, Maniwa et al. (2005) estudaram as proteínas contidas no fluído de cistos foliculares de vacas, a fim de correlacionar esses elementos à etiologia e patogenia da alteração. Diferente dos achados de Mortarino et al. (1999), esse estudo encontrou expressão elevada de 8 *spots* de proteínas nas amostras do líquido dos cistos foliculares: f1-atpase mitocondrial bovina (BMFA); fator associado à eritróide (EAF); metionina sintase (MeS); receptor-VEGF, gliceraldeido 3-fosfato desidrogegenase (GAPDH); proteína 70 de choque térmico (HSP70); β-lactoglobulina (BLG) e subunidade Ip da succinatodesidrogenase (SD).

Angelucci et al. (2006) realizaram uma análise proteômica do fluído folicular de 25 mulheres submetidas à injeção intracitoplasmática de espermatozoide (ICSI) e encontraram 695 *spots* com ponto isoelétrico, variando entre o pH 3 e 10 e massa molecular entre 10 e 200 kDa. Desses *spots*, 625 foram comuns ao do soro humano. Foram identificadas 210 proteínas por espectrometria de massas, sendo que a maioria foram componentes relacionados à inflamação e incluíam principalmente a ceruloplasmina, α e γ-fibrinogênio, hemopexina, haptoglobulina, serpina, glicoproteína leucina-2 e macroglobulina A-2.

Ducolomb et al. (2013) estudaram a adição de frações proteicas e peptídicas do fluído folicular ao meio de cultivo para maturação (MIV) e fertilização *in vitr*o (FIV) em suínos. As amostras de líquido folicular foram separadas em 5 frações (F1-F5) e identificadas por espectrometria de massa. A adição da F1, a qual continha 12 proteínas (fragmentos de imunoglobulinas e imunoglobulinas, albumina, citoqueratina, queratina, α-1-antiquimitripsina 2, transferrina e precursor do plasminogênio) elevou as taxas de MIV e FIV. Já as frações F2 (6 proteínas, fragmentos de imunoglobulinas e imunoglobulinas, pré-albumina), F3 (6 proteínas, fragmentos de imunoglobulinas e imunoglobulinas, 2 isoformas da pré-albumina) e F4 (14 proteínas, proteína da família do inibidor da inter-α-tripsina, α-1-antiquimiotripsina, haptoglobina, endopina 1β, transtiretina, componente C8G do complemento, precursor da albumina sérica, fator-B,

properdina, fragmento da fumaratohidratase, inibidor da anidrase carbônica, fator de coagulação XII e 3 imunoglobulinas) reduziram a porcentagem de oócitos em metáfase I. Já a fração F5 (2 proteínas, albumina sérica e queratina) favoreceu a quebra da vesícula germinativa e a MIV.

Nos bovinos, estudo anterior demonstrou os efeitos mencionados, mas não identificou as diferentes frações contidas no líquido folicular. Romero-Arredondo et al. (1994) investigaram a inclusão de líquido folicular no meio de cultivo. Quando o fluído foi colhido 0 e 4 horas após a onda pré-ovulatória de LH houve efeito inibitório da meiose. Contudo quando colhido 8 horas ou mais após o pico de LH esse efeito foi ausente e induziu a expansão do *cumulus* e a maturação meiótica. Tais resultados comprovam que fatores contidos no fluído folicular podem contribuir para aumentar as taxas de MIV, FIV e PIVE.

Existem poucos estudos relacionados à análise proteômica do fluído folicular de bovinos. Iwata et al. (2005) investigaram a composição química do fluído folicular e do soro de novilhas Nelore. Foram encontradas menores concentrações de magnésio (Mg), asparato amino transferase (AST), ácidos graxos não-esterificados (NEFA), lactato desidrogenase (LDH) no soro, quando comparado ao fluído folicular e observou-se uma correlação negativa entre a capacidade de desenvolvimento, taxa de clivagem e blastulação em relação a concentração do índice de icterícia (TIC) e uréia (BUN) no fluído folicular. Tais resultados podem ser aplicados para a formulação de meios de cultivo oocitário (IWATA et al., 2004).

2.3. Considerações finais

Vários estudos da expressão de genes relacionados a diferentes processos celulares já foram determinados, porém a expressão de proteínas ainda necessita ser elucidada. Em vista da importância da FIV na produção de bovinos, conhecer a fisiologia do desenvolvimento folicular pode contribuir para melhorar estes processos *in vitro*.

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4. HIPÓTESE E OBJETIVO

4.1. Hipótese

Há expressão diferenciada de proteínas do líquido folicular em vista do desenvolvimento dos folículos ovarianos de vacas zebuínas não-gestantes?

4.2. Objetivo principal

Caracterizar o perfil proteico do líquido folicular de vacas zebuínas não-gestantes em diferentes tamanhos de folículos saudáveis.

4.3. Objetivo específico

Caracterizar as proteínas do líquido de folículos saudáveis folículos pequenos (≤6,5 mm), médios (>6,5mm a ≤9mm e) e grandes (>9,0mm) de vacas zebuínas, pela eletroforese unidimensional associada a espectrometria de massas e ontologia gênica a fim de caracterizar as proteínas.

CAPÍTULO 2

Estudo proteômico do desenvolvimento folicular de vacas zebuínas não gestantes

Proteomic study of bovine folicular development

(Artigo redigido segundo as normas da Theriogenology, ISSN 0093-691X, disponível em http://www.elsevier.com/journals/theriogenology/0093-691X/guide-for-authors)

RESUMO

O ciclo estral da vaca é composto por 2-3 ondas de crescimento folicular, onde vários folículos são recrutados. Durante o período denominado desvio folicular um folículo se torna dominante e os outros entram em atresia. Este processo envolve mecanismo ainda não completamente compreendido, incluindo proteínas específicas como já estabelecido pela expressão gênica. Então, o objetivo do presente estudo foi caracterizar as proteínas do fluído folicular a fim de identificar macromoléculas relacionadas ao desenvolvimento dos folículos de vacas zebuínas. Foram colhidos os ovários de 25 vacas adultas não-gestantes. A presença do corpo lúteo foi anotada para cada ovário. O líquido folicular foi colhido com os ovários imersos em líquido e guiado pela ultrassonografia. De acordo com a mensuração do diâmetro folicular, foram separados 3grupos, folículos pequenos (≤6,5mm, n=25), médios (>6,5mm a ≤9mm, n=9)e grandes (>9,0mm, n=11). Após 2 centrifugações (600xg/10 minutos e 15.000xg/30 minutos, 4ºC) o sobrenadante foi separado e utilizado para determinação da concentração de proteína total (método de Bradford). A eletroforese foi conduzida sob condições desnaturantes e redutoras, em gel de separação de poliacrilamidaà 12%. A concentração de progesterona e estradiol do líquido folicular foi determinada a fim de identificar os folículos saudáveis. As proteínas diferenciais identificadas pela eletroforese foram submetidas à espectrometria de massas e a ontologia gênica foi investigada nos bancos de dados disponíveis. Baseado nisto foram encontradas 45 bandas de proteínas na eletroforese em 45 amostras de liquido folicular. A média da concentração ± desvio padrão da progesterona foi de 129,91 ± 186,43, considerando todos os folículos. Houve uma expressão diferenciada de proteínas nas diferentes categorias de folículos.

Palavras-chave: Folículo; MALDI-TOF; Proteína

1. Introdução

A aplicação de técnicas de melhoramento genético animal associada às biotecnologias da reprodução é responsável por parte do crescimento do rebanho bovino mundial. Uma destas biotecnologias é a fertilização *in vitro* (FIV), a qual tem sido aplicada em rebanhos de alto valor genético, a fim de produzir maior número de descentes de matrizes de alto valor zootécnico. Apesar de ser uma técnica já extensivamente estudada em bovinos, a FIV ainda apresenta taxa de produção embrionária modesta. A maturação oocitária *in vitro* (MIV) é um dos principais pontos a ser considerado, quando se pretende elevar estas taxas. Este fato se deve a carência de informações a respeito dos mecanismos envolvidos no desenvolvimento folicular e maturação in vivo, condições que se mimetiza *in vitro* quando se pretende a produção de embriões pela FIV. A análise proteômica do líquido folicular pode elucidar parte destes mecanismos.

O liquido folicular é formado a partir de produtos de secreção das células da granulosa, da teca e difusão dos capilares que irrigam o tecido ovariano, sendo permeável às proteínas com massa molecular <500 kDa (HESS et al., 1998). Os oócitos estão contidos no líquido folicular, e sua composição bioquímica influencia diretamente a qualidade dos oócitos, estando relacionado à condição fisiológica da fêmea, estágio de desenvolvimento e *status* funcional do folículo (IWATA et al., 2006; KIM et al., 2006; BIANCHI et al., 2013).

O líquido folicular contém moléculas ativas e proteínas que estão relacionadas ao crescimento folicular, à fertilização dos oócitos e ao desenvolvimento embrionário. A caracterização proteômica do líquido folicular pode identificar biomarcadores para identificar a competência/qualidade dos oócitos e aumentar a taxa de sucesso na fertilização in vitro (WALLACE et al., 2012; BIANCHI et al., 2013). O envolvimento destas macromoléculas no desenvolvimento folicular é altamente complexo e depende de pequenas alterações (SENGER, 2003).

Apesar de muitos estudos a respeito da maturação e fertilização *in vitro* em bovinos, a análise proteômica do fluído folicular nesta espécie é mencionada em raros trabalhos. A concentração de albumina é maior no líquido folicular do que

no soro. Contrariamente, a concentração de proteína total e gama globulina são mais baixas no fluído folicular, sendo que todos estes componentes são originários do plasma sanguíneo para o folículo (MURANAKA et al., 1986). Outros estudos comparam a composição química do líquido de folículos normais e císticos (MURANAKA et al., 1986; MORTARINO et al., 1999; MANIWA et al., 2005), porém uma análise global e das categorias foliculares ainda não foi descrita nos bovinos.

Assim, o objetivo deste estudo foi caracterizar as proteínas do líquido folicular de vacas vazias zebuínas em diferentes classes de folículos por eletroforese e abordagem MALDI-TOF MS.

2. Materiais e métodos

2.1. Colheita das amostras

Para o estudo foram utilizados ovários de 25 vacas adultas zebuínas não-gestantes, colhidos de um abatedouro. Os ovários foram colhidos imediatamente após o abate e mantidos em tubos plásticos de 50 mL contendo solução salina 0,9% NaCl a 37ºC para o transporte (máximo de 3,5 horas) em caixas térmicas.

No laboratório, os ovários foram retirados dos tubos e depositados em um recipiente contendo solução salina 0,9% de NaCl para execução da ultrassonografia (DOMED SoneScape A6, MedWrench, LLC, Peachtree City, GA, USA). Imagens e mensurações dos folículos foram realizadas usando-se uma probe linear de 7,5 MHz. Após a mensuração, cada folículo foi puncionado com seringa de 5 mL e agulha 30x7 para a colheita do líquido folicular. Os folículos foram classificados de acordo com o diâmetro e separados em 3 grupos, folículos pequenos (≤6,5mm, n=25), médios (>6,5mm a ≤9mm, n=9) e grandes (>9,0mm, n=11). Os folículos dos ovários que possuíam corpo lúteo foram identificados e todos os tamanhos foram anotados. O líquido folicular foi centrifugado a 600 xg, durante 10 minutos, a temperatura ambiente, para retirada do conteúdo celular. O sobrenadante foi recentrifugado a 15.000xg durante 30 minutos, a 4ºC. O novo sobrenadante foi separado e congelado a -20ºC.

2.2. Determinação da concentração de proteína total

A concentração de proteína total foi determinada pelo método de Bradford (Bradford Reagent, B6916, Sigma-Aldrich®, St. Louis, MO, USA) de

acordo com o fabricante, utilizando-se uma curva padrão de 5 pontos de 0,25 a 2,0 mg/mL (R^2 = 0,98). Para a determinação da concentração de proteína total utilizou-se 25 µL da amostra, diluída 1: 60 em água ultra-pura e 750 µL do reagente de Bradford (Bradford Reagent, number B6916, Sigma-Aldrich, St. Louis, CO, UA). A leitura foi realizada em duplicata, em espectrofotômetro sob comprimento de onda 595nm.

2.3. Determinação da concentração hormonal

As concentrações de progesterona (P4) foram mensuradas por radioimunoensaio (RIA Progesterone, ref.IM 1188, Beckman Coulter, Diagnostic Systems Laboratories, Inc., Webster, TX, USA) seguindo as instruções do fabricante. Uma curva padrão foi confeccionada variando de 1,5 a 5,6 ng/mL. As amostras foram diluídas 1: 50 em tampão fosfato salina (PBS) e adicionadas aos tubos testes. O iodo 125 foi adicionado e as amostras incubadas. O conteúdo líquido foi aspirado e a leitura foi realizada em contador gama (WIZARD2 AutomaticGammaCounter, Perkin Elmer, Waltham, MA, USA).

A concentração de estradiol (E2) no líquido folicular foi quantificada pelo ensaio imunoenzimático – ELISA (Estradiol EIA Kit, ref. 582251, Cayman ChemicalCompany, Ann Arbor, MI, USA) de acordo com as recomendações do fabricante, considerando que a metodologia foi validada por Gasperin et al. (2012) para o líquido folicular.

Baseado nas concentrações de progesterona e estradiol (GRIMES; IRELAND, 1986), os folículos foram classificados em saudáveis (E2:P4>1), transicionais (E2:P4>0,01<1) e altamente atrésicos (E2:P4<0,01).

2.4. Eletroforese

Após a determinação da concentração de proteína total, as amostras foram submetidas à eletroforese unidimensional sob condições desnaturantes. Após preparação de acordo com Bollaget al. (1996), em uma concentração de 6,0 µg/µL de proteína total, as amostras foram diluídas em tampão (TRIS-HCl 60 mM, pH 6,8, 50% glicerol, 2% SDS, 23mM 2-mercapetanol, 0,1% bromofenol azul), na proporção de 1 de tampão acrescido de 4 partes de amostra. O volume de 7 µL de amostra/tampão foi aplicado no gel, contendo uma concentração final de 70 µg/uL de proteína. Para a eletroforese, uma mini-cuba (Mini VE, Amersham

Biosciences, Uppsala, Sweden) foi usada. Um gel separador de 12% de poliacrilamida (30% [w/v] de acrilamida e 0,8% [w/v] de bisacrilamida) e de empilhamento de 5% foram utilizados. Para a corrida, o tampão utilizado continha 25 mM TRIS, 192 mM glicina e 0,1% SDS, o qual foi adicionado nos reservatórios da cuba. Uma canaleta em cada gel foi destinada à aplicação de um padrão de massa molecular (Full Range Rainbow RPN800N, Recombinant Protein Molecular Weight Markers, 12 a 225 kDa, GE HealthCare, São Paulo, SP, Brasil). A corrida foi efetuada com uma corrente elétrica constante de 15 mA/gel e voltagem máxima de 300 V.

Os géis foram corados com coomassie coloidal (NEUHOJJ et al., 1985 adaptado por NEUHOFF et al., 1988 e LUO et al., 2006). Após a corrida, os géis foram transferidos para recipientes plásticos e fixados em 40% de álcool etílico e 10% de ácido acético glacial, durante 60 minutos. Preparou-se uma solução estoque contendo 0,1% (p/v) de coomassie azul brilhante G250, 2% (p/v) de ácido fosfórico e 10% (p/v) de sulfato de amônia e posteriormente uma solução trabalho com 80% (v/v) da solução estoque e 20% (v/v) de metanol. Após a fixação, os géis foram imersos na solução trabalho de coloração *overnight*. A seguir, o *background* foi descorado com água destilada e o gel estocado em ácido acético 10% em solução aquosa.

As imagens dos géis foram digitalizadas e um programa analisador de imagens (Image Master v. 3.0, 1993, GE HealthCare, Uppala, Suécia) foi utilizado para determinar a massa molecular de cada banda.

2.5. Espectrometria de massas

2.5.1. Digestão de in-gel de proteínas

Foram selecionadas 16 bandas, as quais foram recortadas dos géis e depositadas em tubos plásticos, formando pools de acordo com os grupos de folículos (folículos saudáveis, transicionais e atrésicos obtidos de ovários sem corpo lúteo, e folículos saudáveis e transicionais obtidos de ovários com corpo lúteo). Os fragmentos foram segmentados em tamanhos de aproximadamente 1 mm^3. A seguir, adicionou-se 15 µL de uma solução de descoloração (50% v/v acetonitrila [ACN] e 25 mM bicarbonato de amônio). A solução foi trocada a cada 15 minutos, até total retirada do corante.

Após desidratação com 100% de ACN, foi realizada redução e alquilação dos fragmentos, submentendo-os a reidratação com 20 mM de DTT em 50 mM de bicarbonato de amônio, durante 40 min, a 55ºC. O líquido excedente foi removido e substituído por 55 mM de iodoacetamida (IAA) em 50 mM de bicarbonato de amônio. Os fragmentos de gel foram mantidos no escuro por 30 minutos à temperatura ambiente, o líquido excedente foi novamente removido e os fragmentos lavados com 25 mM de bicarbonato de amônio, por 15 minutos. Após serem novamente desidratados com 100 % de ACN, os fragmentos foram reidratados em solução de 20 ng/µL de tripsina (cód. WI 53711-5399 Promega Corporation V5111, Madison USA) em 50 mM de bicarbonato de amônio. Após a reidratação total, os fragmentos de gel foram parcialmente cobertos com 25 mM de bicarbonato de amônio e a digestão, realizada a 37ºC por 16 horas.

A ação da tripsina foi bloqueada pela adição de solução contendo 50% ACN v/v, 5% ácido fórmico e 45% água ultrapura, e os peptídeos eluídos dos fragmentos por lavagens sucessivas com solução de eluição I (60% metanol, 1% ácido fórmico e 39% de água ultrapura), solução de eluição II (50% ACN, 1% ácido fórmico, 49% de água ultrapura), seguidas de desidratação final com 100% de ACN. Os sobrenadantes de cada conjunto de bandas foram transferidos para um novo tubo e o volume foi reduzido em concentrador a vácuo, à temperatura ambiente.

2.5.2. Purificação das amostras

Após a secagem a vácuo, adicionou-se 10µL de solução de 0,1% (v/v) ácido trifluoroacético (TFA) em água ultrapura. Então, as amostras foram purificadas utilizando-se micro-colunas de fase reversa (Reverse phase Zip-Tip C18, Millipore). Para isso, as colunas foram equilibradas em solução A (0,1% v/v TFA em 100% ACN), solução B (0,1% v/v TFA, 50% v/v ACN em água ultrapura) e solução C (0,1% v/v TFA em água ultrapura), respectivamente. Após o equilíbrio, as amostras proteicas puderam ser ligadas à coluna, seguindo-se lavagem com solução D (5% v/v metanol, 0,1% v/v TFA em água ultrapura). Para a eluição dos peptídeos, 10µL de solução B foram aspirados e acondicionados em tubos de vidro borosilicato (Waters Total Recovery vials, Manchester, UK). Seguiu-se nova concentração a vácuo.

2.5.3. LC-MS^E

As amostras foram ressuspendidas em 20 µL de formiato de amônio 20 mM pH 10,0. Os peptídeos foram sequenciados no espectrômetro de massas *Synapt*G2 HDMS (Waters, Manchester, UK), acoplado ao sistema *Acquity*UPLC*MClass*, com tecnologia 1D Simulado (Waters, Manchester, UK). Os peptídeos foram capturados por uma coluna Trap2DSymmetry C18 (5 µm, 180 µm x 20 mm) (Waters, Manchester, UK). A separação foi realizada com uma coluna de primeira dimensão Acquity UPLC M-Classpeptide BEH C18 (5 µm, 300 µm x 50 mm) (Waters, Manchester, UK, USA) e uma coluna analítica Acquity UPLC M-Classpeptide CSH C18 (1,7 µm, 75 µm x 150 mm) (Waters, Manchester, UK). As fases móveis da primeira dimensão foram solução de formiato de amônio 20 mM, pH 10,0 e ACN (100%). Na segunda dimensão os eluentes foram 0,1% v/v de ácido fórmico em água ultrapura (eluente A) e 0,1% v/v de ácido fórmico em 100% ACN (eluente B).

O gradiente da primeira dimensão iniciou-se com 97% de formiato de amônio e 3% de ACN (100%). Em 4,6 minutos foi atingido 55% de formiato de amônio e 45% de ACN e até completar 10 minutos a condição inicial foi restabelecida. O fluxo foi de 2 uL/minuto.

O gradiente da fase móvel analítica iniciou-se com 93% do eluente A e 7% do eluente B e por 92 minutos o gradiente se modificou linearmente para 60% de A e 40% de B. Após 2 minutos foi atingido 15% de A e 85% de B. Em 2 minutos a coluna restabeleceu sua condição inicial. O fluxo foi de 0,300 µL/min. Foi injetado 9 µL da amostra.

A aquisição dos dados foi realizada em um espectrômetro de massas do tipo quadrupolo-tempo de voo (Q-TOF) Synapt G2 MS, equipado com uma fonte *nanolockspray*, operando no modo positivo (Waters, Manchester, UK), com *ionmobility*. Para todas as análises, o espectrômetro de massas operou no modo "V", com poder de resolução típico mínimo de 12.500, com a cela de *ionmobility* ativada. O espectrômetro de massas foi calibrado com [Glu1] fibrinopeptídeo B (GFP) humana 1 *p*mol/µL e a mesma solução foi empregada para o *lockmass* utilizando-se o íon de dupla carga com uma amostragem a cada 30 segundos. O estudo foi realizado no modo HDMS^E (análise independente de dados) que consistir na aquisição alternada, entre espectros obtidos à baixa (3 eV) e alta (15 a 50 eV) energia de colisão, aplicadas ao módulo *trap* do *T-wave* CID, em presença

de gás argônio, que produz íons precursores e produtos em sequência. O tempo de varredura foi de 0,8 segundos em cada modo, no intervalo de *m/z* entre 50 e 2000.

2.5.4. Análise dos dados

Os espectros de massas foram processados utilizando o *software Protein Lynx Global Server* (PLGS) versão 3.1 (Waters, Manchester, UK), com o banco de dados reverso de *Bos Taurus UNIPROT* (data do *download* 19 de fevereiro de 2016; 43.705 proteínas). Os parâmetros de processamento incluíram tolerância automática para precursores e íons-produto; mínimo de três íons-fragmento correspondentes por peptídeo; mínimo de 7 íons-fragmento correspondentes por proteína; mínimo de 2 peptídeos correspondentes por proteína; um possível erro de clivagem pela tripsina; carbamidometilação de cisteína como modificação fixa e oxidação de metionina como modificação variável; taxa máxima de descoberta de falso positivo (FDR) a 4%.

2.6. Bioinformática e ontologia gênica

As proteínas identificadas foram buscadas no banco de dados UniprotKB (www.uniprot.org.br), para obter a anotação da ontologia gênica (GO), nas categorias função molecular, processo biológico e componente celular. Um interatoma para cada grupo foi confeccionado utilizando-se um *software* livre *online* (http://string-db.org/). A ontologia gênica foi organizada em gráficos os quais representaram a função molecular, processo biológico, componente celular e classe de proteínas.

3. Resultados

Nos géis de eletroforese foram encontradas 45 bandas (Tabela 1, Figura 1) em todas as categorias de folículos. Houve uma expressão proteica diferenciada entre as categorias foliculares, sendo que a banda de 102,0 kDa foi encontrada apenas nos folículos mensurando <6,5mm, e as bandas de 6,9 e 4,9 kDa foram encontradas apenas nos folículos com >9,0mm. Não houve expressão proteica diferenciada na categoria folicular de >6,5-<9,0mm.

Considerando os folículos colhidos dos ovários com e sem corpo lúteo, a expressão proteica não foi diferenciada (Tabela 2 e 3).

Tabela 1. Resultados das concentrações de progesterona (P4), do estradiol (E2) e da eletroforese do líquido folicular de vacas vazias, de diferentes tamanhos de folículos.

Categoria	N	P4 (ng/mL)	E2 (pg/mL)	nº bandas	Massa mol. mín. e máx. (kDa)
Todas	45	129,9 ± 186,4	135,98±671,47	49	388,2 a 3,9
≤6,5 mm	25	175,1 ± 234,2	0,683±0,594	44	388,2 a 3,9
>6,5- <9,0 mm	9	78,0± 65,2	16,203±16,303	40	388,2 a 3,9
>9,0 mm	11	62,9± 44,8	707,3±1570,8	41	318,8 a 3,9

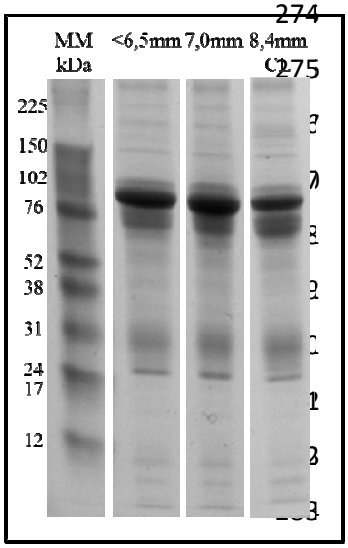


Figura 1. Gel de eletroforese de poliacrilamida do fluído folicular de vacas vazias de diferentes categorias de folículos

Tabela 2. Resultados das concentrações de progesterona (P4), do estradiol (E2) e da eletroforese do líquido folicular de vacas vazias sem corpo lúteo, de diferentes tamanhos de folículos

Categoria	N	P4 (ng/mL)	E2 (pg/mL)	nº bandas	Massa mol. mín. e máx. (kDa)
Todas	30	140,3±199,5	18,5±21,8	49	388,2±3,9
≤6,5 mm	19	185,0±240,0	36,9±53,6	46	388,2±3,9
>6,5 - <9,0 mm	5	66,8±43,7	6,9±8,9	38	388,2±3,9
>9,0 mm	6	59,9±35,4	11,9±3,0	33	250,5±11,1

Tabela 3. Resultados das concentrações de progesterona (P4), do estradiol (E2) e da eletroforese do líquido folicular de vacas vazias com corpo lúteo, de diferentes tamanhos de folículos

Categoria	N	P4 (ng/mL)	E2 (pg/mL)	nº bandas	Massa mol. mín. e máx. (kDa)
Todas	15	124,0±149,5	34,7±49,2	47	388,2±3,9
≤6,5 mm	8	154, 7±195,3	49,0±63,1	46	388,2±3,9
>6,5- <9,0 mm	3	96,9±101,1	3,2±1,7	35	388,2±3,9
>9,0 mm	4	83,2±54,8	33,4±32,2	38	388,2±3,9

A Figura 2 demonstra o interatoma das proteínas obtidas de folículos saudáveis de ovários sem corpo lúteo. A Figura 3 representa a ontologia gênica dos folículos saudáveis de ovários sem corpo lúteo de vacas vazias, nos quais foram identificados 87 espectros MS/MS obtidos pelo LC MS/MS ESI-TOF, nos quais geraram 33 proteínas sendo as principais, albumina, apoliproteína, serotransferrina, proteína de choque térmico, C3 complemento e a tabela 3 que lista as proteínas identificadas no grupo de folículos saudávis, de ovário com corpo lúteo de vacas vazias. Nesta categoria a função molecular que mais se destacou foi atividade catalítica; o processo biológico foi o metabólico; o componente celular foi a região extracelular; e a classe de proteína foi o modulador enzimático.

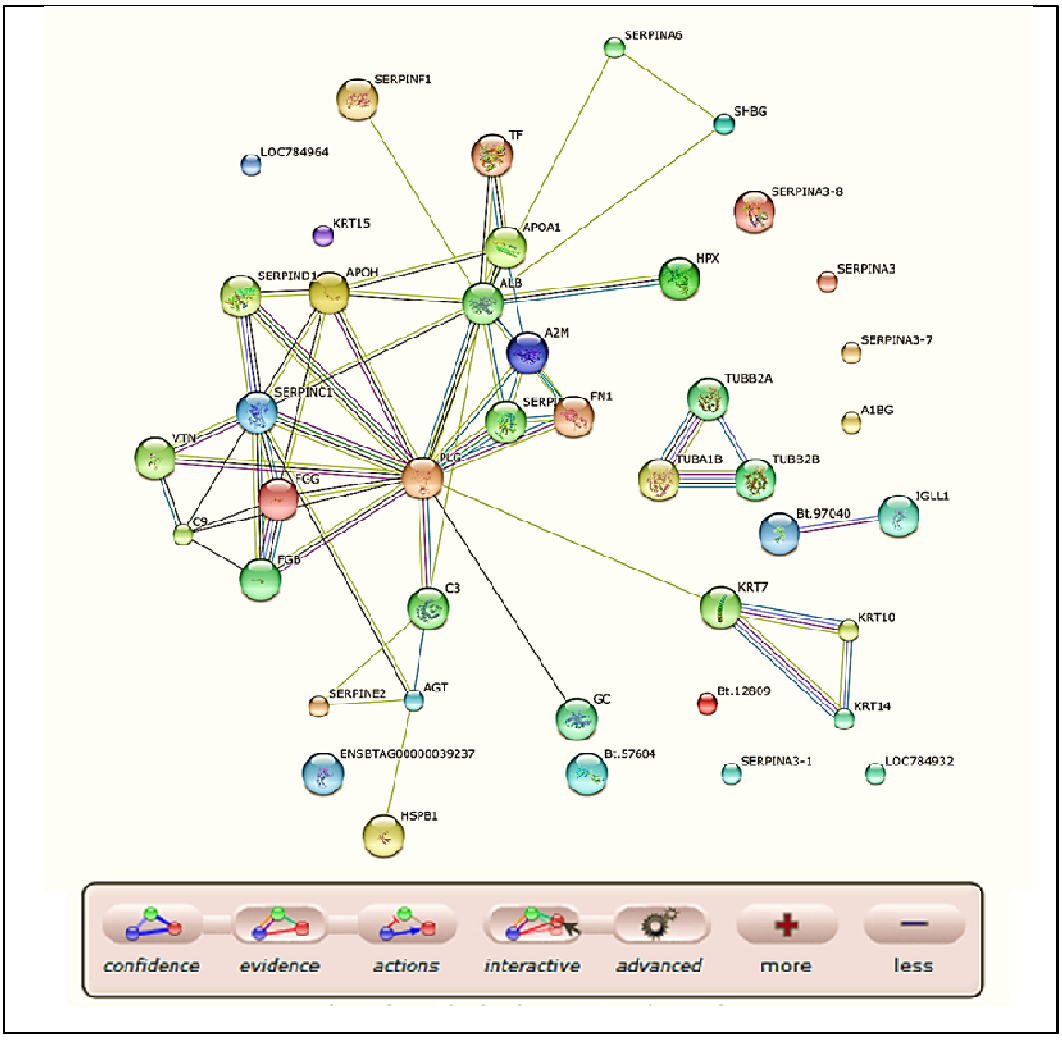
A Figura 4 demonstra o interatoma das proteínas obtidas de folículos transicionais de ovários sem corpo lúteo. Nos folículos transicionais de ovários sem corpo lúteo de vacas vazias foram identificados 55 espectros MS/MS obtidos pelo LC MS/MS ESI TOF, dos quais geraram 21 proteínas. As principais proteínas encontradas foram alpha proteína, apolipoproteína, complemento C3, fibrinogênio e serotransferrina que estão detalhadas na tabela 4, Baseado na análise da ontologia gênica (Figura 5) a principal função molecular foi atividade catalítica; o processo biológico foi processo metabólico; o componente celular foi na região extracelular; e a classe de proteínas foi moduladora enzimática.

A Figura 6 demonstra o interatoma das proteínas obtidas de folículos saudáveis de ovários com corpo lúteo. Os folículos saudáveis de ovários com corpo lúteo de vacas vazias apresentou 95 espectros MS/MS obtidos pelo LC MS/MS ESI TOF,

dos quais geraram 36 proteínas cujas principais foram complemtno C3, apolipoproteína, albumina, serotransferrina e difosfato de fructose essas proteínas dentre outras encontradas estão detalhadas na tabela 5. Baseado na análise da ontologia gênica das proteínas do grupo de folículos saudáveis de ovários com corpo lúteo de vacas vazias a principal função molecular identificada foi a atividade catalítica; a classe de proteínas foi protease; o componente celular foi a região extracelular; e o processo biológico foi o processo metabólico (Figura 7).

A Figura 8 demonstra o interatoma das proteínas obtidas de folículos transicionais de ovários com corpo lúteo. Ainda, nesta categoria foram identificados 34 espectros MS/MS obtidos pelo LC ESI TOF, nos quais geraram 17 proteinas cujas principais foram antitrombina, apolipoproteína, complemento C3, fibrinogênio e serpina. Baseado na análise ontológica a principal função molecular foi atividade catalítica; a classe de proteínas foi sinalizador molecular; o componente celular foi região extracelular; e processo biológico foi processo metabólico(Figura 9).

O interatoma das proteínas obtidas de folículos atrésicos de ovários com corpo lúteo está representado na Figura 10. Nessta classe de folículos foram encontrados 114 espectros MS/MS obtidos pelo LC ESI TOF, nos quais geraram 60 proteínas cujas principais foram complemento C3, apolipoproteína, fibrinogênio, serotransferrina e albumina. A análise da ontologia gênica determinou como principal função molecular atividade catalítica; classe de proteínas, modulador enzimático; componente celular, a região extracelular; e processo biológico, o processo metabólico.



339

340 **Figura 2.** Interatorma das proteinas de folículos saudáveis de ovários sem corpo
341 lúteo de vacas vazias (http://string-db.org/)

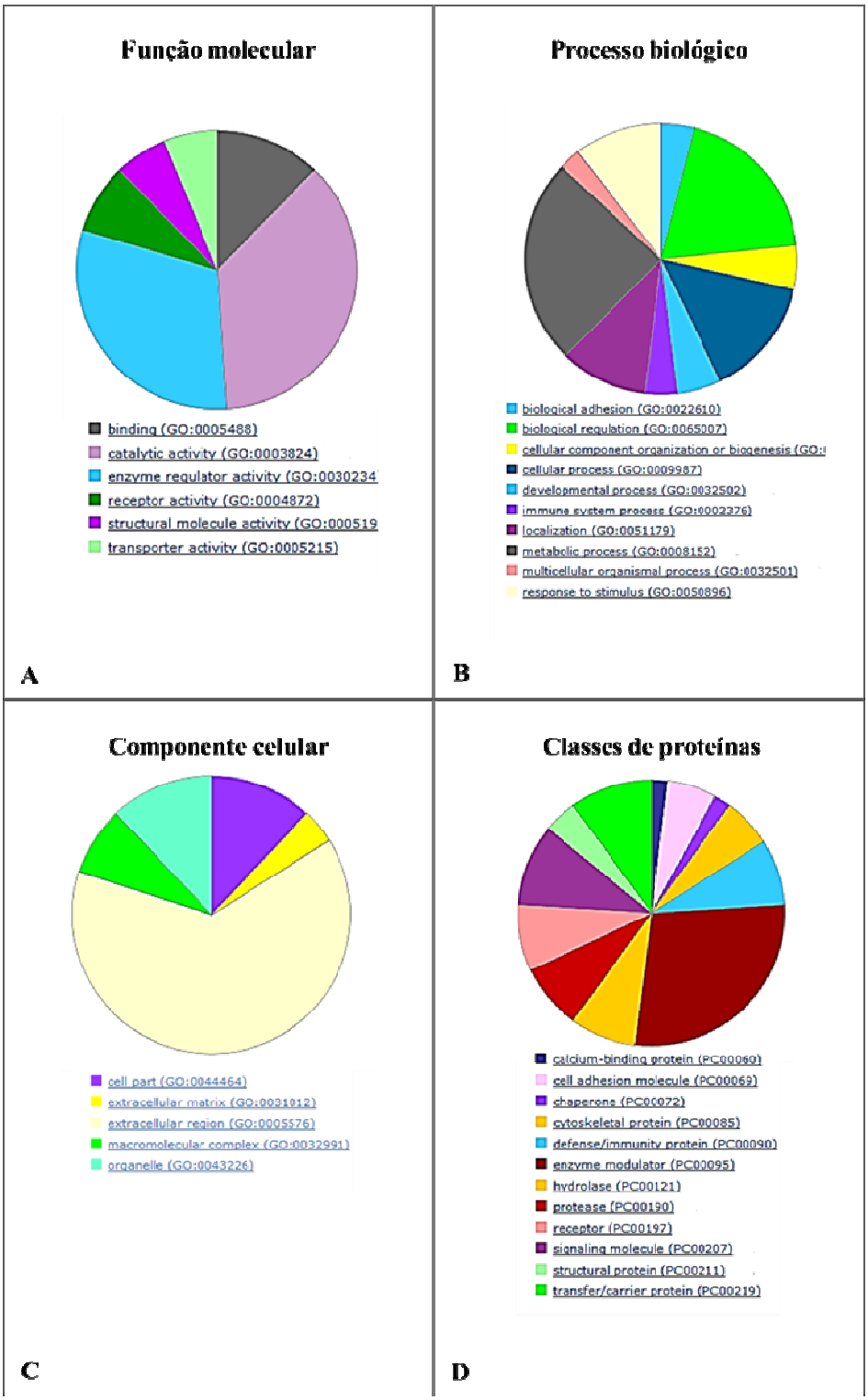


Figura 3. Ontologia gênica das proteínas do líquido de folículos saudáveis de ovários sem corpo lúteo de vacas vazias. A. Função molecular (30 genes com 49 funções moleculares). B. Processo biológico (30 genes envolvidos em 77 processos biológicos). C. Componente celular (30 genes em 25 componentes celulares). D. Classe de proteínas (30 genes distribuidos em 50 classes de proteínas) (http://www.pantherdb.org)

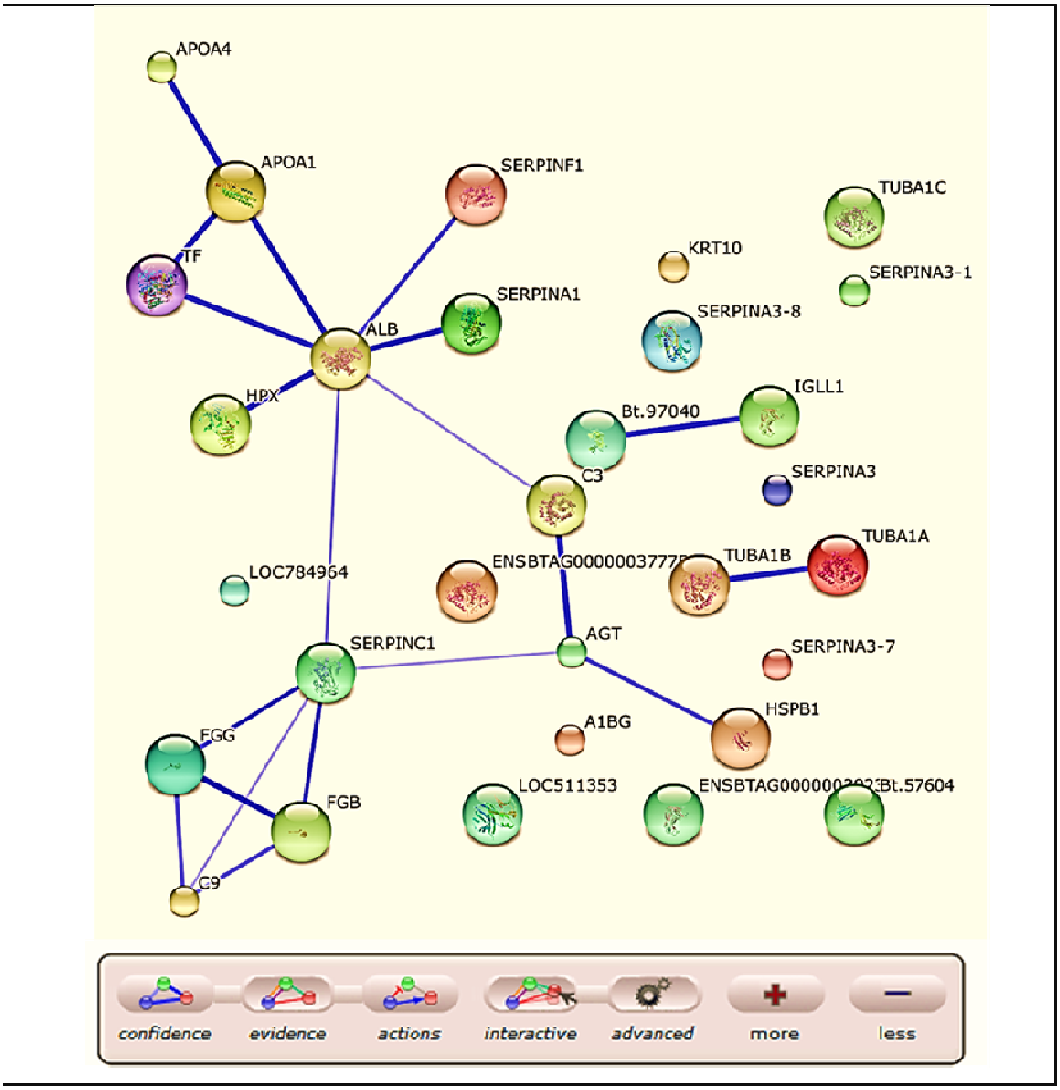


Figura 4. Interatoma das proteinas de folículos transicionais de ovários sem corpo lúteo de vacas vazias (http://string-db.org/)

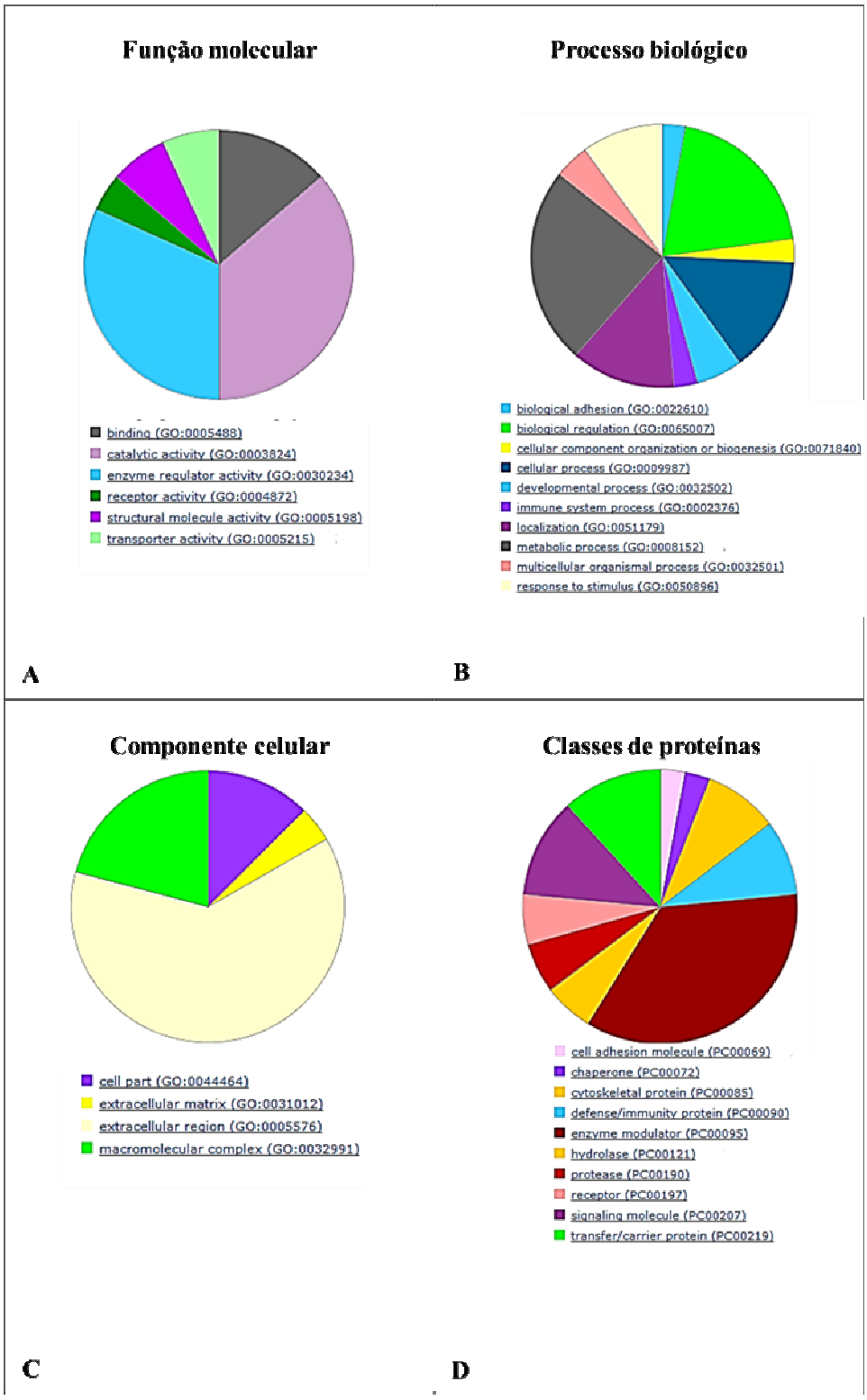
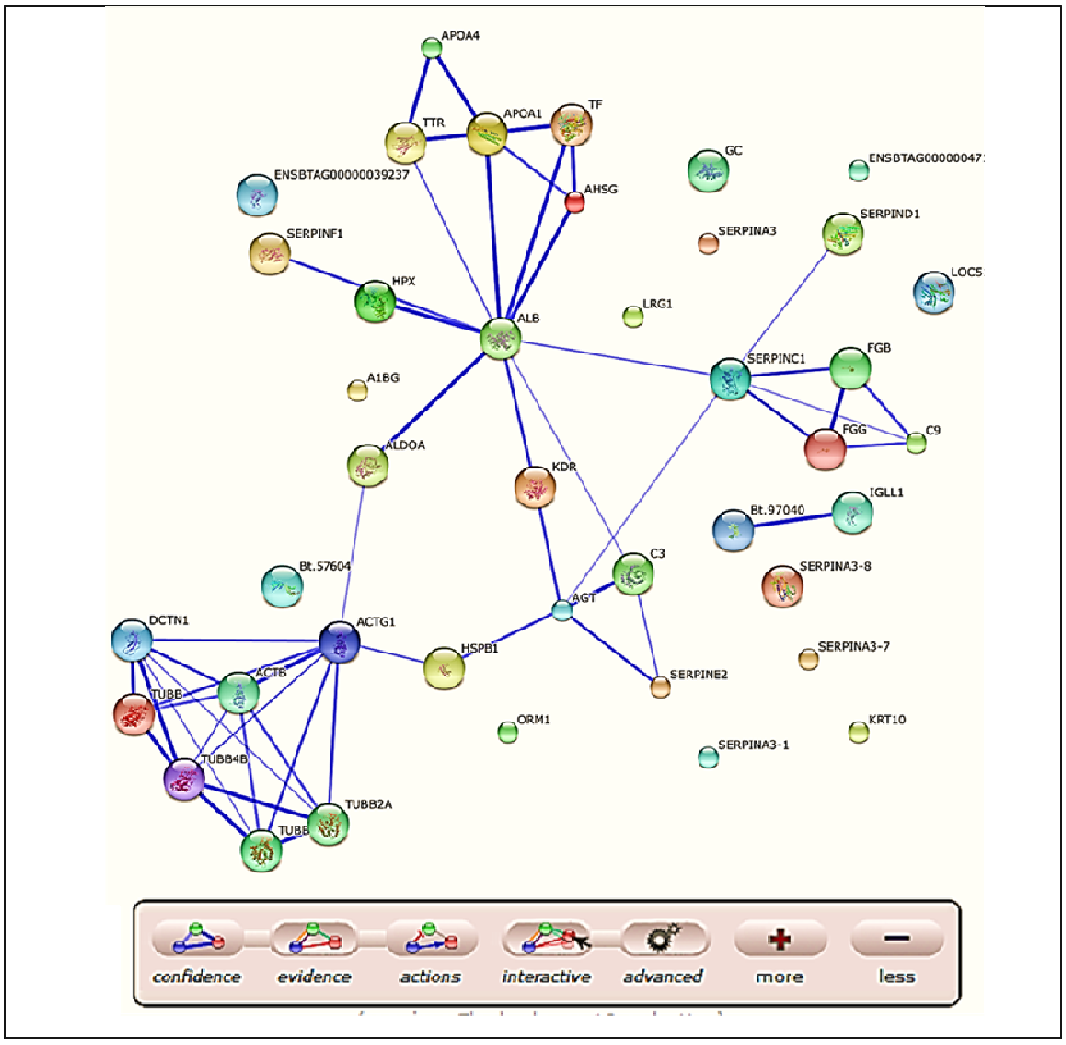


Figura 5. Ontologia gênica das proteínas do líquido de folículos transicionais de ovários sem corpo lúteo de vacas vazias. A. Função molecular (25 genes com 44 funções moleculares). B. Processo biológico (25 genes envolvidos em 70 processos biológicos). C. Componente celular (25 genes em 24 componentes celulares). D. Classe de proteínas (25 genes distribuidos em 34 classes de proteínas) (http://www.pantherdb.org)



360

361 **Figura 6.** Interatoma das proteínas de folículos saudáveis de ovários com corpo
362 lúteo de vacas vazias (http://string-db.org/)

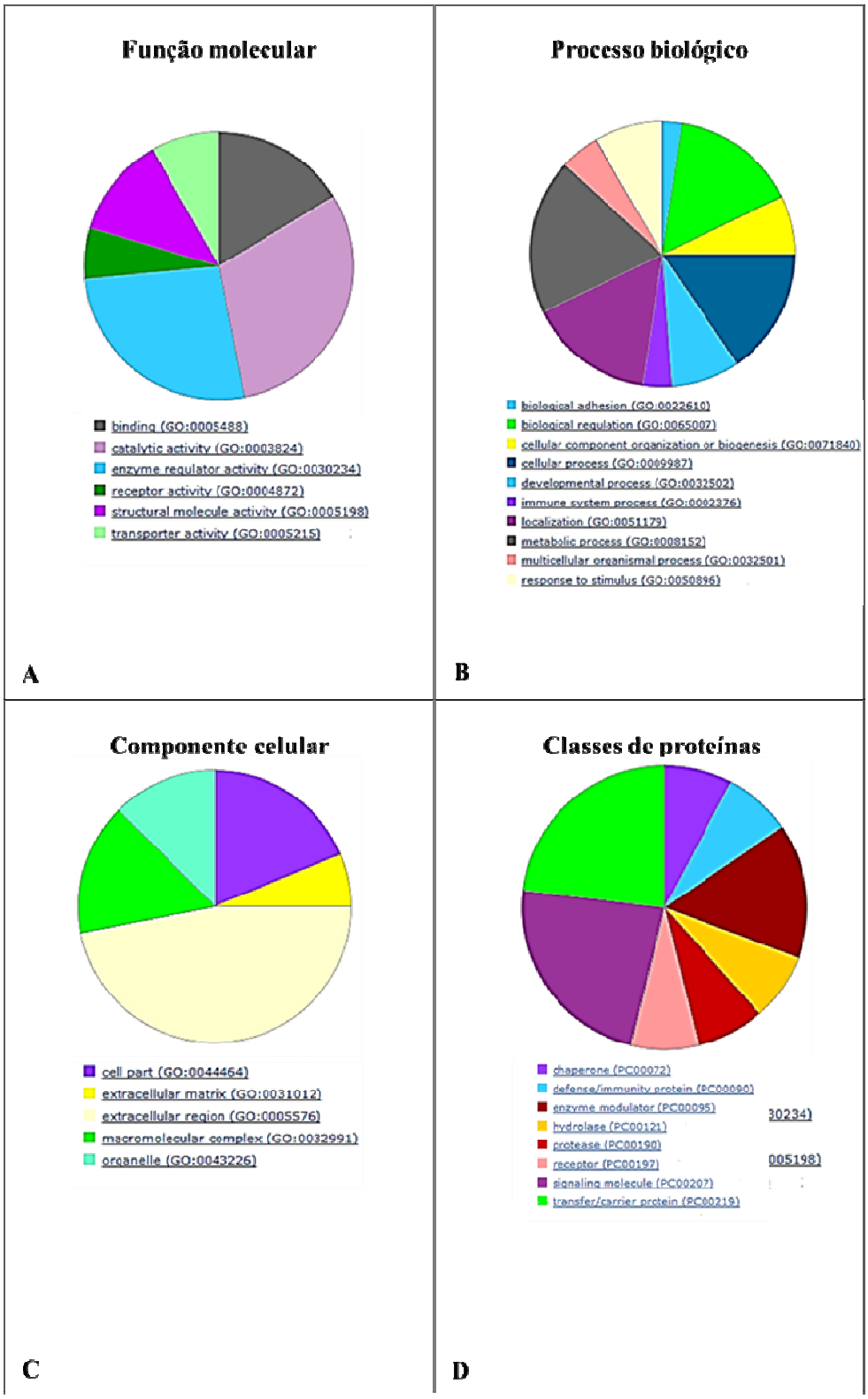


Figura 7. Ontologia gênica das proteínas do líquido de folículos saudáveis de ovários com corpo lúteo de vacas vazias. A. Função molecular (33 genes com 49 funções moleculares). B. Processo biológico (3 genes envolvidos em 84 processos biológicos). C. Componente celular (33 genes em 32 componentes celulares). D. Classe de proteínas (33 genes distribuidos em 41 classes de proteínas) (http://www.pantherdb.org)

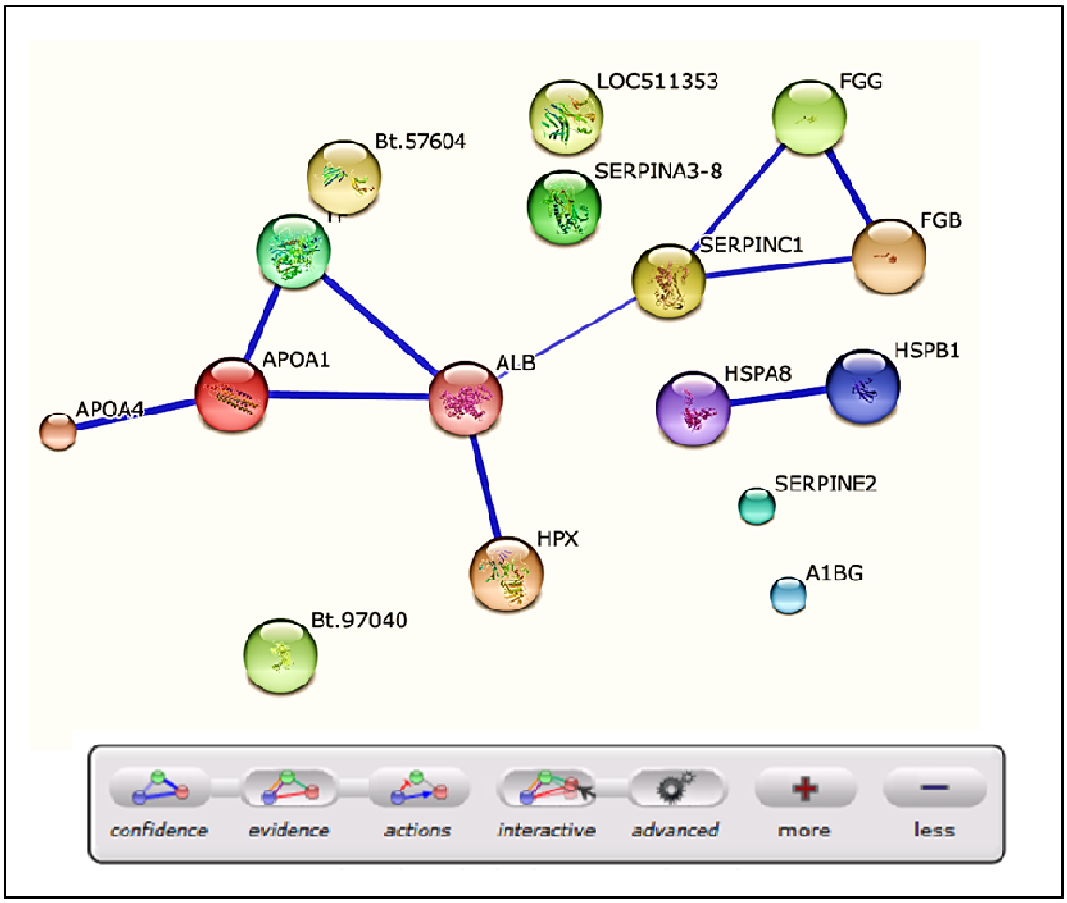


Figura 8. Interatoma das proteínas de folículos transicionais de ovários com corpo lúteo de vacas vazias (http://string-db.org/)

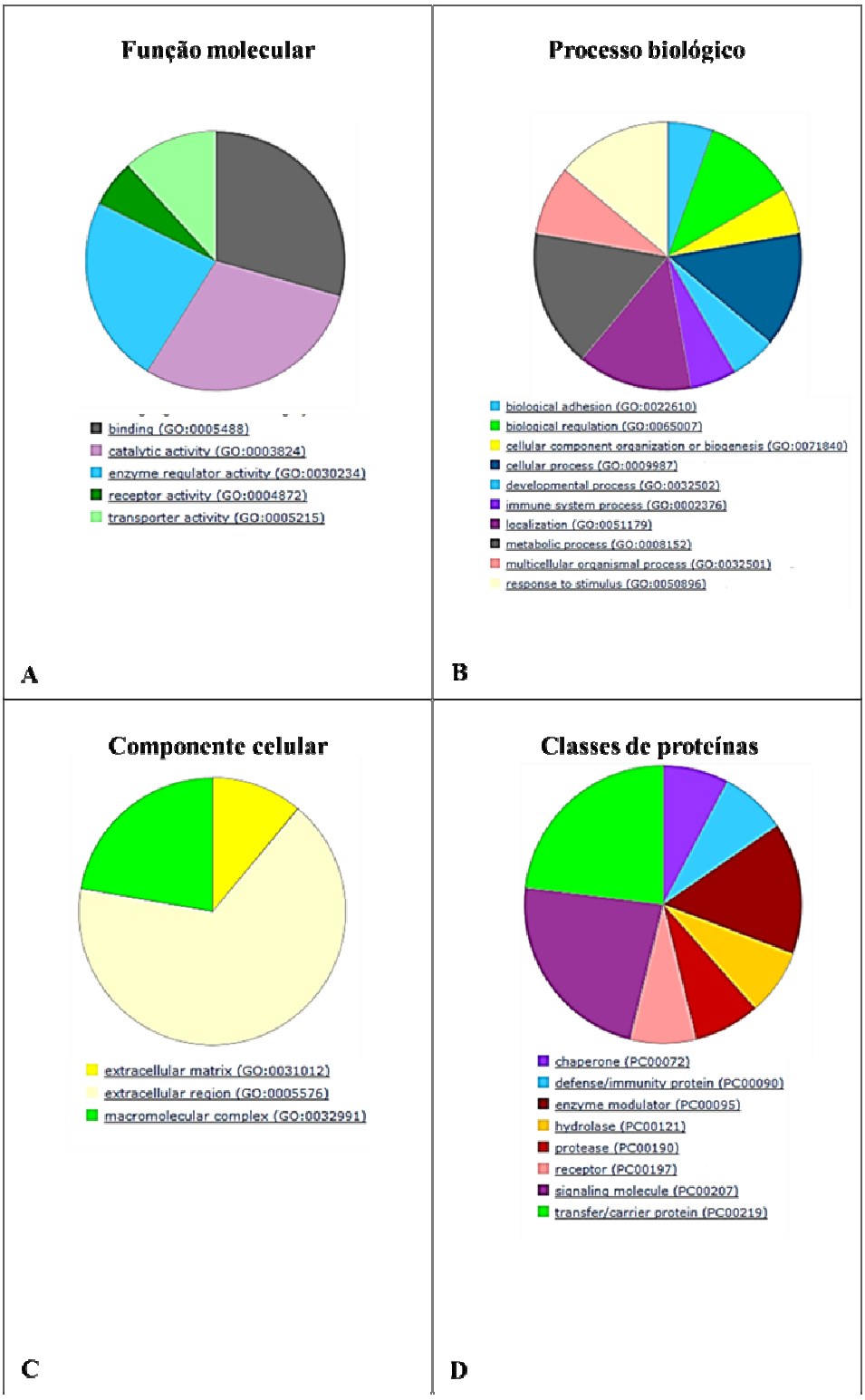


Figura 9. Ontologia gênica das proteínas do líquido de folículos transicionais de ovários com corpo lúteo de vacas vazias. A. Função molecular (11 genes com 17 funções moleculares). B. Processo biológico (11 genes envolvidos em 36 processos biológicos). C. Componente celular (11 genes em 09 componentes celulares). D. Classe de proteínas (11 genes distribuidos em 13 classes de proteínas) (http://www.pantherdb.org)

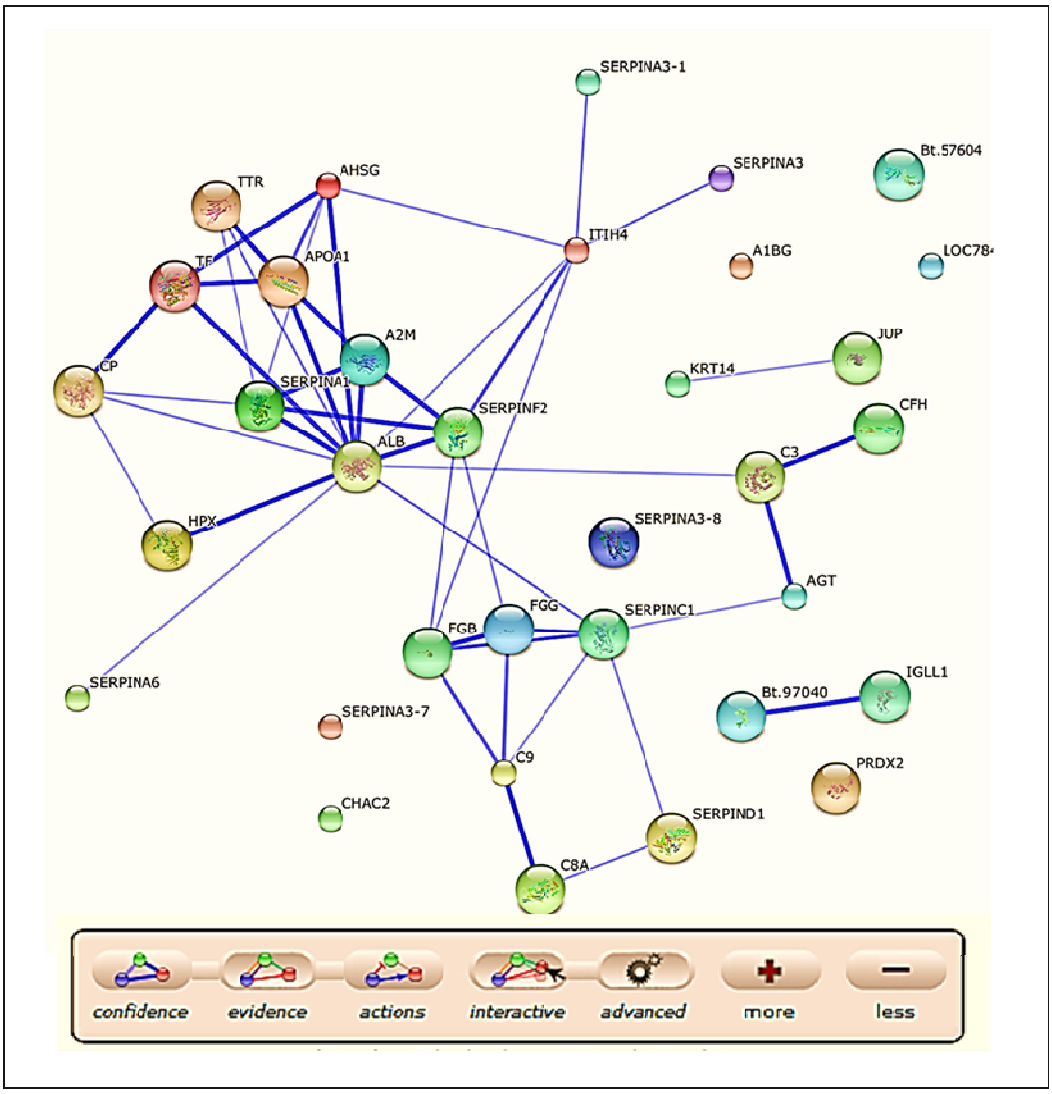


Figura 10. Interatoma das proteínas de folículos atrésicos de ovários com corpo lúteo de vacas vazias (http://string-db.org/)

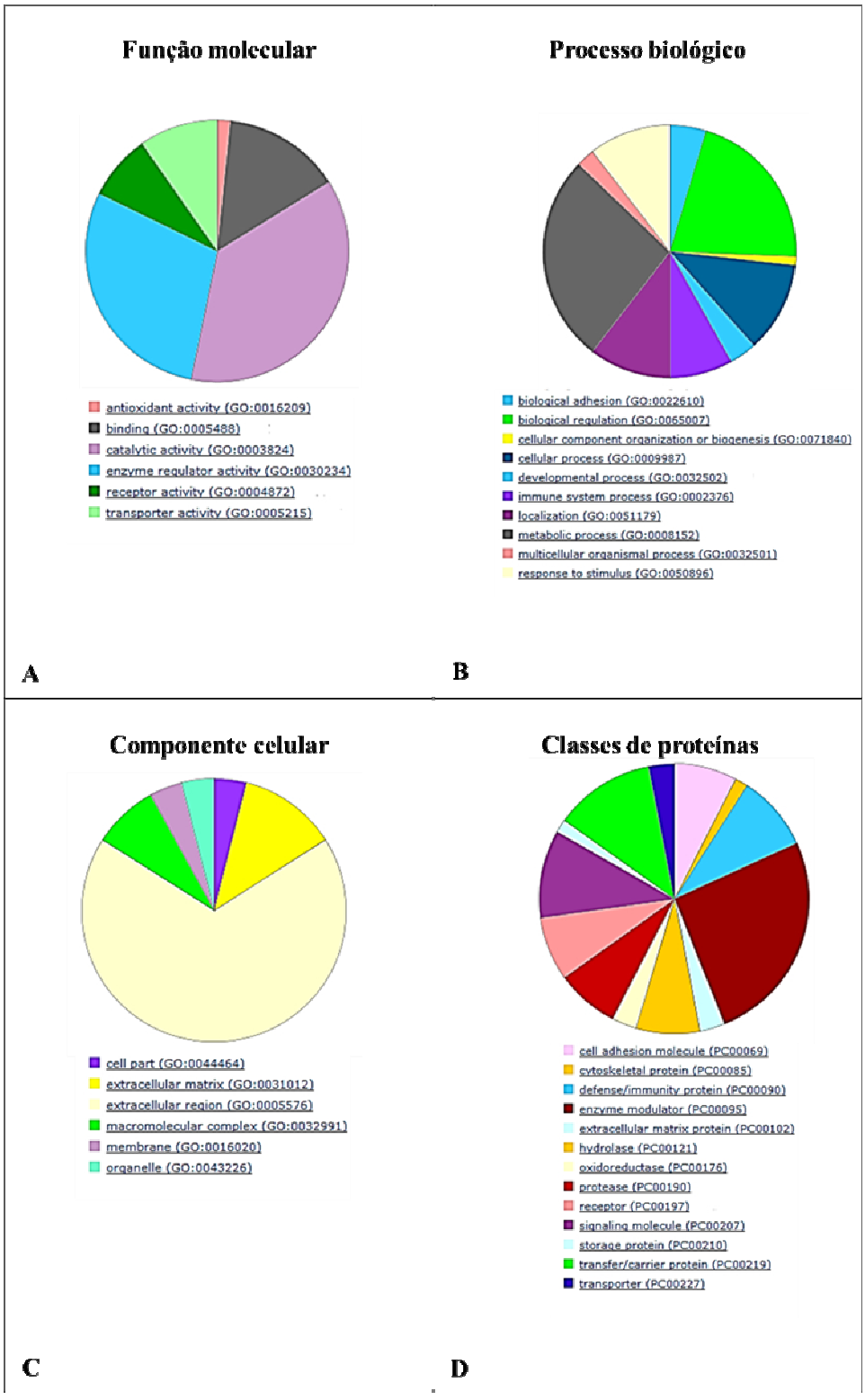


Figura 11. Ontologia gênica das proteínas do líquido de folículos atrésicos de ovários com corpo lúteo de vacas vazias. A. Função molecular (12 genes com 15 funções moleculares). B. Processo biológico (12 genes envolvidos em 35 processos biológicos). C. Componente celular (12 genes em 10 componentes celulares). D. Classe de proteínas (12 genes distribuidos em 12 classes de proteínas) (http://www.pantherdb.org)

4. Discussão

A eletroforese das proteínas do líquido folicular foi capaz de revelar diferenças entre o perfil proteico das categorias de folículos saudáveis, transicionais e atrésicos, contidos em ovários com e sem corpo lúteo de vacas não gestantes. Estes resultados corroboram com o de Gradela et al. (1998), os quais verificaram expressão diferenciada em bovinos. Apesar disso, estes autores não encontraram bandas de massa molecular entre 39 e 43 kDa em folículos com diâmetro inferior a 10 mm, provavelmente em vista do processamento diferente das amostras. Gradela et al. (1998) dialisaram as amostras em membrana de celulose, anterior a eletroforese, o que pode ter gerado perda dos polipetídeos. Já no presente estudo, foram verificados polipetídeos com massas moleculares entre 35 e 45 kDa, especialmente em folículos saudáveis.

Apesar da eletroforese ser uma técnica amplamente utilizada, atualmente é considerada preparatória para análise, não indicando resultados conclusivos que possam identificar as proteínas de interesse. Assim, neste estudo, as bandas principais e as diferenciais foram recortadas e encaminhadas para espectrometria de massas. A espectrometria de massas é uma técnica que permite avaliar a massa molecular dos compostos e quantificá-los, a fim de identificar a sequência de resíduos de aminoácidos de proteínas desconhecidas e determinar as modificações pós-traducionais. É uma técnica que pode ser aplicada à análise de biomoléculas e que fornece informações precisas utilizando a sequência de peptídeos trípticos para identificação de proteínas.

Tal afirmação pôde ser confirmada quando os resultados obtidos no presente estudo foram comparados aos de Ribeiro et al. (2012), os quais utilizaram apenas a eletroforese para o estudo das proteínas do líquido folicular de bovinos. Na espectrometria de massas foi possível identificar várias proteínas contidas em apenas uma banda. Na região da albumina, próximo a 66 kDa, foram identificadas 54 proteínas, incluindo as diferentes subunidades da albumina. Tais resultados contradizem os estudos de Ribeiro et al. (2012) que afirmaram que a banda de 66 kDa continha apenas albumina sérica.

Ademais Ribeiro et al. (2012) observaram as bandas de 30 e 32 kDa em diferentes fases do ciclo estral, o que está de acordo com os resultados do presente estudo, no qual foi encontrada uma banda diferencial em folículos saudáveis (31 kDa) de ovários com corpo lúteo ausente.

Foi verificada uma influência do desenvolvimento folicular na produção de proteínas, já que foi possível identificar uma banda diferencial (102,0 kDa) nos folículos menores que 6,5 mm, o que discorda dos resultados de De La Sota et al. (1996) os quais detectaram proteínas de 22, 28, 30, 35, 43 e 49 kDa nesta categoria de folículos.

Parece haver algum tipo de influência do corpo lúteo sobre a composição proteica do fluido folicular, já que foi encontrada uma banda diferencial (24 kDa) nas classes de folículos saudáveis e transicionais de ovários sem corpo lúteo, e de folículos atrésicos de ovários com corpo lúteo. Apesar de Ribeiro et al. (2012) não ter diferenciado as classes de folículos, como no nosso estudo, a banda de 24 kDa não foi observada.

A banda de 52 kDa foi predominante em quase todas as amostras, incluindo o fluido de folículos obtidos de ovários com ou sem corpo lúteo. Tal banda trata-se da albumina e suas subunidades, resultados confimados pela espectrometria de massas. A albumina sérica apresenta como principal função o transporte de moléculas e segundo os resultados do interatoma foi a principal proteína que interage com outras macromoléculas, especialmente as serpinas e a apolipoproteinas. Em outros fluidos a albumina tem sido considerada um marcador de processos reprodutivos, tal como, a congelabilidade do sêmen de bovinos (Jobim et al., 2002). Também foi indentificada no fluido uterino de vacas sendo atribuída a função de transportar moléculas e já foi especulada como estando presente no líquido folicular (Alavi-Shoushtari et al., 2006), haja vista que a maioria das proteínas presentes nos folículos são originárias do soro sanguíneo (Manarang-pangan et al., 1971), o que foi confirmado no presente estudo pela espectrometria de massas. Tais proteínas são depositadas no fluido folicular por filtração de capilares.

Além da albumina, a apolipoproteína estava presente em todas as classes foliculares. Esta proteína está envolvida na biossíntese, no efluxo, na homeostase, no transporte reverso e na importação de colesterol, elemento essencial para produção de hormônios esteroides contidos no líquido folicular em altas concentrações Apesar dos folículos atrésicos serem folículos em apoptose, os mecanismos de transporte do colesterol ainda ocorrem nesta classe folicular. Outras proteínas então envolvidas neste mecanismo, embora não tenham sido identificadas no nosso estudo. Bottini et al. (1999) apontaram um impacto

significativo da haptoglobina do líquido folicular sobre a fertilidade de mulheres. O transporte da haptoglobina no folículo depende da integridade da barreira hemato-folicular e pode ser associado com o número e qualidade dos oócitos, possivelmente interferindo com a função da apolipoproteína A-1, na troca do colesterol, vitamina E e lipoproteínas de alta densidade com as células da granulosa. Em equinos, a apoliproteína tem sido encontrada em maior abundância no líquido de folículos durante o estágio pré-ovulatório (Rocha et al., 2015).

Em búfalas, a haptoglobina foi também mencionada como um marcador molecular para avaliar o *status* fisiológico da barreira hemato-folicular e para discriminar os folículos atrésicos dos saudáveis (Bergamo et al., 1995). Apesar do envolvimento da haptoglobina na discriminação de classes de folículos, nosso estudo não identificou este tipo proteíco como diferencial entre folículos saudáveis, transicionais e atrésicos. Isto não significa que os bovinos não expressam esta proteína no líquido folicular, pois não foram recortadas todas as bandas gel, apenas as principais e as diferencias.

O fibrinogênio foi identificado em quase todas as classes foliculares, com exceção dos folículos saudáveis contidos em ovários com corpo lúteo, o que pode ter um significado fisiológico, haja vista que esta macromolécula regula positivamente as enzimas ERK 1 e ERK2. A ERK 2, quando em sua forma inativa cataliticamente, pode bloquear a maturação meiótica induzida pela progesterona (Kushni et al., 2012). Assim, acreditamos que os folículos saudáveis contidos em ovários com corpo lúteo, recebem influência da progesterona para que ocorra a maturação meiótica, o que pode ocorrer de maneira diferente nos ovários sem corpo lúteo, indicando um mecanismo local de controle.

Ademais, o fibrinogênio, assim como o angiotensinogênio, apolipoproteína, complemento C3, albumina sérica, hemopexina e a glicoproteína α-2-HS estão envolvidos na resposta inflamatória e são consideradas proteínas de fase aguda, o que sugere um mecanismo de defesa no fluído folicular. Apesar disso, são proteínas multifuncionais e estão envolvidas em vários processos celulares. Resultados superiores na FIV em mulheres tem sido atribuídos a menor expressão do complemento C3 (Estes et al., 2009), o que pode indicar que a resposta inflamatória pode contribuir negativamente para o desenvolvimento oocitário. Estes resultados concordam com os de Angelucci et al. (2006) os quais inferiram que o sistema imunológico desempenha um papel crucial na foliculogênese e a

ovulação poderia ser considerada um processo inflamatório. Esta hipótese também pode ser verdadeira, já que o líquido folicular contem outros mediadores inflamatórios como as interleucinas e fator estimulador de colônias granulócitos-macrófagos encontradas no fluido folicular de humanos.

A serotransferrina foi identificada apenas nos folículos transicionais e atrésicos. Esta molécula apresenta como principal função o transporte de ferro férrico transmembrana. Em equinos, a serotransferrina foi mais abundante nos folículos durante o período de dominância quando comparados aos folículos subordinados, indicando sua participação neste processo (Rocha et al., 2015). Tal diferença pode ser relacionada à ausência de classificação dos folículos no trabalho de Rocha et al. (2015), já que estes autores não diferiram os folículos saudáveis.

Várias proteínas identificadas neste estudo foram relacionadas por Angelucci et al. (2006), os quais realizaram uma análise proteômica do fluído folicular de 25 mulheres submetidas à injeção intracitoplasmática de espermatozoide (ICSI) e encontraram 695 *spots* com ponto isoelétrico, variando entre o pH 3 e 10 e massa molecular entre 10 e 200 kDa. Desses *spots*, 625 foram comuns ao do soro humano. Foram identificadas 210 proteínas por espectrometria de massa, sendo que a maioria foram componentes relacionados à inflamação e incluíam principalmente a ceruloplasmina, α e γ-fibrinogênio, hemopexina, haptoglobulina, serpina, glicoproteína leucina-2 e macroglobulina A-2. No nosso estudo, apesar de não ter sido correlacionado o perfil proteico do soro sanguíneo e líquido folicular, muitas proteínas encontradas estão presentes no soro de bovinos, incluindo algumas determinadas por Angelucci et al. (2006). Tal fato pode confirmar a transferência de algumas proteínas do soro para os folículos e possivelmente a produção local de outras.

Alavi-Shoushtari et al. (2006) relataram altas concentrações de hormônios esteroides tanto estrógeno, assim como progesterona no sangue nas diferentes fases do ciclo estral, os quais tem efeito direto sobre a concentração de proteínas totais do fluido uterino. No presente estudo, as concentrações séricas de hormônios esteroides não foram determinadas, nem tão pouco as fases do ciclo estral, contudo todas as fêmeas apresentaram corpo lúteo e não foi observada diferenças entre os tipos proteicos de acordo com a presença e ausência do corpo lúteo, com exceção do fibrinogênio, da frutose difosfato e de outras proteínas em

menor abundância.

A enzima frutose-1,6-difosfatase participa da biossíntese de ATP e foi identificada apenas nos folículos saudáveis contidos em ovários com corpo lúteo. Esta enzima converte frutose-1,6-difosfato a frutose-6-fosfato na gliconeogênese. A expressão desta enzima é reduzida em células da granulosa envelhecidas de folículos persistentes de mulheres, o que indica uma alteração na produção de energia disponível para o oócito (Brandon et al., 2008). Assim, folículos saudáveis possuem expressão desta enzima em vista da modulação da produção de ATPs para disponibilizá-la pra os oócitos, estando diretamente envolvida no metabolismo e respiração celular folicular.

O plasminogênio também foi encontrado apenas nos folículos saudáveis de ovários que não continham corpo lúteo. A função desta proteína está relacionada à cascata da coagulação, incluindo a atividade de endopeptidase e de serina. Beers (1975) identificou o plasminogênio tanto no fluido folicular quanto na parede do folículo. A presença da enzima no fluido folicular fornece um mecanismo potencial para modular o nível de enzimas proteolíticas dentro do folículo e esse conjunto sugere que o sistema ativador de plasminogênio-plasmina pode estar envolvido durante o processo ovulatório. Ademais, a produção de plasminogênio é estimulada pelas gonadotrofinas, tanto FSH, assim como LH, reforçando seu envolvimento na ovulação (Reich et al., 1985).

Os únicos estudos que envolvem uma abordagem proteômica aprofundada do fluido folicular de bovinos visaram comparar o perfil proteico de folículos normais e císticos. Neste sentido, Maniwa e Jiro (2005) usaram a eletroforese bidimensional para separar as proteínas e analisaram os *spots* por espectrometria de massas com abordagem MALDI-TOF MS. Estes autores encontraram 8 *spots* de proteínas presentes no fluido folicular cístico, dentre elas uma que se destacou foi a proteína de choque térmico as quais são produzidas em condições de estresse, tais como inibição do metabolismo de energia, exposição a metais pesados, estresse oxidativo e inflamação. Sob essas condições as proteínas de choque térmico aumentaram a sobrevivência celular, e em condições não estressantes tiveram múltiplas funções na manutenção celular. Essas proteínas são expressas *in vitro* nas células da granulosa do ovário de mulheres (Benifla et al., 2002), são sintetizadas pelos oócitos e células do *cumulus* em vacas (Edwards et al., 1997) e desempenham um papel importante no desenvolvimento embrionário

inicial. A proteína de choque térmico tem a capacidade de inibir a apoptose podendo contribuir contra o efeito de morte celular. Isobe e Yoshimura (2000) relataram que na teca interna do ovário de bovinos ocorre um aumento na frequência de apoptose em folículos císticos e a diminuição da taxa de apoptose celular pode ser responsável pelo atraso na regressão folicular e que o controle da apoptose pode ser essencial para a redução da incidência de folículos císticos. No presente estudo, foram identificadas várias proteínas de choque térmico apenas nos folículos saudáveis e transicionais de ovários com corpo lúteo, o que pode indicar um mecanismo de proteção, ainda mantido nos folículos durante o período de transição para atrésicos.

Considerações finais

A determinação da composição de proteínas do líquido folicular pode ser uma ferramenta para investigar a fisiologia ovariana, especialmente no que diz respeito ao desenvolvimento folicular e maturação dos oócitos. Também pode ser uma fonte de novas moléculas para otimizar a FIV (Hess et al., 1998). No presente estudo foram identificadas proteínas características utilizando uma nova técnica de proteômica o MALDI-TOF-MS, método que necessita de pequenas quantidades de amostras fornecendo dados confiáveis e reproduzíveis.

O líquido folicular de vacas zebuínas não gestantes possui proteínas semelhantes a outras espécies e que apresentam função crucial no desenvolvimento folicular/oocitário, ovulação, resposta inflamatória, proteção contra apoptose e diferentes proteínas devem ser extensamente estudadas a fim de melhorar os sistemas de FIV. Vários estudos da expressão de genes relacionados a diferentes processos celulares já foram determinados, porém a expressão de proteínas ainda necessita ser elucidada.

587 **Tabela 1.** Proteínas identificadas na espectrometria de massas e suas respectivas ontologias gênicas (função molecular, processo biológico e
588 componente celular) das amostras do grupo de folículos saudáveis, de ovários sem corpo lúteo de vacas vazias.

Descrição proteína	ID Acesso	*Match*	Nº Peptídeos	% Cobertura sequência	Ontologia gênica		
					Função molecular	Processo biológico	Componente celular
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	26	59	43,49	--	--	Extracellular space
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	39	59	63,76	--	--	Extracellular space
Alpha-1B-glycoprotein OS=Bos taurus GN=A1BG PE=1 SV=1	A1BG_BOVIN	14	24	46,92	--	--	Blood microparticle
Alpha-2-macroglobulin variant 21 OS=Bos taurus GN=A2M PE=2 SV=1	K4JBT0_BOVIN	5	16	37,10	Endopeptidase inhibitor activity	--	--
Angiotensinogen OS=Bos taurus GN=AGT PE=2 SV=1	Q3SZH5_BOVIN	12	23	45,05	Sodium channel regulator activity	Activation of nf-kappab-inducing kinase activity; Angiotensin mediated vasoconstriction involved in regulation of systemic arterial blood pressure; Astrocyte activation; Blood vessel development; Brain renin-angiotensin system; Branching involved in ureteric bud morphogenesis; Cell-matrix adhesion; Drinking behavior; Establishment of blood-nerve barrier; Excretion; Extracellular matrix organization; G-protein coupled receptor signaling pathway; Hormone metabolic process; Negative regulation of cell proliferation; Negative regulation of neuron apoptotic process; Negative regulation of neurotrophin trk receptor signaling pathway; Ovarian follicle rupture; Peristalsis; Positive regulation of activation of jak2 kinase activity; Positive regulation of branching involved in ureteric bud morphogenesis; Positive regulation of cholesterol esterification; Positive regulation of endothelial cell migration; Positive regulation of epidermal growth factor receptor signaling pathway; Positive regulation of extrinsic apoptotic signaling pathway; Positive regulation of fatty acid biosynthetic process; Positive regulation of gap junction assembly; Positive regulation of mapk cascade; Positive regulation of membrane hyperpolarization; Positive regulation of multicellular organism growth; Positive regulation of organ growth; Positive regulation of peptidyl-serine phosphorylation; Positive regulation of phosphatidylinositol 3-kinase signaling; Positive regulation of protein kinase c activity; Positive regulation of protein tyrosine kinase activity; Positive regulation of transcription, dna-templated; Regulation of cardiac conduction; Regulation of extracellular matrix assembly; Regulation of inflammatory response; Regulation of renal output by angiotensin; Renal response to blood flow involved in circulatory renin-angiotensin regulation of systemic arterial blood pressure; Renin-angiotensin regulation of aldosterone production; Response to cold; Response to salt stress; Smooth muscle cell differentiation; Smooth muscle cell proliferation	Blood microparticle; Extracellular exosome; Intracellular
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=1	F1MSZ6_BOVIN	27	38	55,70	Heparin binding; Serine-type endopeptidase inhibitor activity	Regulation of blood coagulation, intrinsic pathway source	Blood microparticle; Extracellular exosome
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=2	ANT3_BOVIN	28	38	58,49	Heparin binding; Serine-type endopeptidase inhibitor activity	Blood coagulation; Negative regulation of endopeptidase activity; Regulation of blood coagulation, intrinsic pathway	Extracellular space

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	25	32	68,30	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	16	32	58,11	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	16	32	58,11	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicule; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	13	32	45,66	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling; Vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	25	32	68,30	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response;Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	16	32	58,11	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesteroltransporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling; Vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	11	23	48,56	Lipid binding	Lipid transport; Lipoprotein metabolic process	Extracellular region
Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	7	23	36,54	Lipid binding	Lipid transport; Lipoprotein metabolic process	Extracellular region
Beta-2-glycoprotein 1 OS=Bos taurus GN=APOH PE=1 SV=4	APOH_BOVIN	7	22	35,65	Heparin binding -	--	Extracellular region
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=1	G3X7A5_BOVIN	48	154	36,18	Endopeptidase inhibitor activity	Complement activation; Inflammatory response; Positive regulation of activation of membrane attack complex; Positive regulation of angiogenesis; Positive regulation of apoptotic cell clearance; Positive regulation of glucose transport; Positive regulation of g-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Positive regulation of type iia hypersensitivity; Positive regulation of vascular endothelial growth factor production; Regulation of triglyceride biosynthetic process	Blood microparticle; Extracellular exosome
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=2	CO3_BOVIN	51	154	38,29	C5L2 anaphylatoxin chemotactic receptor binding; Endopeptidase inhibitor activity	Complement activation, alternative pathway; Complement activation, classical pathway;Fatty acid metabolic process; Inflammatory response; Positive regulation of glucose transport; Positive regulation of G-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Regulation of triglyceride biosynthetic process	Extracellular space
Complement component 3 OS=Bos taurus GN=C3 PE=2 SV=1	A0A0F6QNP7_BOVIN	49	156	37,15	Endopeptidase inhibitor activity	Complement activation; Inflammatory response	Extracellular space
Complement component C9 OS=Bos taurus GN=C9 PE=2 SV=1	CO9_BOVIN	16	42	42,70	--	Complement activation, alternative pathway; Complement activation, classical pathway cytolysis	Blood microparticle; Cytoplasm; Extracellular exosome

Continua Tabela 1

Corticosteroid-binding globulin OS=Bos taurus GN=SERPINA6 PE=3 SV=1	CBG_BOVIN	11	28	42,08	Serine-type endopeptidase inhibitor activity; Steroid binding	Glucocorticoid metabolic process; Negative regulation of endopeptidase activity; Transport	Extracellular exosome; Extracellular space
Embryo-specific fibronectin 1 transcript variant OS=Bos taurus GN=FN1 PE=1 SV=1	B8Y9S9_BOVIN	14	145	9,89	--	--	Extracellular region
Endopin 2 OS=Bos taurus GN=SERPINA3-7 PE=2 SV=1	Q3SZQ8_BOVIN	12	29	36,93	--	--	Extracellular space
Endopin 2B OS=Bos taurus PE=2 SV=1	Q5J801_BOVIN	12	29	36,93	--	--	--
Endopin 2C OS=Bos taurus PE=2 SV=1	Q32T06_BOVIN	3	32	8,70	--	--	Extracellular space
Factor XIIa inhibitor OS=Bos taurus PE=1 SV=1	F12AI_BOVIN	3	27	7,48	Serine-type endopeptidase inhibitor activity	Blood coagulation; Fibrinolysis	Extracellular space
FGB protein (Fragment) OS=Bos taurus GN=FGB PE=2 SV=1	A6QPX7_BOVIN	30	28	62,42	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
FGG protein OS=Bos taurus GN=FGG PE=1 SV=1	Q3SZZ9_BOVIN	20	35	54,02	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	FIBB_BOVIN	36	40	60,26	Glycoprotein binding	Adaptive immune response; Innate immune response; Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	F1MAV0_BOVIN	35	43	52,73	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Induction of bacterial agglutination; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	F1MGU7_BOVIN	20	36	53,05	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Protein secretion; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	FIBG_BOVIN	16	36	42,34	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex

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Fibronectin OS=Bos taurus GN=FN1 PE=1 SV=1	G5E5A9_BOVIN	14	146	9,52	Peptidase activator activity	Calcium-independent cell-matrix adhesion; Cell-substrate junction assembly; Endodermal cell differentiation; Integrin activation; Negative regulation of transforming growth factor-beta secretion; Peptide cross-linking; Positive regulation of axon extension; Positive regulation of fibroblast proliferation; Positive regulation of gene expression; Positive regulation of substrate-dependent cell migration, cell attachment to substrate; Regulation of ERK1 and ERK2 cascade; Substrate adhesion-dependent cell spreading; Wound healing	--
Heat shock 27kDa protein 1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	E9RHW1_BOVIN	5	16	35,82	--	--	--
Heat shock 27kDa protein 1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	Q58DP7_BOVIN	4	13	35,48	--	--	--
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=1 SV=1	G3X7S2_BOVIN	4	13	35,71	--	--	--
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=1 SV=2	E1BEL7_BOVIN	5	17	35,47	Poly(A) RNA binding; Protein kinase C inhibitor activity	Intracellular signal transduction; Negative regulation of oxidative stress-induced intrinsic apoptotic signaling pathway; Platelet aggregation; Positive regulation of angiogenesis; Positive regulation of blood vessel endothelial cell migration; Positive regulation of endothelial cell chemotaxis by VEGF-activated vascular endothelial growth factor receptor signaling pathway; Positive regulation of interleukin-1 beta production; Positive regulation of tumor necrosis factor biosynthetic process; Regulation of I-kappab kinase/NF-kappab signalin; Response to virus; Retina homeostasis	Extracellular exosome; Extracellular space; Focal adhesion; Nucleus; Plasma membrane
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	HSPB1_BOVIN	5	16	35,82	--	--	Cytoplasm; Nucleus
Hemopexin OS=Bos taurus GN=HPX PE=2 SV=1	HEMO_BOVIN	17	35	49,46	Heme transporter activity; Metal ion binding	Cellular iron ion homeostasis; Heme metabolic process; Hemoglobin metabolic process; Positive regulation of humoral immune response mediated by circulating immunoglobulin; Positive regulation of immunoglobulin production; Positive regulation of interferon-gamma-mediated signaling pathway; Positive regulation of tyrosine phosphorylation of stat1 protein	Blood microparticle; Cell; Extracellular exosome
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	B0JYP6_BOVIN	7	12	35,83	--	--	--
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	Q05B55_BOVIN	7	13	35,83	--	-	--
KRT15 protein OS=Bos taurus GN=KRT15 PE=1 SV=2	Q17QL7_BOVIN	3	43	4,64	Structural molecule activity	Mitophagy in response to mitochondrial depolarization	Extracellular exosome
Nexin (Fragment) OS=Bos taurus PE=2 SV=1	Q9N1C4_BOVIN	7	12	47,98	--	--	Extracellular space
Pigment epithelium-derived factor OS=Bos taurus GN=SERPINF1 PE=1 SV=1	PEDF_BOVIN	17	30	56,01	Serine-type endopeptidase inhibitor activity	Negative regulation of angiogenesis Negative regulation of endopeptidase activity; Negative regulation of epithelial cell proliferation involved in prostate gland development; Positive regulation of neurogenesis	Extracellular exosome; Extracellular matrix; Extracellular region; Extracellular space
Plasminogen OS=Bos taurus GN=PLG PE=1 SV=2	PLMN_BOVIN	4	68	4,31	Protein domain specific binding; Receptor binding; Serine-type endopeptidase activity	Blood coagulation; Fibrinolysis; Response to heat; Tissue remodeling	Extracellular region

Continua Tabela 1

Plasminogen OS=Bos taurus GN=PLG PE=3 SV=2	E1B726_BOVIN	4	68	4,31	Serine-type endopeptidase activity	Blood coagulation; Fibrinolysis; Labyrinthine layer blood vessel development; Mononuclear cell migration; Muscle cell cellular homeostasis; Myoblast differentiation; Tissue regeneration; Tissue remodeling; Trophoblast giant cell differentiation	Extracellular region; Extrinsic component of plasma membrane
Serine protease inhibitor clade E member 2 OS=Bos taurus GN=SERPINE2 PE=2 SV=1	Q8HZY1_BOVIN	11	29	36,02	Peptidase activity	--	Extracellular space
Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	26	75	43,04	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated endocytosis; Retina homeostasis	Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome; Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; Hfe-transferrin receptor complex; Late endosome; Perinuclear region of cytoplasm; Recycling endosome
Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	49	75	63,21	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated endocytosis retina homeostasis	Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	48	76	62,07	Ferric iron binding; Ferric iron transmembrane transporter activity	Cellular iron ion homeostasis	Cellsource; Extracellular space
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	48	76	62,07	Ferric iron binding; Ferric iron transmembrane transporter activity	Cellular iron ion homeostasis	Cell; Extracellular space
Serpin A3-1 OS=Bos taurus GN=SERPINA3-1 PE=1 SV=3	SPA31_BOVIN	17	28	38,20	Cysteine-type endopeptidase inhibitor activity Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasm
Serpin A3-2 OS=Bos taurus GN=SERPINA3-2 PE=3 SV=1	SPA32_BOVIN	17	28	38,20	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule
Serpin A3-3 OS=Bos taurus GN=SERPINA3-3 PE=1 SV=2	SPA33_BOVIN	19	28	45,50	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule
Serpin A3-4 OS=Bos taurus GN=SERPINA3-4 PE=3 SV=1	SPA34_BOVIN	20	29	56,20	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule

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Serpin A3-5 OS=Bos taurus GN=SERPINA3-5 PE=3 SV=1	SPA35_BOVIN	16	28	38,93	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule
Serpin A3-6 OS=Bos taurus GN=SERPINA3-6 PE=3 SV=1	G3N1U4_BOVIN	17	27	40,88	--	--	Extracellular space
Serpin A3-7 OS=Bos taurus GN=SERPINA3-7 PE=1 SV=1	A0A0A0MP92_BOVIN	12	29	36,93	--	--	Extracellular space
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=2 SV=1	SPA38_BOVIN	12	34	35,89	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=3 SV=1	A0A0A0MP89_BOVIN	12	34	35,89	--	--	Extracellular space
Serpin peptidase inhibitor_ clade E (Nexin_plasminogen activator inhibitor type 1)_ member 2 OS=Bos taurus GN=SERPINE2 PE=2 SV=1	Q08DC0_BOVIN	3	29	9,57	--	--	Extracellular space
SERPIND1 protein OS=Bos taurus GN=SERPIND1 PE=2 SV=1	A6QPP2_BOVIN	19	35	65,73	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular exosome
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	27	59	45,63	DNA binding; drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding; Toxic substance binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Reactome; Extracellular space; Protein complex
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	39	59	63,10	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Extracellular space; Protein complex
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	39	59	63,10	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Extracellular space; Protein complex
Sex hormone-binding globulin (Fragment) OS=Bos taurus GN=SHBG PE=2 SV=1	Q6T182_BOVIN	8	21	43,13	--	--	Extracellular exosome
SHBG protein OS=Bos taurus GN=SHBG PE=2 SV=1	A5PKC2_BOVIN	8	22	39,90	--	--	--

Continua Tabela 1

Similar to alpha-tubulin isoform 1 (Fragment) OS=Bos taurus PE=2 SV=1	Q862L2_BOVIN	3	6	39,39	Gtpase activity	Microtubule-based process	Microtubule
TUBB2A protein OS=Bos taurus GN=TUBB2A PE=2 SV=1	Q148E2_BOVIN	8	19	43,33	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Tubulin alpha-1B chain OS=Bos taurus PE=1 SV=2	TBA1B_BOVIN	12	34	38,36	Double-stranded RNA binding; Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Cellular response to interleukin-4; Microtubule cytoskeleton organization	Cytoplasmic microtubule extracellular exosome myelin sheath
Tubulin beta-2B chain OS=Bos taurus GN=TUBB2B PE=1 SV=2	TBB2B_BOVIN	11	30	44,94	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process; Neuron migration	Cytoplasm; Microtubule; Nucleus
Tubulin beta-2B chain OS=Bos taurus GN=TUBB2B PE=3 SV=1	G3N1W7_BOVIN	8	19	43,33	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Uncharacterized protein (Fragment) OS=Bos taurus GN=IGHM PE=1 SV=1(*)	G5E513_BOVIN	3	35	7,66	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment; Phagocytosis, recognition; Positive regulation of b cell activation	Blood microparticle; External side of plasma membrane; Immunoglobulin complex, circulating
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1(*)	G3N0V0_BOVIN	18	25	76,07	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment; Phagocytosis, recognition; Positive regulation of b cell activation	Blood microparticle; External side of plasma membrane; Immunoglobulin complex, circulating
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1(*)	G5E604_BOVIN	4	6	45,79	--	Immune response; Immunoglobulin production	Extracellular space
Uncharacterized protein OS=Bos taurus GN=IGLL1 PE=1 SV=2(*)	F1MLW7_BOVIN	8	11	43,59	--	--	--
Uncharacterized protein OS=Bos taurus GN=IGLL1 PE=4 SV=1(*)	G3N2D7_BOVIN	3	5	51,72	--	--	--
Uncharacterized protein OS=Bos taurus GN=SERPINA3 PE=3 SV=1(*)	G8JKW7_BOVIN	17	29	49,76	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular space
Uncharacterized protein OS=Bos taurus GN=SERPING1 PE=3 SV=2(*)	E1BMJ0_BOVIN	3	26	7,48	Serine-type endopeptidase inhibitor activity	Negative regulation of complement activation, lectin pathway; Negative regulation of endopeptidase activity	Blood microparticle; Extracelular exosome

Continua Tabela 1

Uncharacterized protein OS=Bos taurus GN=TUBB2A PE=1 SV=1(*)	E1BJB1_BOVIN	10	30	37,53	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Extracellular exosome; Microtubule
Uncharacterized protein OS=Bos taurus GN=TUBB2A PE=1 SV=1(*)	G3X7R7_BOVIN	8	19	43,33	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Uncharacterized protein OS=Bos taurus GN=VTN PE=2 SV=1(*)	Q3ZBS7_BOVIN	4	27	9,03	Extracellular matrix binding; Polysaccharide binding; Scavenger receptor activity	Cell adhesion mediated by integrin; Endodermal cell differentiation; Extracellular matrix organization; Immune response; Negative regulation of endopeptidase activity; Oligodendrocyte differentiation; Positive regulation of cell-substrate adhesion; Positive regulation of peptidyl-tyrosine phosphorylation; Positive regulation of protein binding; Positive regulation of receptor-mediated endocytosis; Positive regulation of smooth muscle cell migration; Smooth muscle cell-matrix adhesion	Blood microparticle; Extracellular exosome; Proteinaceous extracellular matrix
Uncharacterized protein OS=Bos taurus PE=1 SV=2(*)	F1MZ96_BOVIN	7	13	35,83	--	B cell differentiation	--
Uncharacterized protein OS=Bos taurus PE=1 SV=2(*)	F1MH40_BOVIN	7	13	35,83	--	Immune response; Immunoglobulin production	Extracellular space
Vitamin D binding protein OS=Bos taurus PE=2 SV=1	I7CT57_BOVIN	11	44	37,13	Vitamin D binding	--	Extracellular space
Vitamin D-binding protein OS=Bos taurus GN=GC PE=1 SV=2	F1N5M2_BOVIN	12	44	39,45	Calcidiol binding	Vitamin d metabolic process	Blood microparticle
Vitamin D-binding protein OS=Bos taurus GN=GC PE=2 SV=1	VTDB_BOVIN	10	44	35,02	Vitamin D binding	--	Extracellular space

(*) Uncharacterized protein: Proteins which are NOT conserved or with no known or predicted function orcharacteristics (http://www.uniprot.org/docs/nameprot)

Tabela 2. Proteínas identificadas na espectrometria de massas e suas respectivas ontologias gênicas (função molecular, processo biológico e componente celular) das amostras do grupo de folículos transicionais, de ovários sem corpo lúteo de vacas vazias

Descrição proteína	ID Acesso	*Match*	Nº Peptídeos	% Cobertura sequência	Ontologia gênica		
					Função molecular	Processo biológico	Componente celular
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	36	59	59,47	--	Transport	Extracellular space
Alpha-1-antiproteinase OS=Bos taurus GN=SERPINA1 PE=1 SV=1	A1AT_BOVIN	16	28	39,18	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Endoplasmic reticulum
Alpha-1B-glycoprotein OS=Bos taurus GN=A1BG PE=1 SV=1	A1BG_BOVIN	14	24	45,92	--	--	Blood microparticle
Angiotensinogen OS=Bos taurus GN=AGT PE=2 SV=1	Q3SZH5_BOVIN	12	23	38,68	Sodium channel regulator activity	Activation of NF-kappab-inducing kinase activity; Angiotensin mediated vasoconstriction involved in regulation of systemic arterial blood pressure; Astrocyte activation; Blood vessel development; Brain renin-angiotensin system; Branching involved in ureteric bud morphogenesis; Cell-matrix adhesion; Drinking behavior; Establishment of blood-nerve barrier; Excretion; Extracellular matrix organization; G-protein coupled receptor signaling pathway hormone metabolic process; Negative regulation of cell proliferation; Negative regulation of neuron apoptotic process; Negative regulation of neurotrophin TRK receptor signaling pathway; Ovarian follicle rupture; Peristalsis; Positive regulation of activation of JAK2 kinase activity; Positive regulation of branching involved in ureteric bud morphogenesis; Positive regulation of cholesterol esterification; Positive regulation of endothelial cell migration; Positive regulation of epidermal growth factor receptor signaling pathway; Positive regulation of extrinsic apoptotic signaling pathway; Positive regulation of fatty acid biosynthetic process; Positive regulation of gap junction assembly; Positive regulation of MAPK cascade; Positive regulation of membrane hyperpolarization positive regulation of multicellular organism growth; Positive regulation of organ growth; Positive regulation of peptidyl-serine phosphorylation; Positive regulation of phosphatidylinositol 3-kinase signaling; Positive regulation of protein kinase C activity positive regulation of protein tyrosine kinase activity; Positive regulation of transcription, DNA-templated regulation of cardiac conduction; Regulation of extracellular matrix assembly; Regulation of inflammatory response; Regulation of renal output by angiotensin; Renal response to blood flow involved in circulatory renin-angiotensin regulation of systemic arterial blood pressure; Renin-angiotensin regulation of aldosterone production; Response to cold; Response to salt stress;Smooth muscle cell differentiation; Smooth muscle cell proliferation	Blood microparticle; Extracellular exosome; Intracellular
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=1	F1MSZ6_BOVIN	23	38	54,62	Heparin binding	Regulation of blood coagulation, intrinsic pathway	Blood microparticle
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=2	ANT3_BOVIN	23	38	54,62	Heparin binding	Blood coagulation	Extracellular space

Continua Tabela 2

Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	27	32	67,92	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	17	32	50,57	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	27	32	67,92	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3APOA1_BOVIN	3APOA1_BOVIN	17	32	50,57	Beta-amyloid binding; Chemorepellent activity;Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling; Vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	13	23	49,52	Lipid binding	Lipid transport; Lipoprotein metabolic process	Extracellular region
Apolipoprotein A-IV OS=Bos taurus GN=APOA4 PE=2 SV=1	APOA4_BOVIN	11	36	36,32	Cholesterol binding; Cholesterol transporter activity; Phosphatidylcholine binding; Phosphatidylcholine-sterol O-acyltransferase activator activity	Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; High-density lipoprotein particle assembly; Lipoprotein metabolic process; Neuron projection regeneration; Phosphatidylcholine metabolic process; Phospholipid efflux; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of triglyceride catabolic process; Regulation of intestinal cholesterol absorption; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling	Blood microparticle; Chylomicron; High-density lipoprotein particle
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=1	G3X7A5_BOVIN	43	154	36,91	Endopeptidase inhibitor activity Source: interpro	Complement activation; Inflammatory response; Positive regulation of activation of membrane attack complex; Positive regulation of angiogenesis; Positive regulation of apoptotic cell clearance positive regulation of glucose transport; Positive regulation of G-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage Positive regulation of protein phosphorylation; Positive regulation of type iia hypersensitivity; Positive regulation of vascular endothelial growth factor production; Regulation of triglyceride biosynthetic process	Blood microparticle; Extracellular exosome
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=2	CO3_BOVIN	46	154	39,55	C5L2 anaphylatoxin chemotactic receptor binding; Endopeptidase inhibitor activity	Complement activation, alternative pathway; Complement activation, classical pathway; Fatty acid metabolic process; Inflammatory response; Positive regulation of glucose transport; Positive regulation of G-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Regulation of triglyceride biosynthetic process	Extracellular space
Complement component 3 OS=Bos taurus GN=C3 PE=2 SV=1	A0A0F6QNP7_BOVIN	44	156	37,87	Endopeptidase inhibitor activity	Complement activation; Inflammatory response	Extracellular space
Complement component C9 OS=Bos taurus GN=C9 PE=2 SV=1	CO9_BOVIN	15	42	35,77	--	Complement activation, alternative pathway; Complement activation, classical pathway; Cytolysis	Blood microparticle; Cytoplasm; Extracellular exosome

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Endopin 2 OS=Bos taurus GN=SERPINA3-7 PE=2 SV=1	Q3SZQ8_BOVIN	15	29	40,77	--	--	Extracellular space
Endopin 2B OS=Bos taurus PE=2 SV=1	Q5J801_BOVIN	15	29	40,77	--	--	Extracellular space
FGB protein (Fragment) OS=Bos taurus GN=FGB PE=2 SV=1	A6QPX7_BOVIN	25	28	56,67	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
FGG protein OS=Bos taurus GN=FGG PE=1 SV=1	Q3SZZ9_BOVIN	16	35	46,21	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	F1MAV0_BOVIN	30	43	48,89	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Induction of bacterial agglutination; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	FIBB_BOVIN	30	40	51,71	Glycoprotein binding	Adaptive immune response; Innate immune response; Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	F1MGU7_BOVIN	16	36	45,37	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Protein secretion; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	FIBG_BOVIN	16	36	43,69	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	HSPB1_BOVIN	5	16	35,82	--	--	Cytoplasmsource: uniprotkb
Hemopexin OS=Bos taurus GN=HPX PE=2 SV=1	HEMO_BOVIN	17	35	47,71	Heme transporter activity; Metal ion binding	Cellular iron ion homeostasis; Heme metabolic process; Hemoglobin metabolic process; Positive regulation of humoral immune response mediated by circulating immunoglobulin; Positive regulation of immunoglobulin production; Positive regulation of interferon-gamma-mediated signaling pathway; Positive regulation of tyrosine phosphorylation of stat1 protein	Blood microparticle; Cell; Extracellular exosome
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	B0JYP6_BOVIN	8	12	36,67	--	--	--
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	Q05B55_BOVIN	9	13	41,67	--	--	--

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IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	B0JYP6_BOVIN	6	12	35,83	--	--	--
IGL@ protein OS=Bos taurus GN=IGL@ PE=1 SV=1	Q3T101_BOVIN	8	12	48,94	--	--	--
Pigment epithelium-derived factor OS=Bos taurus GN=SERPINF1 PE=1 SV=1	PEDF_BOVIN	13	30	45,91	Serine-type endopeptidase inhibitor activity	Negative regulation of angiogenesis; Negative regulation of endopeptidase activity; Negative regulation of epithelial cell proliferation involved in prostate gland development; Positive regulation of neurogenesis	Extracellular exosome; Extracellular matrix; Extracellular region; Extracellular space
Putative uncharacterized protein OS=Bos taurus PE=2 SV=1 (*)	A5PK72_BOVIN	7	12	39,41	--	--	--
Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	53	75	69,60	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated endocytosis; Retina homeostasis	Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	52	76	68,47	Ferric iron binding; Ferric iron transmembrane transporter activity	cellular iron ion homeostasis	Cell; Extracellular;
Serpin A3-1 OS=Bos taurus GN=SERPINA3-1 PE=1 SV=3	SPA31_BOVIN	17	28	35,77	Cysteine-type endopeptidase inhibitor activity; Serine-type endopeptidase inhibitor activity	negative regulation of endopeptidase activity	Chromaffin granule; -subcell; Cytoplasm cytoplasmic vesicle; Extracellular space;
Serpin A3-2 OS=Bos taurus GN=SERPINA3-2 PE=3 SV=1	SPA32_BOVIN	18	28	42,58	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-3 OS=Bos taurus GN=SERPINA3-3 PE=1 SV=2	SPA33_BOVIN	16	28	36,98	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-4 OS=Bos taurus GN=SERPINA3-4 PE=3 SV=1	SPA34_BOVIN	16	29	36,98	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-5 OS=Bos taurus GN=SERPINA3-5 PE=3 SV=1	SPA35_BOVIN	14	28	37,96	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-6 OS=Bos taurus GN=SERPINA3-6 PE=3 SV=1	SPA36_BOVIN	16	26	48,31	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule Cytoplasmic vesicle Extracellular space
Serpin A3-7 OS=Bos taurus GN=SERPINA3-7 PE=1 SV=1	A0A0A0MP92_BOVIN	15	29	40,77	--	--	--
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=2 SV=1	SPA38_BOVIN	13	34	37,56	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space

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Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	39	59	64,09	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Extracellular space; Protein complex
Tubulin alpha-1B chain OS=Bos taurus PE=1 SV=2	TBA1B_BOVIN	13	34	45,45	Double-stranded RNA binding; Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Cellular response to interleukin-4; Microtubule cytoskeleton organization	Cytoplasmic microtubule; Extracellular exosome; Myelin sheath
Tubulin alpha-1C chain OS=Bos taurus GN=TUBA1C PE=1 SV=1	TBA1C_BOVIN	10	34	40,09	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1(**)	G3N0V0_BOVIN	12	25	46,32	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment; Phagocytosis, recognition; Positive regulation of b cell activation	Blood microparticle; External side of plasma membrane; Immunoglobulin complex, circulating
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1(**)	G5E604_BOVIN	4	6	52,34	--	Immune respons; Immunoglobulin production	Extracellular space
Uncharacterized protein OS=Bos taurus GN=IGLL1 PE=1 SV=2(**)	F1MLW7_BOVIN	7	11	39,74	--	--	--
Uncharacterized protein OS=Bos taurus GN=LOC100141266 PE=3 SV=1(**)	F1MNF8_BOVIN	9	34	36,97	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Uncharacterized protein OS=Bos taurus GN=SERPINA3 PE=3 SV=1(**)	G8JKW7_BOVIN	15	29	37,86	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular space
Uncharacterized protein OS=Bos taurus GN=TUBA1A PE=3 SV=1(**)	F2Z4C1_BOVIN	11	34	42,57	Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasmic microtubule; Cytoplasmic ribonucleoprotein granule; Extracellular exosome; Myelin sheath; Nucleus; Recycling endosome
Uncharacterized protein OS=Bos taurus PE=1 SV=2(*)	F1MH40_BOVIN	6	13	35,83	--	Immune response; Immunoglobulin production	Extracellular space
Uncharacterized protein OS=Bos taurus PE=1 SV=2(**)	F1MZ96_BOVIN	8	13	36,67	--	B cell differentiation	--

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Continua Tabela 2

Uncharacterized protein OS=Bos taurus PE=1 SV=2(**)	F1MH40_BOVIN	8	13	36,67	--	Immune response; Immunoglobulin production	Extracellular space
Uncharacterized protein OS=Bos taurus PE=1 SV=2(**)	F1MZ96_BOVIN	6	13	35,83	--	B cell differentiation	--

(*) Putative uncharacterized protein: means that this protein may be identified by computer, and the function is still unknown. This protein is not homologous to any well characterised proteins and thus its function cannot be predicted. Putative means that it was only predicted based on ORF (open reading frame) and promoter sequence.

(**) Uncharacterized protein: Proteins which are NOT conserved or with no known or predicted function orcharacteristics (http://www.uniprot.org/docs/nameprot)

623 **Tabela 3.** Proteínas identificadas na espectrometria de massas e suas respectivas ontologias gênicas (função molecular, processo biológico e
624 componente celular) das amostras do grupo de folículos saudáveis, de ovários com corpo lúteo de vacas vazias

Descrição proteína	ID Acesso	*Match*	Nº Peptídeos	% Cobertura sequência	Ontologia gênica		
					Função molecular	Processo biológico	Componente celular
Actin_ cytoplasmic 1 OS=Bos taurus GN=ACTB PE=1 SV=1	ACTB_BOVIN	15	34	47,73	ATP binding	Chaperone mediated protein folding independent of cofactor; Protein folding	Cytoskeleton; Cytosol; Dense body; Focal adhesion; Nua4 histone acetyltransferase complex; Plasma membrane
Actin_ cytoplasmic 1 OS=Bos taurus GN=ACTB PE=3 SV=2	F1MRD0_BOVIN	10	34	38,93	ATP binding; RNA polymerase II core promoter proximal region sequence-specific DNA binding; RNA polymerase II distal enhancer sequence-specific DNA binding	ATP-dependent chromatin remodeling; Platelet aggregation; Retina homeostasis; Substantia nigra development	Blood microparticle; Cortical cytoskeleton; Cytoplasmic ribonucleoprotein granule; Cytoskeleton; Cytosol; Dense body; Extracellular exosome; Focal adhesion; MLL5-L complex; Myelin sheath; Nua4 histone acetyltransferase complex; Nuclear chromatin; Plasma membrane
Actin_ cytoplasmic 2 OS=Bos taurus GN=ACTG1 PE=1 SV=1	ACTG_BOVIN	16	34	50,67	ATP binding; Structural constituent of cytoskeleton	Platelet aggregation; Retina homeostasis; Sarcomere organization	Blood microparticle; Cytoskeleton; Dense body; Extracellular exosome; Filamentous actin; Focal adhesion; Myelin sheath; Myofibril; Nucleus; Plasma membrane
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	40	59	61,78	--	Transport	Extracellular space
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	40	59	61,78	--	Transport	Extracellular space
Alpha 1-antichymotrypsin (Fragment) OS=Bos taurus GN=alpha 1-antichymotrypsin/ ACT PE=2 SV=1	Q28921_BOVIN	11	18	42,46	--	--	Extracellular space
Alpha-1-acid glycoprotein OS=Bos taurus GN=agp PE=2 SV=2	Q5GN72_BOVIN	10	20	38,61	--	Regulation of immune system process; Transport	Extracellular space
Alpha-1-acid glycoprotein OS=Bos taurus GN=ORM1 PE=2 SV=1	A1AG_BOVIN	10	20	38,61	--	Acute-phase response; Regulation of immune system process; Transport	Extracellular space

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Alpha1-antichymotrypsin isoform pHHK11 (Fragment) OS=Bos taurus PE=2 SV=1	Q27983_BOVIN	9	16	42,86	--	--	Extracellular space
Alpha-1B-glycoprotein OS=Bos Taurus GN=A1BG	A1BG_BOVIN	18	24	55,67	--	--	Blood microparticle; Extracellular exosome
Alpha-2-HS-glycoprotein OS=Bos taurus GN=AHSG PE=1 SV=1	B0JYN6_BOVIN	7	19	36,49	Cysteine-type endopeptidase inhibitor activity	Acute-phase response; Negative regulation of bone mineralization; Ossification; Positive regulation of phagocytosis; Regulation of inflammatory response	Blood microparticle; Extracellular exosome; Extracellular membrane-bounded organelle; Plasma membrane; Vesicle
Alpha-2-HS-glycoprotein OS=Bos taurus GN=AHSG PE=1 SV=2	FETUA_BOVIN	7	19	36,49	Cysteine-type endopeptidase inhibitor activity; Endopeptidase inhibitor activity	Acute-phase response; Negative regulation of biomineral tissue development; Negative regulation of bone mineralization; Negative regulation of endopeptidase activity; Ossification; Positive regulation of phagocytosis; Regulation of inflammatory response	Blood microparticle; Extracellular exosome; Extracellular matrix; Extracellular membrane-bounded organelle source: agbase; Plasma membrane; Vesicle
Angiotensinogen OS=Bos taurus GN=AGT PE=2 SV=1	Q3SZH5_BOVIN	13	23	45,05	Sodium channel regulator activity	Activation of nf-kappab-inducing kinase activity; Angiotensin mediated vasoconstriction involved in regulation of systemic arterial blood pressure; Astrocyte activation; Blood vessel development; Brain renin-angiotensin system; Branching involved in ureteric bud morphogenesis; Cell-matrix adhesion; Drinking behavior; Establishment of blood-nerve barrier; Excretion; Extracellular matrix organization; G-protein coupled receptor signaling; Hormone metabolic process; Negative regulation of cell proliferation; Negative regulation of neuron apoptotic process; Negative regulation of neurotrophin trk receptor signaling pathway; Ovarian follicle rupture; Peristalsis; Positive regulation of activation of jak2 kinase activity; Positive regulation of branching involved in ureteric bud morphogenesis; Positive regulation of cholesterol esterification; Positive regulation of endothelial cell migration; Positive regulation of epidermal growth factor receptor signaling pathway; Positive regulation of extrinsic apoptotic signaling pathway; Positive regulation of fatty acid biosynthetic; Positive regulation of gap junction assembly; Positive regulation of mapk cascade; Positive regulation of membrane hyperpolarization; Positive regulation of multicellular organism growth; Positive regulation of organ growth; Positive regulation of peptidyl-serine phosphorylation; Positive regulation of phosphatidylinositol 3-kinase signaling; Positive regulation of protein kinase c activity; Positive regulation of protein tyrosine kinase activity; Positive regulation of transcription, DNA-templated; Regulation of cardiac conduction; Regulation of extracellular matrix assembly; Regulation of inflammatory response ; egulation of renal output by angiotensin; Renal response to blood flow involved in circulatory renin-angiotensin regulation of systemic arterial blood pressure; Renin-angiotensin regulation of aldosterone production; Response to cold; Response to salt stress; Smooth muscle cell differentiation; Smooth muscle cell proliferation	Blood microparticle; Extracellular exosome; Intracellular
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=1	F1MSZ6_BOVIN	25	38	50,75	Heparin binding; Serine-type endopeptidase inhibitor activity	Regulation of blood coagulation, intrinsic pathway	Blood microparticle; Extracellular exosome

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Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=2	ANT3_BOVIN	26	38	55,91	Heparin binding; Serine-type endopeptidase inhibitor activity	Blood coagulation; Negative regulation of endopeptidase activity; Regulation of blood coagulation, intrinsic pathway	Extracellular space
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	24	32	63,77	Beta-amyloid binding; chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	16	32	52,08	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol O-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of Rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	24	32	63,77	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response ; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	24	32	63,77	Beta-amyloid binding; Chemorepellent activity ; Cholesterol binding; Cholesterol transporteractivity; High-density lipoprotein; Particle binding; High-density lipoprotein; Particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol O-acyltransferase activator activity;	Adrenal gland development ; Blood vessel endothelial cell migration ; Cholesterol biosynthetic; process; Cholesterol efflux;Cholesterol homeostasis;Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell; Adhesion molecule production;Negative regulation of cytokine secretion involved in immune response;Negative regulation of heterotypic cell-cell adhesion;Negative regulation of hydrolase activity; Negative regulation of inflammatory response;Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway;Negative regulation of very-low-density lipoprotein particle remodeling;Neuron projection regeneration; Peptidyl-methionine modification;Phosphatidylcholine biosynthetic process;Phosphatidylcholine metabolic process;Phospholipid efflux;Phospholipid homeostasis;Positive regulation of cholesterol esterification;Positive regulation of fatty acid biosynthetic process;Positive regulation of lipoprotein lipase activity;Positive regulation of Rho protein signal transduction;Positive regulation of stress fiber assembly;Positive regulation of substrate adhesion-dependent cell spreading;Positive regulation of triglyceride catabolic process ;Protein oxidation;Protein stabilization;Regulation of Cdc42 protein signal transduction;Regulation of intestinal cholesterol absorption;Regulation of protein phosphorylation;Reverse cholesterol transport;Triglyceride catabolic process;Triglyceride homeostasis;Very-low-density lipoprotein particle remodeling;Vitamin transport;	Blood microparticle; Chylomicron endocytic vesicle; Extracellular exosome; High-density lipoprotein; Particle spherical high-density lipoprotein particle; Very-low-density lipoprotein particle

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN		32	50,57	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	24	32	63,77	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol O-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of Rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of Cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling; Vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	12	23	49,52	Lipid binding	Lipid transport; Lipoprotein metabolic process	Extracellular region
Apolipoprotein A-IV OS=Bos taurus GN=APOA4 PE=2 SV=1	APOA4_BOVIN	26	36	58,16	Cholesterol binding; Cholesterol transporter activity; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; High-density lipoprotein particle assembly; Lipoprotein metabolic process; Neuron projection regeneration; Phosphatidylcholine metabolic process; Phospholipid efflux; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process positive regulation of lipoprotein lipase activity; Positive regulation of triglyceride catabolic process; Regulation of intestinal cholesterol absorption; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling	Blood microparticle; Chylomicron; High-density lipoprotein particle

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Apolipoprotein A-IV OS=Bos taurus GN=APOA4 PE=2 SV=1	APOA4_BOVIN	15	36	51,05	Cholesterol binding; Cholesterol transporter activity; Phosphatidylcholine binding; Phosphatidylcholine-sterol O-acyltransferase activator activity	Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; High-density lipoprotein particle assembly; Lipoprotein metabolic process; Neuron projection regeneration; Phosphatidylcholine metabolic process; Phospholipid efflux; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of triglyceride catabolic process; Regulation of intestinal cholesterol absorption; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling	Blood microparticle; Chylomicron; High-density lipoprotein particle
Apolipoprotein A-IV OS=Bos taurus GN=APOA4 PE=4 SV=1	F1N3Q7_BOVIN	15	36	51,05	Antioxidant activity; Cholesterol transporter activity; Copper ion binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Cholesterol efflux; Cholesterol homeostasis; Cholesterol metabolic process; Hydrogen peroxide catabolic process; Innate immune response in mucosa; Leukocyte cell-cell adhesion; Lipoprotein metabolic process; Multicellular organismal lipid catabolic process; Negative regulation of plasma lipoprotein particle oxidation; Phosphatidylcholine metabolic processs; Phospholipid efflux; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of triglyceride catabolic process; Protein-lipid complex assembly; Regulation of intestinal cholesterol absorption; Removal of superoxide radicals; Response to lipid hydroperoxide; Response to stilbenoid; Reverse cholesterol transport; Very-low-density lipoprotein particle remodeling	Blood microparticle; Cell surface; Chylomicron; Extracellular exosome; High-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-IV OS=Bos taurus GN=APOA4 PE=4 SV=1	F1N3Q7_BOVIN	15	36	51,05	Antioxidant activity; Cholesterol transporter activity; Copper ion binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol O-acyltransferase activator activity	Cholesterol efflux; Cholesterol homeostasis; Cholesterol metabolic process; Hydrogen peroxide catabolic process; Innate immune response in mucosa; Leukocyte cell-cell adhesion; Lipoprotein metabolic process; Multicellular organismal lipid catabolic process; Negative regulation of plasma lipoprotein particle oxidation; Phosphatidylcholine metabolic process; Phospholipid efflux; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of triglyceride catabolic process; Protein-lipid complex assembly; Regulation of intestinal cholesterol absorption; Removal of superoxide radicals; Response to lipid hydroperoxide; Response to stilbenoid; Reverse cholesterol transport; Very-low-density lipoprotein particle remodeling	Blood microparticle; Cell surface; Chylomicron; Extracellular exosome; High-density lipoprotein particle; Very-low-density lipoprotein particle
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=1	G3X7A5_BOVIN	55	154	41,12	Endopeptidase inhibitor activity	Complement activation; Inflammatory response; Positive regulation of activation of membrane attack complex; Positive regulation of angiogenesis; Positive regulation of apoptotic cell; Positive regulation of glucose transport; Positive regulation of g-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Positive regulation of type iia hypersensitivity; Positive regulation of vascular endothelial growth factor production; Regulation of triglyceride biosynthetic process	Blood microparticle; Extracellular exosome
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=1	G3X7A5_BOVIN	54	154	40,40	Endopeptidase inhibitor activity	Complement activation; Inflammatory response; Positive regulation of activation of membrane attack complex; Positive regulation of angiogenesis; Positive regulation of apoptotic cell clearance; Positive regulation of glucose transport; Positive regulation of g-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Positive regulation of type iia hypersensitivity; Positive regulation of vascular endothelial growth factor production; Regulation of triglyceride biosynthetic process	Blood microparticle; Extracellular exosome
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=2	CO3_BOVIN	60	154	44,73	C5L2 anaphylatoxin chemotactic receptor binding; endopeptidase inhibitor activity	Complement activation, alternative pathway; Complement activation, classical pathway	Extracellular space
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=2	CO3_BOVIN	55	154	41,36	C5L2 anaphylatoxin chemotactic receptor binding; Endopeptidase inhibitor activity	Complement activation, alternative pathway; Complement activation, classical pathway; Fatty acid metabolic process; Inflammatory response; Positive regulation of glucose transport; Positive regulation of G-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Regulation of triglyceride biosynthetic process	Extracellular space

Continua Tabela 3

Complement component 3 OS=Bos taurus GN=C3 PE=2 SV=1	A0A0F6QNP7_BOVIN	54	156	40,94	Endopeptidase inhibitor activity	Complement activation; Inflammatory response	Extracellular space
Complement component 3d (Fragment) OS=Bos taurus PE=2 SV=1	Q693V9_BOVIN	12	35	50,50	--	--	Extracellular space
Complement component C9 OS=Bos taurus GN=C9 PE=2 SV=1	CO9_BOVIN	15	42	38,50	--	Complement activation, alternative pathway; Complement activation, classical pathway; Cytolysis	Blood microparticle; Cytoplasm; Extracellular exosome; Membrane attack complex
DCTN1 protein OS=Bos taurus GN=DCTN1 PE=2 SV=1	A5PKJ3_BOVIN	8	105	5,57	--	Microtubule-based transport	Dynactin complex
Endopin 2 OS=Bos taurus GN=SERPINA3-7 PE=2 SV=1	Q3SZQ8_BOVIN	15	29	39,81	--	--	Extracellular space
Endopin 2B OS=Bos taurus PE=2 SV=1	Q5J801_BOVIN	16	29	41,49	--	--	Extracellular space
FGB protein (Fragment) OS=Bos taurus GN=FGB PE=2 SV=1	A6QPX7_BOVIN	28	28	60,91	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
FGG protein OS=Bos taurus GN=FGG PE=1 SV=1	Q3SZZ9_BOVIN	18	35	54,71	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	FIBB_BOVIN	35	40	61,54	Glycoprotein binding	Adaptive immune response; Innate immune response; Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	F1MAV0_BOVIN	35	43	58,18	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Induction of bacterial agglutination; Negative regulation of endothelial cell apoptotic process negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	F1MGU7_BOVIN	18	36	50,56	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Protein secretion; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	FIBG_BOVIN	18	36	58,11	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex

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Fructose-bisphosphate aldolase OS=Bos taurus GN=ALDOA PE=1 SV=1	A6QLL8_BOVIN	10	31	39,01	Fructose binding; Fructose-bisphosphate aldolase activity; Poly(a) rna binding	Atp biosynthetic process; Fructose 1,6-bisphosphate metabolic process; Fructose metabolic process; Glycolytic process; Muscle cell cellular homeostasis; Regulation of cell shape; Striated muscle contraction	Actin cytoskeleton; Extracellular exosome; Extracellular space; Membrane; Nucleus
Genome polyprotein OS=Bovine viral diarrhea virus PE=4 SV=1	I1XC72_BVDV	25	310	4,19	ATP binding; ATP-dependent helicase activity; Cysteine-type endopeptidase activity; Ribonuclease T2 activity; RNA binding; RNA-directed RNA polymerase activity; Serine-type endopeptidase activity; Serine-type exopeptidase activity	Induction by virus of host autophagy; Viral entry into host cell; Viral protein processing; Viral RNA genome replication; Virion attachment to host cell	Host cell membrane; Integral component of membrane; Virion
Heat shock 27kDa protein 1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	E9RHW1_BOVIN	6	16	39,80	--	--	--
Heat shock 27kDa protein 1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	Q58DP7_BOVIN	5	13	40,65	--	--	--
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=1 SV=1	G3X7S2_BOVIN	5	13	40,91	--	--	--
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=1 SV=2	E1BEL7_BOVIN	6	17	39,41	Poly(A) RNA binding; Protein kinase C inhibitor activity	Intracellular signal transduction; Negative regulation of oxidative stress-induced intrinsic apoptotic signaling pathway; Platelet aggregation; Positive regulation of angiogenesis; Positive regulation of blood vessel endothelial cell migration; Positive regulation of endothelial cell chemotaxis by VEGF-activated vascular endothelial growth factor receptor signaling pathway; Positive regulation of interleukin-1 beta production; Positive regulation of tumor necrosis factor biosynthetic process; Regulation of I-kappab kinase/NF-kappab signaling; Response to virus; Retina homeostasis	Extracellular exosome; Extracellular space; Focal adhesion; Nucleus; Plasma membrane; Z disc
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	HSPB1_BOVIN	6	16	39,80	--	--	Cytoplasm; Nucleus; Spindle
Hemopexin OS=Bos taurus GN=HPX PE=2 SV=1	HEMO_BOVIN	21	35	49,46	Heme transporter activity; Metal ion binding	Cellular iron ion homeostasis; Heme metabolic process; Hemoglobin metabolic process; Positive regulation of humoral immune response mediated by circulating immunoglobulin; Positive regulation of immunoglobulin production; Positive regulation of interferon-gamma-mediated signaling pathway; Positive regulation of tyrosine phosphorylation of STAT1 protein	Blood microparticle; Cell; Extracellular exosome
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	B0JYP6_BOVIN	8	12	36,67	--	Immune response; Immunoglobulin production	Extracellular space
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	B0JYP6_BOVIN	8	12	36,67	--	--	--
Immunoglobulin light chain_ lambda gene cluster OS=Bos taurus GN=IGL@ PE=2 SV=1	Q1RMN8_BOVIN	7	13	44,44	--	--	--

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Leucine-rich alpha-2-glycoprotein 1 OS=Bos taurus GN=LRG1 PE=2 SV=1	Q2KIF2_BOVIN	13	21	42,20	--	Brown fat cell differentiation; Positive regulation of angiogenesis; Positive regulation of endothelial cell proliferation; Positive regulation of transforming growth factor beta receptor signaling pathway	Extracellular exosome; Extracellular space
Nexin (Fragment) OS=Bos taurus PE=2 SV=1	Q9N1C4_BOVIN	8	12	45,09	Serine-type endopeptidase inhibitor activity	Negative regulation of angiogenesis; Negative regulation of endopeptidase activity; Negative regulation of epithelial cell proliferation involved in prostate gland development; Positive regulation of neurogenesis	Extracellular exosome; Extracellular matrix; Extracellular region; Extracellular space; Melanosome; Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome; Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; Hfe-transferrin receptor complex; Late endosome; Perinuclear region of cytoplasm; Recycling endosome
Pigment epithelium-derived factor OS=Bos taurus GN=SERPINF1 PE=1 SV=1	PEDF_BOVIN	18	30	56,49	Serine-type endopeptidase inhibitor activity	Negative regulation of angiogenesis; Negative regulation of endopeptidase activity; Negative regulation of epithelial cell proliferation involved in prostate gland development; Positive regulation of neurogenesis	Extracellular exosome; Extracellular matrix; Extracellular region; Extracellular space
Putative uncharacterized protein OS=Bos taurus PE=2 SV=1	A6QM09_BOVIN	8	16	62,07	--	--	--
Putative uncharacterized protein OS=Bos taurus PE=2 SV=1(*)	A5PK72_BOVIN	6	12	38,56	--	--	--
Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	23	75	42,05	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated endocytosis; Retina homeostasi	Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome; Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; Hfe-transferrin receptor complex; Late endosome; Perinuclear region of cytoplasm; Recycling endosome

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Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	56	75	67,76	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell positive regulation of receptor-mediated endocytosis; Retina homeostasis	Extracellular exosome; Extracellular matrix; Extracellular region; Extracellular space; Melanosome; Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome; Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; Hfe-transferrin receptor complex; Late endosome; Perinuclear region of cytoplas; Recycling endosome
Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	23	75	42,05	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated endocytosis; Retina homeostasis	Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome; Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; Hfe-transferrin receptor complex; Late endosome; Perinuclear region of cytoplasm; Recycling endosome
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	51	76	63,49	Ferric iron binding; Ferric iron transmembrane transporter activity	Cellular iron ion homeostasis	Cell; Extracellular space
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	27	76	48,30	Ferric iron binding; Ferric iron transmembrane transporter activity Source: interpro	Cellular iron ion homeostasis Source: interpro	Cell; Extracellular space
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	27	76	48,30	Ferric iron binding Ferric iron transmembrane transporter activity s	Cellular iron ion homeostasis	Cell Extracellular space
Serpin A3-1 OS=Bos taurus GN=SERPINA3-1 PE=1 SV=3	SPA31_BOVIN	18	28	42,34	Cysteine-type endopeptidase inhibitor activity; Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasm; Cytoplasmic vesicle; Extracellular space

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Serpin A3-2 OS=Bos taurus GN=SERPINA3-2 PE=3 SV=1	SPA32_BOVIN	19	28	45,26	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-5 OS=Bos taurus GN=SERPINA3-5 PE=3 SV=1	SPA35_BOVIN	17	28	39,90	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-7 OS=Bos taurus GN=SERPINA3-7 PE=1 SV=1	A0A0A0MP92_BOVIN	16	29	41,49	--	--	Extracellular space
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=2 SV=1	SPA38_BOVIN	11	34	37,80	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
SERPIND1 protein OS=Bos taurus GN=SERPIND1 PE=2 SV=1	A6QPP2_BOVIN	16	35	43,95	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular space; Extracellular exosome; Extracellular space
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	45	59	66,89	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Extracellular space; Protein complex
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	45	59	66,89	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding; Toxic substance binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Extracellular space; Protein complex
Similar to alpha-tubulin isoform 1 (Fragment) OS=Bos taurus PE=2 SV=1	Q862L2_BOVIN	2	6	35,35	GTPase activity; GTP binding	Microtubule-based process	Microtubule
Transthyretin OS=Bos taurus GN=TTR PE=1 SV=1	TTHY_BOVIN	5	7	55,10	Thyroid hormone binding	Retinol metabolic process; Thyroid hormone transport	Extracellular exosome; Extracellular space
TUBB2A protein OS=Bos taurus GN=TUBB2A PE=2 SV=1	Q148E2_BOVIN	8	19	38,18	Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Tubulin beta-2B chain OS=Bos taurus GN=TUBB2B PE=1 SV=2	TBB2B_BOVIN	12	30	37,30	Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process; Neuron migration	Cytoplasm; Microtubule; Nucleus
Tubulin beta-2B chain OS=Bos taurus GN=TUBB2B PE=3 SV=1	G3N1W7_BOVIN	8	19	38,18	GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Tubulin beta-4B chain OS=Bos taurus GN=TUBB4B PE=2 SV=1	TBB4B_BOVIN	13	30	35,96	Double-stranded RNA binding; GTPase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Extracellular exosome; Microtubule; Myelin sheath; Nucleus

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Tubulin beta-5 chain OS=Bos taurus GN=TUBB5 PE=2 SV=1	TBB5_BOVIN	17	30	45,95	Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cell body; Cytoplasmic ribonucleoprotein granule; Extracellular exosome; Microtubule; Nuclear envelope lumen
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1 (**)	G3N0V0_BOVIN	13	25	48,16	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment; Phagocytosis, recognition	Blood microparticle; External side of plasma membrane; Immunoglobulin complex, circulating
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1 (**)	G5E604_BOVIN	3	6	36,45	--	Immune response; Immunoglobulin production	Extracellular space
Uncharacterized protein OS=Bos taurus GN=DCTN1 PE=4 SV=1 (**)	F1MIC9_BOVIN	11	106	5,57	--	Melanosome transport; Microtubule-based transport; Retrograde transport, endosome to Golgi	Cell leading edge; Centrosome; Dynactin complex; Kinetochore; Microtubule; Retromer complex; Spindle pole
Uncharacterized protein OS=Bos taurus GN=LOC784932 PE=3 SV=1 (**)	A0A0A0MPA0_BOVIN	12	31	36,69	--	--	Extracellular space
Uncharacterized protein OS=Bos taurus GN=SERPINA3 PE=3 SV=1 (**)	G8JKW7_BOVIN	16	29	46,36	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular space
Uncharacterized protein OS=Bos taurus GN=SERPINE2 PE=3 SV=2 (**)	F1MZX2_BOVIN	18	28	39,04	Heparin binding serine-type endopeptidase inhibitor activity	Blood coagulation; Cerebellar granular layer morphogenesis; Detection of mechanical stimulus involved in sensory perception; Innervation; Long-term synaptic potentiation; Mating plug formation; Negative regulation of cell growth; Negative regulation of cell proliferation; Negative regulation of endopeptidase activity; Negative regulation of phosphatidylinositol 3-kinase signaling; Negative regulation of plasminogen activation; Negative regulation of platelet aggregation; Negative regulation of smoothened signaling pathway; Negative regulation of sodium ion; Positive regulation of astrocyte differentiation; Regulation of synaptic transmission, glutamatergic; Regulation of timing of cell differentiation; Seminal vesicle epithelium development	Cytosol; Extracellular matrix; Extracellular space; Extracellular vesicle; Extrinsic component of external side of plasma membrane; Neuromuscular junction; Platelet alpha granule
Uncharacterized protein OS=Bos taurus GN=TUBB2A PE=1 SV=1 (**)	G3X7R7_BOVIN	8	19	38,18	Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; Microtubule
Uncharacterized protein OS=Bos taurus GN=TUBB2A PE=1 SV=1 (**)	E1BJB1_BOVIN	12	30	37,30	Gtpase activity; GTP binding; Structural constituent of cytoskeleton	Microtubule-based process	Cytoplasm; xtracellular exosome; Microtubule; Nucleus
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MZ96_BOVIN	8	13	36,67	--	B cell differentiation	--
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MH40_BOVIN	6	13	35,83	--	Immune response; Immunoglobulin production	Extracellular space

Continua Tabela 3

Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MZ96_BOVIN	8	13	36,67	--	B cell differentiation	--
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MH40_BOVIN	8	13	36,67	--	Immune response; Immunoglobulin production	Extracellular space
Uncharacterized protein OS=Bos taurus PE=4 SV=2 (**)	F1MLW8_BOVIN	4	10	38,20	--	Immune response; Immunoglobulin production	Extracellular space
Vitamin D binding protein OS=Bos taurus PE=2 SV=1 (**)	I7CT57_BOVIN	14	44	40,08	Vitamin D binding; Vitamin transporter activity	Extracellular space	--
Vitamin D-binding protein OS=Bos taurus GN=GC PE=1 SV=2 (**)	F1N5M2_BOVIN	14	44	40,08	Calcidiol binding; Vitamin transporter activity	Vitamin D metabolic process	Blood microparticle; Extracellular exosome
Vitamin D-binding protein OS=Bos taurus GN=GC PE=2 SV=1 (**)	VTDB_BOVIN	12	44	37,97	Vitamin D binding; Vitamin transporter activity	--	Extracellular space Source: interpro

(*) Putative uncharacterized protein: means that this protein may be identified by computer, and the function is still unknown. This protein is not homologous to any well characterised proteins and thus its function cannot be predicted. Putative means that it was only predicted based on ORF (open reading frame) and promoter sequence.

(**) Uncharacterized protein: Proteins which are NOT conserved or with no known or predicted function orcharacteristics (http://www.uniprot.org/docs/nameprot)

Tabela 4. Proteínas identificadas na espectrometria de massas e suas respectivas ontologias gênicas (função molecular, processo biológico e componente celular) das amostras do grupo de folículos transicionais, de ovários sem corpo lúteo de vacas vazias

Descrição proteína	ID Acesso	*Match*	Nº Peptídeos	% Cobertura sequência	Ontologia gênica		
					Função molecular	Processo biológico	Componente celular
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	39	59	62,27	--	Transport	Extracellular space
Alpha-1B-glycoprotein OS=Bos taurus GN=A1BG PE=1 SV=1	A1BG_BOVIN	17	24	56,26	--	--	Blood microparticlesource; Extracellular exosome
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=1	F1MSZ6_BOVIN	21	38	45,38	Heparin binding; Serine-type endopeptidase inhibitor activity	Regulation of blood coagulation, intrinsic pathway	Blood microparticles; Extracellular exosome
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=2	ANT3_BOVIN	21	38	45,38	Heparin binding; Serine-type endopeptidase inhibitor activity	Blood coagulationsource negative regulation of endopeptidase activity; Regulation of blood coagulation, intrinsic pathway	Extracellular space
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	23	32	64,15	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	23	32	64,15	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol O-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of Rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle

Continua Tabela 4

Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	14	32	49,06	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import Endothelial cell proliferati; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterificationl; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activitysource; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading;Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	23	32	64,15	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol O-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase; Positive regulation of Rho protein signal; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	10	23	45,67	Lipid binding Source: interpro	Lipid transport; Lipoprotein metabolic process	Extracellular region
Apolipoprotein A-IV OS=Bos taurus GN=APOA4 PE=2 SV=1	APOA4_BOVIN	10	36	36,58	Cholesterol binding; Cholesterol transporter activity; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; High-density lipoprotein particle assembly; Lipoprotein metabolic process; Neuron projection regeneration; Phosphatidylcholine metabolic process; Phospholipid efflux; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of triglyceride catabolic process; Regulation of intestinal cholesterol absorption; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling	Blood microparticle; Chylomicronsource; High-density lipoprotein particle

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Apolipoprotein A-IV OS=Bos taurus GN=APOA4 PE=4 SV=1	F1N3Q7_BOVIN	10	36	36,58	Antioxidant activity; Cholesterol transporter activity; Copper ion binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Cholesterol efflux; Cholesterol homeostasis; Cholesterol metabolic process; Hydrogen peroxide catabolic process; Innate immune response in mucosa; Leukocyte cell-cell adhesion; Lipoprotein metabolic process; Multicellular organismal lipid catabolic process; Negative regulation of plasma lipoprotein particle oxidation; Phosphatidylcholine metabolic process; Phospholipid efflux; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of triglyceride catabolic process; Protein-lipid complex assembly; Regulation of intestinal cholesterol absorption; Removal of superoxide radicals; Response to lipid hydroperoxide; Response to stilbenoid; Reverse cholesterol transport; Very-low-density lipoprotein particle remodeling	Blood microparticle; Cell surface; Chylomicron; Extracellular exosome; High-density lipoprotein particle; Very-low-density lipoprotein particle
FGB protein (Fragment) OS=Bos taurus GN=FGB PE=2 SV=1	A6QPX7_BOVIN	24	28	58,48	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
FGG protein OS=Bos taurus GN=FGG PE=1 SV=1	Q3SZZ9_BOVIN	14	35	38,85	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	FIBB_BOVIN	30	40	62,18	Glycoprotein binding	Adaptive immune response; Innate immune response; Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	F1MAV0_BOVIN	29	43	54,55	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Induction of bacterial agglutination; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	F1MGU7_BOVIN	14	36	38,15	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Protein secretion; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	FIBG_BOVIN	12	36	35,14	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Heat shock 27kDa protein 1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	Q58DP7_BOVIN	4	13	35,48	--	--	--
Heat shock 27kDa protein 1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	E9RHW1_BOVIN	5	16	35,82	--	--	--
Heat shock 27kDa protein 1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	Q58DP7_BOVIN	4	13	35,48	--	--	--

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Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=1 SV=1	G3X7S2_BOVIN	4	13	35,71	--	--	--
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=1 SV=2	E1BEL7_BOVIN	5	17	35,47	Poly(A) RNA binding; Protein kinase C inhibitor activity Source: Ensembl	Intracellular signal transduction; Negative regulation of oxidative stress-induced intrinsic apoptotic signaling pathway; Platelet aggregation; Positive regulation of angiogenesis; Positive regulation of blood vessel endothelial cell migration; Positive regulation of endothelial cell chemotaxis by VEGF-activated vascular endothelial growth factor receptor signaling pathway; Positive regulation of interleukin-1 beta production; Positive regulation of tumor necrosis factor biosynthetic process; Regulation of I-kappab kinase/NF-kappab signaling; Response to virus; Retina homeostasis	Extracellular exosome; Extracellular space; Focal adhesion; Nucleus; Plasma membrane; Z disc
Heat shock protein beta-1 OS=Bos taurus GN=HSPB1 PE=2 SV=1	HSPB1_BOVIN	5	16	35,82	--	--	Cytoplasm; Nucleus; Spindle
Hemopexin OS=Bos taurus GN=HPX PE=2 SV=1	HEMO_BOVIN	17	35	45,53	Heme transporter activitysource: interpro; Metal ion binding	Cellular iron ion homeostasis; Heme metabolic process; Hemoglobin metabolic process; Positive regulation of humoral immune response mediated by circulating immunoglobulin; Positive regulation of immunoglobulin production; Positive regulation of interferon-gamma-mediated signaling pathway; Positive regulation of tyrosine phosphorylation of Stat1 protein	Blood microparticle; Cell; Extracellular exosome
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	Q05B55_BOVIN	6	13	35,83	--	--	--
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	B0JYP6_BOVIN	6	12	35,83	--	--	--
Putative uncharacterized protein OS=Bos taurus PE=2 SV=1 (*)	A5PK72_BOVIN	6	12	38,56	--	--	--
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	47	76	62,50	Ferric iron transmembrane transporter activity; Ferrous iron binding; Ferric iron binding; Ferric iron transmembrane transporter activity	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated retina homeostasis; Cellular iron ion homeostasis	Extracellular space; Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome; Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; HFE-transferrin receptor complex; Late endosome; Perinuclear region of cytoplasm; Recycling endosome; Cell; Extracellular space
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=2 SV=1	SPA38_BOVIN	14	34	44,26	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule – SubCell; Cytoplasmic vesicle; Extracellular space

Continua Tabela 4

Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=3 SV=1	A0A0A0MP89_BOVIN	13	34	39,95	--	--	Extracellular space
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	40	59	64,42	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding; Toxic substance binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Extracellular space; Protein complex
Similar to 7O kDa heat shock cognate protein (Fragment) OS=Bos taurus PE=2 SV=1	Q861V2_BOVIN	2	6	41,79	ATP binding	--	--
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1 (**)	G3N0V0_BOVIN	10	25	45,09	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment; Phagocytosis, recognition; Positive regulation of b cell activation	Blood microparticle; Immunoglobulin complex, circulating
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MZ96_BOVIN	6	13	35,83	--	B cell differentiation	--
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MH40_BOVIN	6	13	35,83	--	Immune response; Immunoglobulin production	Extracellular space

(*) Putative uncharacterized protein: means that this protein may be identified by computer, and the function is still unknown. This protein is not homologous to any well characterised proteins and thus its function cannot be predicted. Putative means that it was only predicted based on ORF (open reading frame) and promoter sequence.
(**) Uncharacterized protein: Proteins which are NOT conserved or with no known or predicted function orcharacteristics (http://www.uniprot.org/docs/nameprot)

Tabela 5. Proteínas identificadas na espectrometria de massas e suas respectivas ontologias gênicas (função molecular, processo biológico e componente celular) das amostras do grupo de folículos atrésicos, de ovários com corpo lúteo de vacas vazias

Descrição proteína	ID Acesso	*Match*	Nº Peptídeos	% Cobertura sequência	Ontologia gênica		
					Função molecular	Processo biológico	Componente celular
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	33	59	56,34	--	Transport	Extracellular space
ALB protein OS=Bos taurus GN=ALB PE=2 SV=1	B0JYQ0_BOVIN	40	59	62,27	--	Transport	Extracellular space
Alpha 1-antichymotrypsin (Fragment) OS=Bos taurus GN=alpha 1-antichymotrypsin/ ACT PE=2 SV=1	Q28922_BOVIN	3	7	73,12	--	--	Extracellular space
Alpha-1-antiproteinase OS=Bos taurus GN=SERPINA1 PE=1 SV=1	A1AT_BOVIN	15	28	42,79	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Endoplasmic reticulum extracellular exosome; Extracellular space
Alpha-1B-glycoprotein OS=Bos taurus GN=A1BG PE=1 SV=1	A1BG_BOVIN	19	24	58,05	--	--	Blood microparticle
Alpha-1B-glycoprotein OS=Bos taurus GN=A1BG PE=1 SV=1 A2AP_BOVIN	A1BG_BOVIN	19	24	58,05	Serine-type endopeptidase inhibitor activity	Acute-phase response; Blood vessel morphogenesis; Collagen fibril organization; Negative regulation of endopeptidase activity; Negative regulation of fibrinolysis; Negative regulation of plasminogen activation; Positive regulation of cell differentiation; Positive regulation of collagen biosynthetic process; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of JNK cascade; Positive regulation of smooth muscle cell proliferation; Positive regulation of stress fiber assembly; Positive regulation of transcription from rna polymerase II promoter; Positive regulation of transforming growth factor beta production; Regulation of blood vessel size by renin-angiotensin	Blood microparticle; Extracellular exosome; Blood microparticle; Cell surface; Extracellular exosome; Extracellular space; Fibrinogen complex
Alpha-2-HS-glycoprotein OS=Bos taurus GN=AHSG PE=1 SV=2	FETUA_BOVIN	6	19	35,93	Serine-type endopeptidase inhibitor activity; Endopeptidase inhibitor activity	Acute-phase response; Negative regulation of biomineral tissue development; Negative regulation of bone mineralization; Negative regulation of endopeptidase activity; Ossification; Positive regulation of phagocytosis; Regulation of inflammatory response	Blood microparticle; Extracellular exosome; Extracellular matrix; Extracellular membrane-bounded organelle; Plasma membrane; Vesicle
Alpha-2-macroglobulin OS=Bos taurus GN=A2M PE=1 SV=2	A2MG_BOVIN	55	108	57,22	Serine-type endopeptidase inhibitor activity	Negative regulation of complement activation, lectin pathway; Stem cell differentiation	Blood microparticle ; Extracellular exosome
Alpha-2-macroglobulin OS=Bos taurus GN=A2M PE=2 SV=1	R9QSM8_BOVIN	44	82	55,51	Endopeptidase inhibitor activity	--	Extracellular space

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Alpha-2-macroglobulin variant 1 OS=Bos taurus GN=A2M PE=2 SV=1	K4JBR5_BOVIN	29	73	46,13	Endopeptidase inhibitor activity	--	Extracellular region
Alpha-2-macroglobulin variant 10 OS=Bos taurus GN=A2M PE=2 SV=1	K4JDS3_BOVIN	15	34	51,37	--	--	Extracellular space
Alpha-2-macroglobulin variant 11 OS=Bos taurus GN=A2M PE=2 SV=1	K4JBS4_BOVIN	12	27	53,69	Endopeptidase inhibitor activity	--	--
Alpha-2-macroglobulin variant 12 OS=Bos taurus GN=A2M PE=2 SV=1	K4JR81_BOVIN	18	38	48,29	--	--	Extracellular space
Alpha-2-macroglobulin variant 14 OS=Bos taurus GN=A2M PE=2 SV=1	K4JBA5_BOVIN	4	11	41,06	--	--	--
Alpha-2-macroglobulin variant 15 OS=Bos taurus GN=A2M PE=2 SV=1	K4JDS8_BOVIN	6	17	41,12	Endopeptidase inhibitor activity	--	--
Alpha-2-macroglobulin variant 17 OS=Bos taurus GN=A2M PE=2 SV=1	K4JR84_BOVIN	4	9	48,44	--	--	--
Alpha-2-macroglobulin variant 18 OS=Bos taurus GN=A2M PE=2 SV=1	K4JF13_BOVIN	10	29	41,03	--	--	Extracellular space
Alpha-2-macroglobulin variant 2 OS=Bos taurus GN=A2M PE=2 SV=1	K4JR71_BOVIN	10	20	56,32	Endopeptidase inhibitor activity	--	--
Alpha-2-macroglobulin variant 20 OS=Bos taurus GN=A2M PE=2 SV=1	K4JDT2_BOVIN	27	61	47,56	Endopeptidase inhibitor activity	--	--
Alpha-2-macroglobulin variant 21 OS=Bos taurus GN=A2M PE=2 SV=1	K4JBT0_BOVIN	8	16	55,48	Endopeptidase inhibitor activity	--	--
Alpha-2-macroglobulin variant 22 OS=Bos taurus GN=A2M PE=2 SV=1	K4JR88_BOVIN	22	46	52,24	Endopeptidase inhibitor activity	--	--
Alpha-2-macroglobulin variant 23 OS=Bos taurus GN=A2M PE=2 SV=1	K4JF16_BOVIN	28	64	48,23	Endopeptidase inhibitor activity	--	Extracellular region
Alpha-2-macroglobulin variant 4 OS=Bos taurus GN=A2M PE=2 SV=1	K4JB97_BOVIN	9	27	42,30	--	--	Extracellular space
Alpha-2-macroglobulin variant 5 OS=Bos taurus GN=A2M PE=2 SV=1	K4JDR8_BOVIN	11	30	45,10	--	--	Extracellular space

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Alpha-2-macroglobulin variant 6 OS=Bos taurus GN=A2M PE=2 SV=1	K4JBR9_BOVIN	14	32	53,52	Endopeptidase inhibitor activity	--	Extracellular region
Alpha-2-macroglobulin variant 9 OS=Bos taurus GN=A2M PE=2 SV=1	K4JBA2_BOVIN	11	29	46,35	--	--	Extracellular space
Angiotensinogen OS=Bos taurus GN=AGT PE=2 SV=1	Q3SZH5_BOVIN	10	23	36,56	Sodium channel regulator activity	Activation of nf-kappab-inducing kinase activity; Angiotensin mediated vasoconstriction involved in regulation of systemic arterial blood pressure; Astrocyte activation; Blood vessel development; Brain renin-angiotensin system; Branching involved in ureteric bud morphogenesis; Cell-matrix adhesion; Drinking behavior; Establishment of blood-nerve barrier; Excretion; Extracellular matrix organization; G-protein coupled receptor signaling pathway; Hormone metabolic process; Negative regulation of cell proliferation; Negative regulation of neuron apoptotic process; Negative regulation of neurotrophin trk receptor signaling pathway; Peristalsis; Positive regulation of activation of jak2 kinase activity; Positive regulation of branching involved in ureteric bud morphogenesis; Positive regulation of cholesterol esterification; Positive regulation of endothelial cell migration; Positive regulation of epidermal growth factor receptor signaling pathway; Positive regulation of extrinsic apoptotic signaling pathway; Positive regulation of fatty acid biosynthetic process; Positive regulation of gap junction assembly; Positive regulation of mapk cascade; Positive regulation of membrane hyperpolarization; Positive regulation of multicellular organism growth; Positive regulation of organ growth; Response to cold; Response to salt stress; Smooth muscle cell differentiation; Smooth muscle cell proliferation	Blood microparticle; Extracellular exosome; Intracellular; Ovarian follicle rupture; Positive regulation of peptidyl-serine phosphorylation; Positive regulation of phosphatidylinositol 3-kinase signaling; Positive regulation of protein kinase c activity; Positive regulation of protein tyrosine kinase activity; Positive regulation of transcription, dna-templated; Regulation of cardiac conduction; Regulation of extracellular matrix assembly; Regulation of inflammatory response; Regulation of renal output by angiotensin; Renal response to blood flow involved in circulatory renin-angiotensin regulation of systemic arterial blood pressure; Renin-angiotensin regulation of aldosterone production
ANT3_BOVIN	Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=2	29	38	62,58	Heparin binding; Serine-type endopeptidase inhibitor activity	Blood coagulation; Negative regulation of endopeptidase activity; Regulation of blood coagulation, intrinsic pathway	Extracellular space
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=1	F1MSZ6_BOVIN	14	38	44,30	Heparin binding	Regulation of blood coagulation, intrinsic pathway	Blood microparticle
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=2	ANT3_BOVIN	29	38	62,58	Serine-type endopeptidase inhibitor activity; Heparin binding; Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity; Blood coagulatio	Extracellular exosome; Extracellular space

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	32	32	75,47	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Protein oxidation; Protein stabilization; Regulation of CDC42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis; Vitamin transport	Blood microparticle;Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle
Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	V6F9A2_BOVIN	22	32	73,21	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride homeostasis

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Continua Tabela 5

Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	32	32	75,47	Beta-amyloid binding; Chemorepellent activity cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; High-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling; Vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	22	32	73,21	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding; Phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration source; Peptidyl-methionine modification; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Vitamin transport	Blood microparticle; Chylomicron; Endocytic vesicle; Extracellular exosome; High-density lipoprotein particle; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle high-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Phosphatidylcholine biosynthetic process; Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling

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Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=3	APOA1_BOVIN	22	32	73,21	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity high-density lipoprotein particle binding; High-density lipoprotein particle receptor binding; Phosphatidylcholine binding phosphatidylcholine-sterol o-acyltransferase activator activity	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Lipoprotein metabolic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Neuron projection regeneration; Peptidyl-methionine modification; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Regulation of protein phosphorylation; Vitamin transport	Blood microparticle; Chylomicron Endocytic vesicle: Extracellular exosome High-density lipoprotein particle Spherical high-density lipoprotein particle Very-low-density lipoprotein particle High-density lipoprotein particle assembly Integrin-mediated signaling pathway Phosphatidylcholine biosynthetic process Phosphatidylcholine metabolic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of fatty acid biosynthetic process; Positive regulation of lipoprotein lipase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Positive regulation of triglyceride catabolic process; Reverse cholesterol transport; Triglyceride catabolic process; Triglyceride homeostasis; Very-low-density lipoprotein particle remodeling
Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	7	23	35,58	Lipid binding	Lipid transport; Lipoprotein metabolic process	Extracellular region source
Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	8	23	40,38	Lipid binding	Lipid transport; Lipoprotein metabolic process	Extracellular region

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Apolipoprotein A-I-like OS=Bos taurus GN=LOC100297695 PE=4 SV=1	V6F869_BOVIN	8	23	40,38	Lipid binding	Lipid transport; Lipoprotein metabolic process source: interpro	Extracellular region
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=1	G3X7A5_BOVIN	75	154	56,65	Endopeptidase inhibitor activity	Complement activation; Inflammatory response; Positive regulation of activation of membrane attack complex; Positive regulation of angiogenesis; Positive regulation of apoptotic cell clearance; Positive regulation of glucose transport; Positive regulation of g-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Positive regulation of type iia hypersensitivity; Positive regulation of vascular endothelial growth factor production; Regulation of triglyceride biosynthetic process	Blood microparticle; Extracellular exosome
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=1	G3X7A5_BOVIN	53	154	42,99	Endopeptidase inhibitor activity	Complement activation; Inflammatory response; Positive regulation of activation of membrane attack complex; Positive regulation of angiogenesis; Positive regulation of apoptotic cell clearance; Positive regulation of glucose transport; Positive regulation of g-protein coupled receptor protein signaling pathway	Blood microparticle; Extracellular exosome; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Positive regulation of type IIa hypersensitivity; Positive regulation of vascular endothelial growth factor production; Regulation of triglyceride biosynthetic process
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=2	CO3_BOVIN	56	154	46,24	C5L2 anaphylatoxin chemotactic receptor binding; Endopeptidase inhibitor activity	Complement activation, alternative pathway; Complement activation, classical pathway; Fatty acid metabolic process; Inflammatory response; Positive regulation of glucose transport; Positive regulation of G-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Regulation of triglyceride biosynthetic process	Extracellular space
Complement C3 OS=Bos taurus GN=C3 PE=1 SV=2	CO3_BOVIN	56	154	46,24	C5L2 anaphylatoxin chemotactic receptor binding; Endopeptidase inhibitor activity	Complement activation, alternative pathway; Complement activation, classical pathway; Fatty acid metabolic process; Inflammatory response; Positive regulation of glucose transport	Extracellular space; Positive regulation of G-protein coupled receptor protein signaling pathway; Positive regulation of lipid storage; Positive regulation of protein phosphorylation; Regulation of triglyceride biosynthetic process
Complement component 3 (Fragment) OS=Bos taurus GN=c3 PE=2 SV=1	Q6KDN5_BOVIN	3	5	66,67	--	--	Extracellular region
Complement component 3 OS=Bos taurus GN=C3 PE=2 SV=1	A0A0F6QNP7_BOVIN	75	156	57,44	Endopeptidase inhibitor activity	Complement activation; Inflammatory response	Extracellular region

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Complement component 3 OS=Bos taurus GN=C3 PE=2 SV=1	A0A0F6QNP7_BOVI	52	156	41,96	--	Complement activation; Inflammatory response	Extracellular space
Complement component 3d (Fragment) OS=Bos taurus PE=2 SV=1	Q693V9_BOVIN	14	35	58,75	--	--	Extracellular space
Complement component 8_ alpha polypeptide (Fragment) OS=Bos taurus GN=C8A PE=2 SV=1	Q1JPD0_BOVIN	6	24	40,97	--	Immune response	Membrane attack complex
Complement component 8_ alpha polypeptide (Fragment) OS=Bos taurus GN=C8A PE=2 SV=1	Q1JPD0_BOVIN	6	24	40,97	Immune response	--	Membrane attack complex source: interpro
Complement component 8_ alpha polypeptide OS=Bos taurus GN=C8A PE=2 SV=1	Q2KIH5_BOVIN	15	44	40,24	--	Immune response	Membrane attack complex
Complement component C9 OS=Bos taurus GN=C9 PE=2 SV=1	CO9_BOVIN	19	42	35,77	--	Complement activation, alternative pathway; Complement activation, classical pathway; Cytolysis	Blood microparticle; Cytoplasm; Extracellular exosome; Membrane attack complex
Complement factor H OS=Bos taurus GN=CFH PE=1 SV=3	CFAH_BOVIN	44	91	52,10	--	Complement activation, alternative pathway	Extracellular region
Corticosteroid-binding globulin OS=Bos taurus GN=SERPINA6 PE=3 SV=1	CBG_BOVIN	8	28	37,87	Serine-type endopeptidase inhibitor activity; Steroid binding	Glucocorticoid metabolic process; Negative regulation of endopeptidase activity; Transport	Extracellular exosome; Extracellular space
Endopin 2 OS=Bos taurus GN=SERPINA3-7 PE=2 SV=1	Q3SZQ8_BOVIN	12	29	35,73	--	--	Extracellular space
Endopin 2 OS=Bos taurus GN=SERPINA3-7 PE=2 SV=1	Q3SZQ8_BOVIN	15	29	41,25	--	--	Extracellular space
Antithrombin-III OS=Bos taurus GN=SERPINC1 PE=1 SV=1	F1MSZ6_BOVIN	29	38	62,58	Heparin binding; Serine-type endopeptidase inhibitor activity	Regulation of blood coagulation, intrinsic pathway	Blood microparticle; Extracellular exosome

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FGB protein (Fragment) OS=Bos taurus GN=FGB PE=2 SV=1	A6QPX7_BOVIN	15	28	52,42	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
FGB protein (Fragment) OS=Bos taurus GN=FGB PE=2 SV=1	A6QPX7_BOVIN	27	28	59,70	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
FGG protein OS=Bos taurus GN=FGG PE=1 SV=1	Q3SZZ9_BOVIN	16	35	48,51	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
FGG protein OS=Bos taurus GN=FGG PE=1 SV=1	Q3SZZ9_BOVIN	14	35	39,08	--	Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	F1MAV0_BOVIN	20	43	50,71	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Induction of bacterial agglutination; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion source: ensemble; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	FIBB_BOVIN	34	40	61,97	Glycoprotein binding	Adaptive immune response; Innate immune response; Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	F1MAV0_BOVIN	35	43	58,59	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Induction of bacterial agglutination; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Response to calcium ion
Fibrinogen beta chain OS=Bos taurus GN=FGB PE=1 SV=2	FIBB_BOVIN	34	40	61,97	Glycoprotein binding	Adaptive immune response; Innate immune response; Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex

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Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	F1MGU7_BOVIN	15	36	47,63	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization; Protein secretion; Response to calcium ion; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	FIBG_BOVIN	14	36	39,19	--	Platelet activation ; Protein polymerization; Signal transduction	Fibrinogen complex
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	F1MGU7_BOVIN	13	36	35,67	Structural molecule activity	Blood coagulation, fibrin clot formation; Cell-matrix adhesion; Fibrinolysis; Negative regulation of endothelial cell apoptotic process; Negative regulation of extrinsic apoptotic signaling pathway via death domain receptors; Plasminogen activation; Platelet aggregation; Positive regulation of ERK1 and ERK2 cascade; Positive regulation of exocytosis; Positive regulation of heterotypic cell-cell adhesion; Protein secretion; Response to calcium ion source; Signal transduction	Blood microparticle; Cell cortex; External side of plasma membrane; Extracellular exosome; Fibrinogen complex; Platelet alpha granule; Positive regulation of peptide hormone secretion; Positive regulation of protein secretion; Positive regulation of vasoconstriction; Protein polymerization
Fibrinogen gamma-B chain OS=Bos taurus GN=FGG PE=1 SV=1	FIBG_BOVIN	14	36	39,19		Platelet activation; Protein polymerization; Signal transduction	Fibrinogen complex
Hemopexin OS=Bos taurus GN=HPX PE=2 SV=1	HEMO_BOVIN	15	35	49,24	Heme transporter activity; Metal ion binding	Cellular iron ion homeostasis; Heme metabolic process; Hemoglobin metabolic process; Positive regulation of humoral immune response mediated by circulating immunoglobulin; Positive regulation of immunoglobulin production; Positive regulation of interferon-gamma-mediated signaling pathway; Positive regulation of tyrosine phosphorylation of stat1 protein	Blood microparticle; Cell; Extracellular exosome
Hemopexin OS=Bos taurus GN=HPX PE=2 SV=1	HEMO_BOVIN	22	35	49,67	Heme transporter activity; Metal ion binding	Cellular iron ion homeostasis; Heme metabolic process; Hemoglobin metabolic process; Positive regulation of humoral immune response mediated by circulating immunoglobulin; Positive regulation of immunoglobulin production source: ensembl	Blood microparticle; Cell; Extracellular exosome; Positive regulation of interferon-gamma-mediated signaling pathway; Positive regulation of tyrosine phosphorylation of stat1 protein
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	B0JYP6_BOVIN	7	12	36,67	--	--	--
IGK protein OS=Bos taurus GN=IGK PE=2 SV=1	Q05B55_BOVIN	7	13	36,67	--	--	--

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Inter-alpha (Globulin) inhibitor H4 (Plasma Kallikrein-sensitive glycoprotein) OS=Bos taurus GN=ITIH4 PE=2 SV=1	Q5EA67_BOVIN	24	62	40,28	Serine-type endopeptidase inhibitor activity	Hyaluronan metabolic process	--
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Bos taurus GN=ITIH4 PE=1 SV=1	ITIH4_BOVIN	26	62	42,03	Serine-type endopeptidase inhibitor activity	Acute-phase response; Hyaluronan metabolic process	Extracellular region
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Bos taurus GN=ITIH4 PE=1 SV=2	F1MMD7_BOVIN	24	62	40,28	Serine-type endopeptidase inhibitor activity	Acute-phase response; Hyaluronan metabolic process; Response to cytokine	Blood microparticle; Cytoplasm; Extracellular exosome; Plasma membrane
Junction plakoglobin OS=Bos taurus GN=JUP PE=2 SV=1	PLAK_BOVIN	19	50	38,66	Alpha-catenin binding; Cadherin binding; Protein homodimerization activity; Protein phosphatase binding; Signal transducer activity; Structural molecule activity; Transcription coactivator activity	Adherens junction assembly; Bundle of his cell-purkinje myocyte adhesion involved in cell communication; Cell migration; Cellular response to indole-3-methanol; Desmosome assembly; Detection of mechanical stimulus; Endothelial cell-cell adhesion; Establishment of protein localization to plasma membrane; Positive regulation of protein import into nucleus; Positive regulation of sequence-specific dna binding transcription factor activity; Regulation of cell proliferation; Regulation of heart rate by cardiac conduction; Regulation of ventricular cardiac muscle cell action potential ; kin development	Catenin complex; Cell-cell adherens junction; Cytoplasmic side of plasma membrane; Cytoskeleton; Cytosol; Desmosome; Extracellular exosome; Focal adhesion; Gamma-catenin-tcf7l2 complex; Intercalated disc; Intermediate filament; Protein-dna complex; Z disc; Zonula adherens
Peroxiredoxin-2 OS=Bos taurus GN=PRDX2 PE=2 SV=1	PRDX2_BOVIN	4	16	37,69	Peroxidase activity; Peroxiredoxin activity	Regulation of apoptotic process; Removal of superoxide radicals	Cytoplasm; Extracellular exosome
Putative glutathione-specific gamma-glutamylcyclotransferase 2 OS=Bos taurus GN=CHAC2 PE=2 SV=1 (*)	CHAC2_BOVIN	4	19	36,93	--	--	--
Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	44	75	63,64	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated endocytosis; Retina homeostasis	Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome; Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; Hfe-transferrin receptor complex; Late endosome; Perinuclear region of cytoplasm; Recycling endosome

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Serotransferrin OS=Bos taurus GN=TF PE=1 SV=1	G3X6N3_BOVIN	59	75	69,32	Ferric iron binding; Ferric iron transmembrane transporter activity; Ferrous iron binding	Cellular iron ion homeostasis; Cellular response to iron ion; Ferrous iron import into cell; Positive regulation of receptor-mediated endocytosis; Retina homeostasis	Apical plasma membrane; Basal plasma membrane; Blood microparticle; Coated pit; Early endosome Endocytic vesicle; Extracellular exosome; Extrinsic component of external side of plasma membrane; Hfe-transferrin receptor complex; Late endosome; Perinuclear region of cytoplasm; Recycling endosome
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	41	76	62,22	Ferric iron binding; Ferric iron transmembrane transporter activity	Cellular iron ion homeostasis	Cell; Extracellular space
Serotransferrin OS=Bos taurus GN=TF PE=2 SV=1	TRFE_BOVIN	55	76	65,06	Ferric iron binding; Ferric iron transmembrane transporter activity	Cellular iron ion homeostasis	Cell; Extracellular space
Serpin A3-1 OS=Bos taurus GN=SERPINA3-1 PE=1 SV=3	SPA31_BOVIN	16	28	42,58	Cysteine-type endopeptidase inhibitor activity; Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasm; Cytoplasmic vesicle; Extracellular space
Serpin A3-1 OS=Bos taurus GN=SERPINA3-1 PE=1 SV=3	SPA31_BOVIN	21	28	45,26	Cysteine-type endopeptidase inhibitor activity; Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule – subcell; Cytoplasm; Cytoplasmic vesicle; Extracellular space
Serpin A3-2 OS=Bos taurus GN=SERPINA3-2 PE=3 SV=1	SPA32_BOVIN	21	28	45,26	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity Source: GOC	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-2 OS=Bos taurus GN=SERPINA3-2 PE=3 SV=1	SPA32_BOVIN	21	28	45,26	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-3 OS=Bos taurus GN=SERPINA3-3 PE=1 SV=2	SPA33_BOVIN	22	28	58,39	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space

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Continua Tabela 5

Serpin A3-3 OS=Bos taurus GN=SERPINA3-3 PE=1 SV=2	SPA33_BOVIN	22	28	58,39	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-4 OS=Bos taurus GN=SERPINA3-4 PE=3 SV=1	SPA34_BOVIN	22	29	58,39	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-4 OS=Bos taurus GN=SERPINA3-4 PE=3 SV=1	SPA34_BOVIN	22	29	58,39	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-5 OS=Bos taurus GN=SERPINA3-5 PE=3 SV=1	SPA35_BOVIN	20	28	52,07	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-6 OS=Bos taurus GN=SERPINA3-6 PE=3 SV=1	SPA36_BOVIN	18	26	57,00	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-6 OS=Bos taurus GN=SERPINA3-6 PE=3 SV=1	G3N1U4_BOVIN	21	27	71,53	--	--	Extracellular space
Serpin A3-6 OS=Bos taurus GN=SERPINA3-6 PE=3 SV=1	G3N1U4_BOVIN	22	27	58,64	--	--	Extracellular space
Serpin A3-6 OS=Bos taurus GN=SERPINA3-6 PE=3 SV=1	SPA36_BOVIN	18	26	57,00	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=2 SV=1	SPA38_BOVIN	15	34	45,22	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=2 SV=1	SPA38_BOVIN	15	34	45,22	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Serpin A3-8 OS=Bos taurus GN=SERPINA3-8 PE=3 SV=1	A0A0A0MP89_BOVIN	15	34	45,22	--	--	Extracellular space

Continua Tabela 5

SERPIND1 protein OS=Bos taurus GN=SERPIND1 PE=2 SV=1	A6QPP2_BOVIN	14	35	44,76	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular exosome
SERPIND1 protein OS=Bos taurus GN=SERPIND1 PE=2 SV=1	A6QPP2_BOVIN	16	35	46,77	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular exosome; Extracellular space
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	41	59	63,43	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding; Toxic substance binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular space; Extracellular region; Extracellular space; Protein complex
Serum albumin OS=Bos taurus GN=ALB PE=1 SV=4	ALBU_BOVIN	41	59	63,43	DNA binding; Drug binding; Fatty acid binding; Metal ion binding; Pyridoxal phosphate binding; Toxic substance binding	Cellular response to starvation; Hemolysis by symbiont of host erythrocytes; Maintenance of mitochondrion location; Negative regulation of apoptotic process; Transport	Extracellular region; Extracellular space; Protein complex
SPA35_BOVIN	Serpin A3-5 OS=Bos taurus GN=SERPINA3-5 PE=3 SV=1	20	28	52,07	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Chromaffin granule; Cytoplasmic vesicle; Extracellular space
Transthyretin OS=Bos taurus GN=TTR PE=1 SV=1	TTHY_BOVIN	7	**7**	55,78	Thyroid hormone binding	Thyroid hormone binding	Thyroid hormone binding
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1 (**)	G3N0V0_BOVIN	13	25	50,00	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment; Phagocytosis, recognition; Positive regulation of b cell activation	Blood microparticle; External side of plasma membrane; Immunoglobulin complex, circulating
Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1 (**)	G3N0V0_BOVIN	6	25	39,26	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment	Blood microparticle; External side of plasma membrane; Immunoglobulin complex, circulating; Phagocytosis, recognition; Positive regulation of B cell activation

699 *Continua Tabela 5*

Uncharacterized protein (Fragment) OS=Bos taurus PE=1 SV=1 (**)	G3N0V0_BOVIN	16	25	64,42	Antigen binding; Immunoglobulin receptor binding	B cell receptor signaling pathway; Complement activation, classical pathway; Defense response to bacterium; Innate immune response; Phagocytosis, engulfment	Blood microparticle; External side of plasma membrane; Immunoglobulin complex, circulating; Phagocytosis, recognition; Positive regulation of B cell activation
Uncharacterized protein OS=Bos taurus GN=C8A PE=4 SV=1 (**)	F1MX87_BOVIN	13	45	36,67	--	Complement activation	Blood microparticle; Extracellular exosome; Membrane attack complex
Uncharacterized protein OS=Bos taurus GN=CP PE=1 SV=2 (**)	F1N076_BOVIN	30	**88**	43,78	Copper ion binding; Ferroxidase activity	--	Blood microparticle; Extracellular exosome; Lysosomal membrane
Uncharacterized protein OS=Bos taurus GN=SERPINA3 PE=3 SV=1 (**)	G8JKW7_BOVIN	19	29	66,02	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	Extracellular space
Uncharacterized protein OS=Bos taurus GN=SERPINA3 PE=3 SV=1 (**)	G8JKW7_BOVIN	26	29	58,74	Serine-type endopeptidase inhibitor activity	Negative regulation of endopeptidase activity	--
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MZ96_BOVIN	7	13	36,67	--	B cell differentiation	Extracellular space
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MZ96_BOVIN	6	13	35,83	--	B cell differentiation	--
Uncharacterized protein OS=Bos taurus PE=1 SV=2 (**)	F1MH40_BOVIN	7	13	36,67	--	Immune response; Immunoglobulin production	Extracellular space
Uncharacterized protein OS=Bos taurus PE=4 SV=2 (**)	F1MC45_BOVIN	33	64	58,75	--	--	--

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Continua Tabela 5

V6F9A2_BOVIN	Apolipoprotein A-I OS=Bos taurus GN=APOA1 PE=1 SV=1	22	32	73,21	Beta-amyloid binding; Chemorepellent activity; Cholesterol binding; Cholesterol transporter activity; High-density lipoprotein particle bindin; Phosphatidylcholine-sterol o-acyltransferase activator activity; Phospholipid binding	Adrenal gland development; Blood vessel endothelial cell migration; Cholesterol biosynthetic process; Cholesterol efflux; Cholesterol homeostasis; Cholesterol import; Endothelial cell proliferation; Glucocorticoid metabolic process; G-protein coupled receptor signaling pathway; Lipid storage; Lipoprotein biosynthetic process; Negative regulation of cell adhesion molecule production; Negative regulation of cytokine secretion involved in immune response; Negative regulation of heterotypic cell-cell adhesion; Negative regulation of hydrolase activity; Negative regulation of inflammatory response; Negative regulation of interleukin-1 beta secretion; Negative regulation of tumor necrosis factor-mediated signaling pathway; Negative regulation of very-low-density lipoprotein particle remodeling; Protein oxidation; Protein stabilization; Regulation of cdc42 protein signal transduction; Regulation of intestinal cholesterol absorption; Vitamin transport	Blood microparticle; Endocytic vesicle; Extracellular exosome; Spherical high-density lipoprotein particle; Very-low-density lipoprotein particle high-density lipoprotein particle assembly; Integrin-mediated signaling pathway; Peptidyl-methionine modification; Phosphatidylcholine biosynthetic process; Phospholipid efflux; Phospholipid homeostasis; Positive regulation of cholesterol esterification; Positive regulation of hydrolase activity; Positive regulation of rho protein signal transduction; Positive regulation of stress fiber assembly; Positive regulation of substrate adhesion-dependent cell spreading; Regulation of protein phosphorylation l; Reverse cholesterol transport; Triglyceride homeostasis

(*) Putative uncharacterized protein: means that this protein may be identified by computer, and the function is still unknown. This protein is not homologous to any well characterised proteins and thus its function cannot be predicted. Putative means that it was only predicted based on ORF (open reading frame) and promoter sequence.
(**) Uncharacterized protein: Proteins which are NOT conserved or with no known or predicted function orcharacteristics (http://www.uniprot.org/docs/nameprot)

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