Infection, Genetics and Evolution 39 (2016) 194–200

Contents lists available at ScienceDirect

Infection, Genetics and Evolution

journal homepage: www.elsevier.com/locate/meegid

Research paper

The *GATA3* gene is involved in leprosy susceptibility in Brazilian patients

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ARTICLE INFO

Article history:
Received 20 August 2015
Received in revised form 23 November 2015
Accepted 21 January 2016
Available online 23 January 2016

Keywords:
Leprosy
GATA3
Polymorphisms
Association study
GATA-3 transcription factor
rs10905284

ABSTRACT

Leprosy outcome is a complex trait and the host–pathogen–environment interaction defines the emergence of the disease. Host genetic risk factors have been successfully associated to leprosy. The 10p13 chromosomal region was linked to leprosy in familial studies and *GATA3* gene is a strong candidate to be part of this association. Here, we tested tag single nucleotide polymorphisms at *GATA3* in two case–control samples from Brazil comprising a total of 1633 individuals using stepwise strategy. The A allele of rs10905284 marker was associated with leprosy resistance. Then, a functional analysis was conducted and showed that individuals carrying AA genotype express higher levels of GATA-3 protein in lymphocytes. So, we confirmed that the rs10905284 is a locus associated to leprosy and influences the levels of this transcription factor in the Brazilian population.

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1. Introduction

Leprosy is still a public health problem exhibiting around 225,000 new cases by year, while Brazil ranks second in the number of patients in the world (World Health Organization, 2014).

The disease is caused by the intracellular pathogen *Mycobacterium leprae*, which has tropism for macrophages in skin and Schwann cells in the nerves turning leprosy the primary cause of nerve incapacity due to an infectious agent. *M. leprae* exhibits an extremely conserved and compact genome associated with long generation time. This bacillus is well adapted to the humans, but a large range of outcomes may emerge from the interplay between host and mycobacterium, and individuals can either eliminate the bacteria or develop infection.

The spectrum of clinical forms of leprosy is based on clinical, immunological, microbiological and histopathological criteria. The patients can evolve to a localized form, known as tuberculoid (TT), or to a disseminated form, named lepromatous (LL). This polar pattern of leprosy, TT or LL disease, resembles a Th1 or Th2 profiles of immune response, respectively (Modlin, 1994). The TT patients prevent the replication of the bacillus by a cell mediated immune (CMI) response, while LL patients present a poor CMI resulting in bacterial persistence, replication and spread throughout the body. Focusing on the treatment, the World Health Organization (WHO) proposed a clinical classification based on the number of skin lesions, that includes paucibacillary (PB) and multibacillary (MB) forms (World Health Organization, 1998).

Due to the low genetic variability of the pathogen and the diversity of phenotypes emerging from its interaction to the host, it is assumed that the host genetic background has a main role in the control of the leprosy development (Monot et al., 2005; Alter et al., 2011). In fact, twin studies showed the genetic influence in leprosy, revealing the higher concordance rate of disease per se and clinical forms in monozygotic than dizygotic pairs (Chakravartti and Vogel, 1973). Afterwards, complex segregation analysis demonstrated the presence of a major gene controlling the disease susceptibility (Abel and Demenais, 1988; Lázaro et al., 2010). Noteworthy, genetic epidemiology approaches are consistently emphasizing the presence of a genetic control in leprosy. A variety of genes and single nucleotide polymorphisms (SNPs) influencing the susceptibility to leprosy were identified in different populations: *TNF/LTA/HLA* (Roy et al., 1997; Santos et al., 2002; Cardoso et al., 2011; Vanderborght et al., 2007; Alcaïs et al., 2007), *IL10* (Santos et al., 2002; Malhotra et al., 2005; Pereira et al., 2009), *PARK2* and *PACRG* (Mira et al., 2004), *NOD2* (Zhang et al., 2009; Grant et al., 2012; Sales-Marques et al., 2014), *CCDC122* (Zhang et al., 2009; Grant et al., 2012; Sales-Marques et al., 2014), *IFNG* (Cardoso et al., 2010), and *TLR1* (Marques et al., 2013).

Two genome-wide linkage studies for leprosy pointed peaks at the 10p13 chromosomal region. The first one, from India, described the peak linked to the leprosy per se (Siddiqui et al., 2001). However, the second, from Vietnam, concluded that this region is involved in PB leprosy (Mira et al., 2003). The region contains many candidate genes and among them some were associated to leprosy. Markers at the *MRC1*

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http://dx.doi.org/10.1016/j.meegid.2016.01.015
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(mannose receptor, C type 1) gene were associated to the disease per se or clinical forms in Vietnamese, Brazilian and Chinese populations (Alter et al., 2010; Wang et al., 2012). Recently, a high-density association scan was performed in two family-based samples from Vietnam, and two SNPs were associated to MB leprosy at the *CUBN* and *NEBL* genes (Grant et al., 2014).

GATA3 gene is located at 10p15 chromosomal region and is a strong candidate gene to leprosy susceptibility since encodes the GATA-3 transcription factor that induces Th2 immune response that favors the permissiveness to *M. leprae* replication and spread (Yang et al., 2014). Besides, GATA-3 acts in other points of innate and adaptive immunity such as T cells development, innate lymphoid cell development and function, regulatory and CD8 + T cells as well as thymic natural killer cells (Tindemans et al., 2014).

Here, we investigated the association of *GATA3* gene to leprosy using a stepwise strategy in two case–control samples from Brazil enrolling 922 patients and 737 controls. Then, we verified the functional effect of rs10905284 SNP at *GATA3* on the expression of this gene.

2. Methods

2.1. Subjects and study design

The genetic epidemiology study enrolled 1659 individuals distributed in two independent case–control samples. A stepwise strategy was adopted using a discovery and a replication population. These populations are well-characterized in previous studies (Marques et al., 2013; Sales-Marques et al., 2014) and are detailed at the Supplementary Table 1.

First, we tested seven markers in 768 individuals in the discovery sample from endemic region of Rondonopolis, Mato Grosso State, located at the west center of Brazil. Four-hundred eleven cases were assembled from a specialized clinic and three-hundred fifty seven healthy controls were recruited during the campaigns for detecting new leprosy cases in public places of the region.

Then, SNPs associated in the discovery sample were investigated in a replication sample comprising 871 individuals from São Paulo State, located at the southeastern region of Brazil that presents lower number of leprosy cases. All leprosy cases (511 patients) were enrolled from the outpatient clinic specialized in leprosy from Instituto Lauro de Souza Lima. The control group (380 individuals) was derived from blood donors.

Patients were classified according to the Ridley and Jopling criteria (Ridley and Jopling, 1966). However, to evaluate the genetic effect of *GATA3* SNPs in the severity of leprosy, patients were classified into PB and MB according to bacillary index. Patients presenting a positive index were classified as MB and a negative index was condition to the PB patients. The leprosy subtype distribution was 75% MB and 23% PB in the discovery sample, and 76% MB and 19% PB in the replication sample.

The maximum power of our sample to reveal the same effect of the rs10905284 observed to leprosy per se in the leprosy subsets was 0.83, using an additive model and one-side type I error rate of 0.05 for PB and MB subsets (Table 1). In practice, a power of 80% to detect what we want to test is advisable (Pacheco and Moraes, 2009).

Table 1
Power to detect the association of OR = 0.73 in the PB (n = 185) and MB subsets (n = 655) considering the minor allele frequencies of the combined sample.

Stratum	MAF[a]	Model[b]	Power ($\alpha = 0.05$)	Power ($\alpha = 0.01$)
PB	0.44	ADD	0.83	0.61
MB	0.43	ADD	0.83	0.61

Abbreviation: PB — paucibacillary, MB — multibacillary.
[a] MAF — minor allele frequency of each stratum in the combined sample.
[b] Genetic model — ADD (additive).

The study of the functional effect of rs10905284 at *GATA3* gene was based on the homozygous genotypes. We studied healthcare workers of the Instituto Lauro de Souza Lima, all of them were women (eight presenting the AA genotype and eight presenting the CC genotype).

This work was approved by the Ethics Committee from Instituto Lauro de Souza Lima and all the protocols required were followed.

2.2. SNPs selection

To select tag SNPs to cover *GATA3* gene we used the tagger multimaker method considering the minor allele frequency of 0.1 in the Yoruba population and a cutoff r^2 of 0.8 in International HapMap Project database (http://hapmap.ncbi.nlm.nih.gov/). Thus, seven tag SNPs across the *GATA3* gene were picked, as follows: rs10905284, rs1399180, rs2280015, rs3781094, rs3802604, rs444929 and rs569421.

2.3. DNA extraction and SNP genotyping

Genomic DNA was extracted from peripheral blood leukocytes samples by salting-out method. The genotyping of the discovery sample was made using the GoldenGate assay with VeraCode technology in BeadXpress reader (Illumina, Inc., San Diego, CA, USA). For the replication sample and to select the genotypes for the functional study, the genotyping was made by allelic discrimination using fluorogenic probes in TaqMan SNP genotyping assay in StepOnePlus equipment (Applied Biosystems, Foster City, CA, USA), according to the manufacturer's instructions.

2.4. Peripheral blood mononuclear cell (PBMC) culture

Twenty-four milliliters of peripheral blood were collected from each individual in heparinized tubes by venipuncture. PBMCs were obtained by gradient centrifugation using Histopaque - 1077 (Sigma-Aldrich – Saint Louis – USA) and total cell number was estimated by counting in a Neubauer chamber. The concentration of the cell suspension was adjusted to 1.2×10^6 cells/ml and the cells were cultured for 48 h in 24-well polystyrene plates at 37 °C in a humidified atmosphere of 5% CO_2. RPMI 1640 medium supplemented with 10% serum fetal bovine and 1% antibiotics was used. Phytohemagglutinin (PHA, 8 μg/ml) or *M. leprae* sonicated antigen (ML, 10 μg/ml) were used as stimuli; unstimulated cultures (US) were kept on the same conditions as controls. After 48 h, the supernatants were collected and stored at − 80 °C for cytokine assay. Cells were used to analyze GATA-3 expression by flow cytometry.

2.5. Flow cytometry

For the analysis of GATA-3 expression, cells were harvested, washed in phosphate buffered saline (PBS) pH 7.4 and submitted to blockage of nonspecific sites for 1 h at 4 °C with normal mouse serum and normal human serum. Lymphocytes were labeled employing anti-CD4 FITC and CD69 PE (BD Biosciences, San Jose, CA, USA) for 1 h at 4 °C in the dark. The cell suspension was washed twice with PBS containing 5% fetal bovine serum. For GATA-3 labeling, cells were fixed and permeabilized using a specific kit (Buffer TranscriptionFactor Set BD Biosciences, San Jose, CA, USA) and then incubated with anti-GATA-3 antibody labeled with AlexaFluor-647 (BD Biosciences, San Jose, CA, USA) for 1 h at 4 °C in the dark. To control the specificity of the reactions we employed unrelated antibodies presenting the same isotype and conjugated with the same fluorochrome (isotype controls, BD Biosciences, San Jose, CA, USA).

Data collection was performed in a FACSCalibur flow cytometry (BD Biosciences, San Jose, CA, USA), including a minimum of 10,000 events. For data analyses we used the FlowJo software version 7.6.5 (2011) and consider the mean fluorescence intensity values (MFI).

2.6. Cytokines measurement by CBA

The cytokines IL-2, IL-4, IL-5, IL-10, TNF and IFN-γ were measured using a multiplex bead-based assay for Th1/Th2 profiles (CBA, BD Biosciences, San Jose, CA, USA) according to the manufacturer's instructions. Data collection was performed in a FACSCalibur flow cytometry (BD Biosciences, San Jose, CA, USA) and data were analyzed using FCAP software version 3 (2011).

2.7. Statistical analyses

The frequencies of alleles, genotypes and minor allele carriers were analyzed using logistic regression model to calculate the values of odds ratio (OR). Besides, we performed analyses with adjusting for sex and ethnicity covariates. The combined analysis was done applying the same method and adjusting by origin population as a variable. The analyses were performed using the R statistical software for Windows (version 2.14.0). The p values ≤0.01 were taken as statistically significant. We excluded from analyses the markers that failed the Hardy–Weinberg test and/or presented a call rate lower than 95%. To confirm the independent signals of the SNPs at *GATA3* we measured the linkage disequilibrium (LD) through r^2 statistics using the Haploview software, version 4.2 (Barrett et al., 2005).

In both group of cases, the set of MB is more representative than PB set. Therefore, we calculated if the subsets have a sufficient power to detect the same association found for leprosy per se. The power estimate was done using sample size and the minor allele frequency (MAF) of each subset of cases and the odds ratio obtained for leprosy per se, from the combined samples. For this analysis we used QUANTO Power and Sample Size Program version 1.2.4 (Gauderman and Morrison, 2006).

Statistical analyses for the functional study were done using non-parametric tests. A p-value lower than 0.05 was considered significant. All analyses were performed using GraphPad Prism software version 5.01 (La Jolla, CA, USA; 2007).

3. Results

3.1. A allele of the rs10905284 SNP at GATA3 gene is associated to leprosy resistance in Brazilian patients

Seven SNPs at the *GATA3* gene were tested in 762 individuals of the discovery sample. Among them, the rs10905284 marker was associated to leprosy per se at p-value <0.01 (Table 2). The other six markers did not present any association with leprosy (Supplementary Table 3).

The association of the rs10905284 in the discovery sample was observed for CA genotype (OR 0.65; 95% CI 0.47–0.90; p = 0.0099) and for carriers of the A allele (OR 0.67; 95% CI 0.50–0.92; p = 0.0117) (Table 2). Thus, we tested this marker in a replication sample from Sao Paulo State and the findings confirmed the association of the rs10905284 to leprosy per se for A carriers (OR 0.67; 95% CI 0.48–0.92; p = 0.0151), heterozygous CA (OR 0.69; 95% CI 0.49–0.97; p = 0.0344), and also for homozygous AA (OR 0.61; 95% CI 0.40–0.93; p = 0.0201) (Table 2).

A combined analysis was conducted joining the data from both samples and using the population covariate for adjustment of the analysis. Significant associations with the combined population were observed for CA (OR 0.67; 95% CI 0.53–0.85; p = 0.0009) and AA (OR 0.67; 95% CI 0.50–0.89; p = 0.0056) genotypes; A carriers (OR 0.67; 95% CI 0.53–0.84; p = 0.0004), and for the A allele (OR 0.81; 95% CI 0.66–0.98; p = 0.0341) (Table 3). We also made analyses considering clinical forms for both samples but we did not find any statistical significance (Supplementary Tables 4 and 2).

Ethnicity stratified analyses were performed and the same effect was seen for Caucasoid and Mestizo subsets in both populations and for the combined population (data not shown).

The linkage disequilibrium analysis including the seven markers showed that rs10905284 has an independent signal (Fig. 1). From LD analyses, two markers (rs3781094 and rs3802604) were in the same bin in our population ($r^2 = 0.96$).

None of the SNPs evaluated deviated from Hardy–Weinberg equilibrium (HWE).

3.2. rs10905284 SNP at GATA3 gene modulates in vitro expression of GATA-3 in T cells

Next, we evaluated the expression of GATA-3 in CD4+ lymphocytes by flow cytometry to verify the influence of the rs10905284 genotype in the response against *M. leprae* antigens (Fig. 2). Unstimulated cultures (US) showed a low expression of GATA-3. When cells were stimulated with ML a subtle increase in the expression of GATA-3 was observed. After stimulation with PHA, an important increase in the expression of this transcription factor in most of the subjects, mainly in the individuals with AA genotype, was detected (Fig. 2). When GATA-3 expression in stimulated cultures was normalized by the values found in US cultures we observed a higher expression of GATA-3 in AA individuals when compared to CC after stimulation with PHA (Fig. 2, p = 0.0415).

We also investigated the T cells activation using CD69 as a marker. However, there were no significant differences considering the genotypes AA and CC to the expression of CD69 (Fig. 2).

3.3. rs10905284 SNP at GATA3 gene has no effect in the production of cytokines

We also evaluated the production of the cytokines IL-2 (interleukin-2), TNF (tumor necrosis factor), IFN-γ (interferon-gamma), IL-4 (interleukin-4), IL-5 (interleukin-5) and IL-10 (interleukin-10), according to the genotype for the rs10905284 variant. There was no significant variation in the levels of these cytokines related to the genotype for

Table 2
Allele, genotype and carrier frequencies of the rs10905284 polymorphism in case and control groups and logistic regression data for association with leprosy per se in the discovery sample from Rondonopolis and replication sample from Sao Paulo State.

SNP rs10905284	Discovery sample (n = 762)				Replication sample (n = 871)			
	Control	Case	OR(95% CI) p-value	OR(95% CI) p-value[a]	Control	Case	OR(95% CI) p-value	OR(95% CI) p-value[a]
Allele A	0.47	0.42	0.82 (0.62–1.10) 0.1813	0.82 (0.61–1.09) 0.1690	0.5	0.45	0.85 (0.65–1.11) 0.2346	0.79 (0.59–1.05) 0.0985
Allele C	0.53	0.58	*	*	0.5	0.55	*	*
AA	80 (0.22)	87 (0.21)	0.73 (0.49–1.08) 0.1186	0.72 (0.48–1.07) 0.1066	83 (0.23)	105 (0.21)	0.72 (0.49–1.07) 0.1004	**0.61 (0.40–0.93) 0.0201**
CA	176 (0.49)	170 (0.42)	**0.65 (0.47–0.90) 0.0099**	**0.64 (0.46–0.89) 0.0084**	191 (0.53)	255 (0.50)	0.76 (0.55–1.05) 0.0980	**0.69 (0.49–0.97) 0.0344**
CC	100 (0.28)	149 (0.37)	*	*	86 (0.24)	151 (0.30)	*	*
A Carrier			**0.67 (0.50–0.92) 0.0117**	**0.67 (0.49–0.91) 0.0097**			0.75 (0.55–1.02) 0.0649	**0.67 (0.48–0.92) 0.0151**

Bold values denote statistically significant results.
Abbreviation: OR — odds ratio; CI — confidence interval of 95%.
*Indicates the baseline for comparison.
[a] OR e p-value were adjusted for covariates sex and ethnicity.

Table 3
Allele, genotype and carrier frequencies of the rs10905284 polymorphism and logistic regression data for association with leprosy per se in the combined populations.

SNP rs10905284	Combined samples (n = 1633)			
	Control	Case	OR(95% CI) p-value	OR(95% CI) p-value[b]
Allele A	0.48	0.44	0.84 (0.69–1.02) 0.085	**0.81 (0.66–0.98) 0.0341**
Allele C	0.52	0.56	*	*
AA	163 (0.23)	192 (0.21)	**0.73 (0.55–0.96) 0.0265**	**0.67 (0.50–0.89) 0.0056**
CA	367 (0.51)	425 (0.46)	**0.72 (0.57–0.90) 0.0048**	**0.67 (0.53–0.85) 0.0009**
CC	186 (0.26)	300 (0.33)	*	*
A carrier			**0.72 (0.58–0.90) 0.0032**	**0.67 (0.54–0.84) 0.0004**

Bold values denote statistically significant results.
Abbreviation: OR — odds ratio; CI — confidence interval of 95%.
*Indicates the baseline for comparison.
[b] OR e p-value were adjusted for covariates sex, ethnicity and study.

rs10905284 SNP (Fig. 3). PHA and ML stimulated TNF and IL-10 production in peripheral blood mononuclear cells (PBMCs), while only PHA induced IFN-γ and IL-5. The production of IL-2 and IL-4 was very low regardless of the stimulus (data not shown). Of note, individuals with CC genotype for rs10905284 SNP presented negative correlation between the levels of GATA-3 expression and the production of cytokines IL-5 ($r = -0.90$; $p < 0.01$) and IL-10 ($r = -0.71$; $p = 0.03$).

4. Discussion

Here, we investigated if *GATA3* gene is associated to leprosy, since it is a strong candidate because it is located in an interval of 6.5 Mb from the previously published peak of linkage on chromosome 10p13 and has an important role in immunology (Siddiqui et al., 2001; Mira et al., 2003). For this, we applied a stepwise strategy in two Brazilian case–control samples and we focused on markers covering the gene based on linkage disequilibrium data of the HapMap. We found an association of the rs10905284 polymorphism to leprosy per se that could be confirmed for the Brazilian population since we used two samples from different regions of the country. Besides, we looked for a functional evidence for our data and we found changes in the expression of GATA-3 dependent on the rs10905284 genotype.

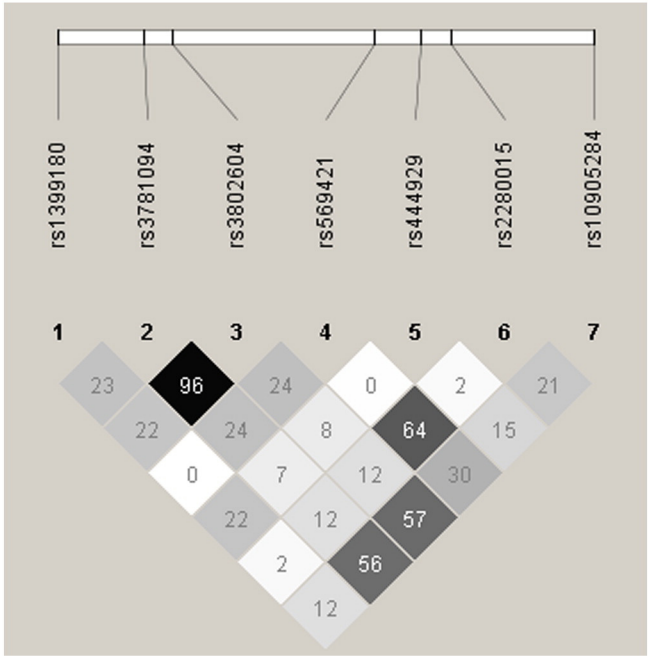

Fig. 1. Linkage disequilibrium (LD) map at seven polymorphisms (tagSNPs) from *GATA3*. The number within boxes represents r^2 values, calculated by Haploview software (4.2).

Three genes at 10p13 region have already been associated to clinical forms of leprosy. Non-synonymous variants at exon 7 of the *MRC1* gene were associated to MB form in Vietnamese and Brazilian (Alter et al., 2010). SNPs at this gene were also associated to PB form in the Chinese population (Wang et al., 2012). At the same region, *CUBN* and *NEBL* genes were associated to MB leprosy in Vietnamese (Grant et al., 2014). Thus, the original involvement of the 10p13 region with the clinical form of leprosy seems to be reliable. However, this hypothesis does not preclude some association of this region to leprosy per se since these genes were also associated to leprosy per se (Alter et al., 2010; Grant et al., 2014). Here, we did not find *GATA3* markers associated to clinical forms of the disease, although we maintained a reasonable power for that (0.83). Thus, we can assume that the association found here also does not explain the PB linkage peak at 10p13, but is indubitably a strong association to leprosy per se.

The rs10905284 marker is located in an intron and close to the 3′UTR region of the *GATA3* gene. It is located just 1200 bp from the rs1058240 in the 3′UTR, which has three potential miRNA binding sites and influences the mRNA expression of *GATA3* (Yang et al., 2014). Thus, is reasonable speculate that the association seen to the rs10905284 can reflect the effect of some causative marker at 3′UTR. Nonetheless, our data allow saying that the rs10905284 is a representative marker of the *GATA3* involvement in the leprosy susceptibility for Brazilian population.

Polymorphisms in *GATA3* gene have been associated with the occurrence of several diseases with inflammatory background such as asthma, allergy and cancer (Guthikonda et al., 2014; Pykäläinen et al., 2005; Glubb et al., 2015; Cook et al., 2014; Andrew et al., 2012; Perez-Andreu et al., 2015; Chang et al., 2010; Arshad et al., 2008; Wang et al., 2008). However, there are no reports regarding infectious diseases. Also, no functional effect of variants at *GATA3* on immune response was already described, in spite of the broad effect of this transcription factor (Tindemans et al., 2014).

Individuals with AA genotype associated to leprosy resistance showed higher expression of GATA-3 protein. Besides, we have observed a negative correlation between the levels of GATA-3 expression and the production of IL-5 and IL-10 in individuals with CC genotype, but no significant difference in the production of classical Th1 and Th2 cytokines considering the genotypes for rs10905284. Recent evidences show that the role of this transcription factor goes beyond the induction of Th2 differentiation, and includes the control of Treg cells function and immune tolerance, since GATA-3 controls FoxP3 expression (Wang et al., 2011). GATA-3 is also involved in proliferation and survival of CD8 + T cells (Wang et al., 2013), and in the development of some subpopulations of natural killer (NK) cells (Vosshenrich et al., 2006). Experiments including *GATA3* knockout mice result in the complete ablation of T-cell development (Yang et al., 2013). This transcription factor is expressed on a variety of cell types and acts as a repressor or activator of the transcription and more than 14,000 binding sites for GATA-3 have been identified in the DNA in human lymphocytes. GATA-3 also influences the pattern of methylation of various genes related to the

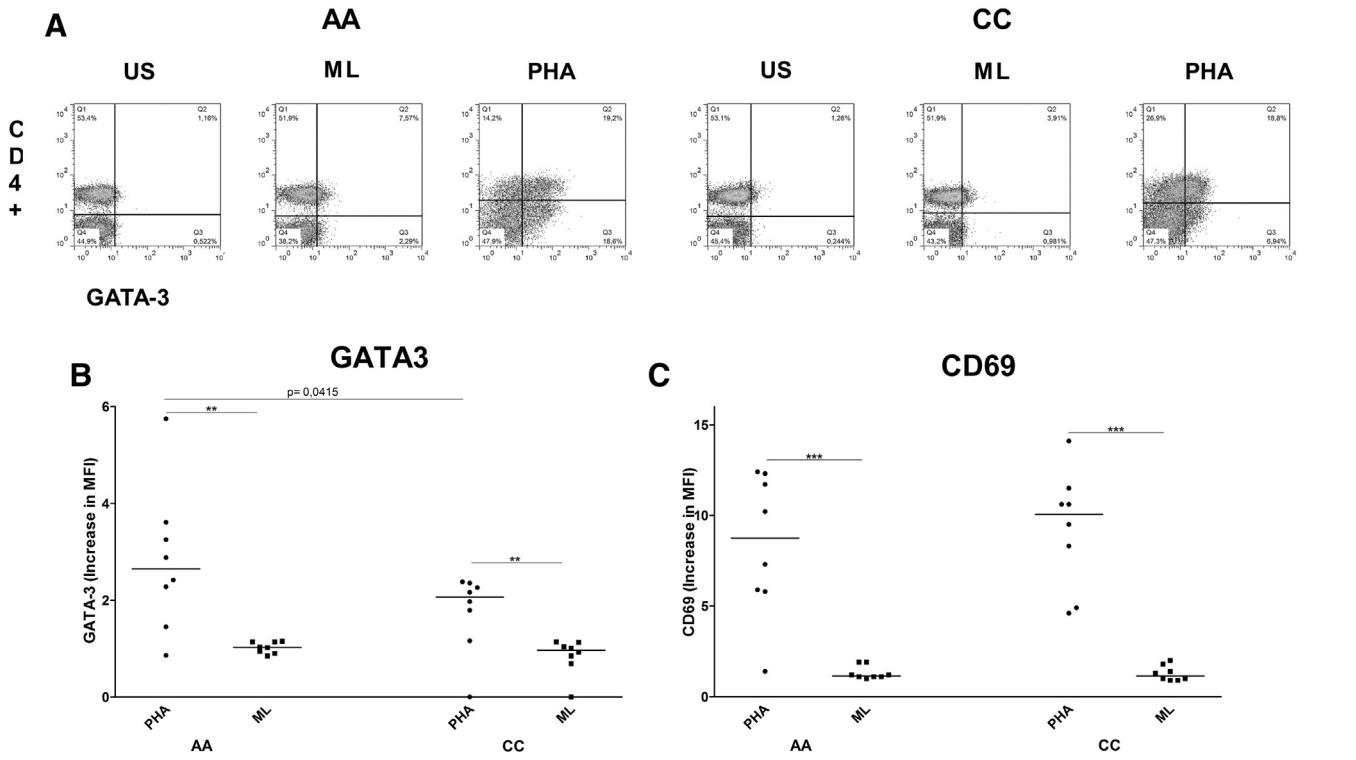

Fig. 2. GATA-3 and CD69 expressions in CD4 + lymphocytes according to the genotypes for rs10905284 SNP. A. GATA-3 expression in AA and CC individuals in unstimulated cultures (US) and after stimulation with *M. leprae* sonicate antigen (ML) and phytohemagglutinin (PHA). B and C. The mean fluorescence intensity (MFI) was normalized by the values observed in unstimulated cultures. *$p < 0.05$; **$p < 0.01$ and ***$p < 0.001$, Mann–Whitney test.

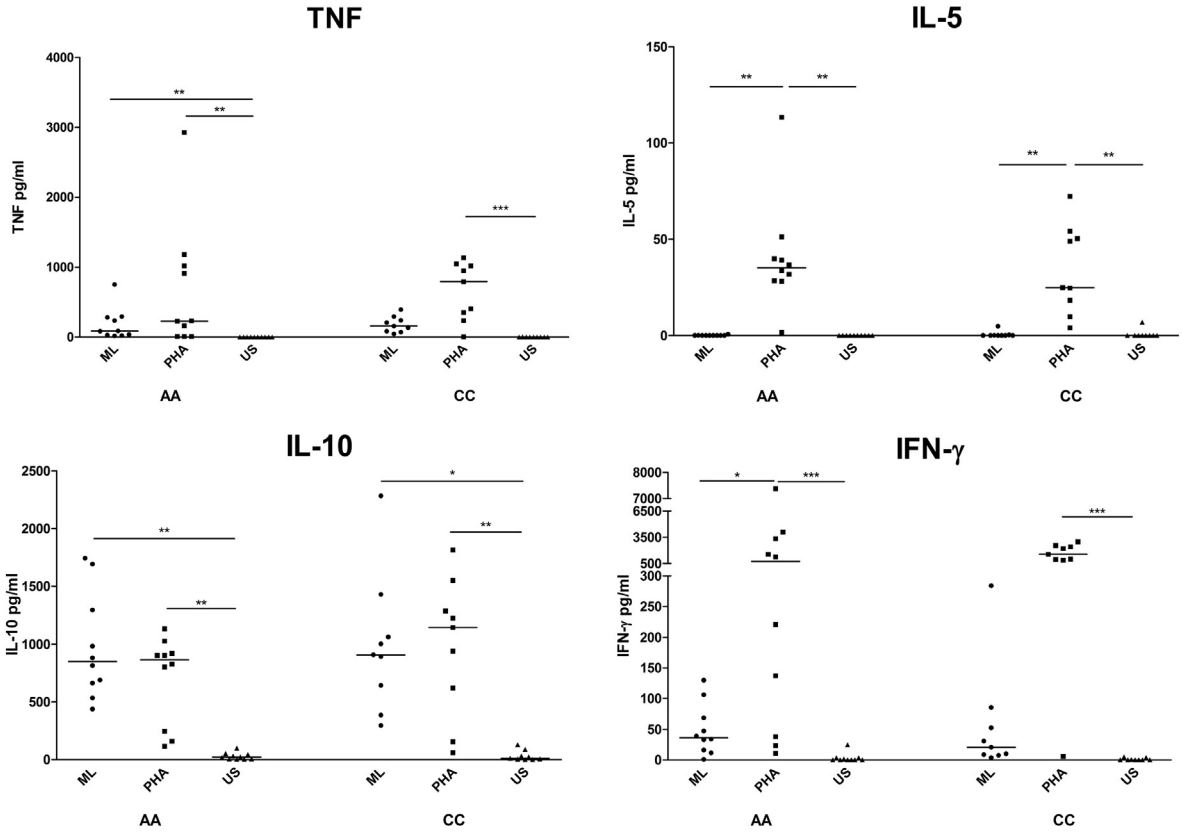

Fig. 3. Cytokine levels in culture supernatants of peripheral blood mononuclear cells (PBMCs) according to the genotypes for rs10905284. PBMCs were stimulated for 48 h with ML (10 mg/ml) or PHA (8 mg/ml) or unstimulated (US). The median value was indicated by a line. *$p < 0.05$; **$p < 0.01$ and ***$p < 0.001$. Friedman nonparametric analysis of variance followed by Dunn's post-test.

immune response (Tindemans et al., 2014). Considering its broad range of action, it is possible that GATA-3 acts in other points of the immune response further than Th2 polarization, influencing the host–parasite interaction and contributing to leprosy susceptibility. One of these points can be the involvement of GATA-3 in the survival of CD8 + T cells (Wang et al., 2013), that are important in the response against *M. leprae* (Steinhoff and Kaufmann, 1988; Sasiain et al., 1992; De la Barrera et al., 1997). In line with this idea, our data show association of *GATA3* with leprosy per se and not with the clinical form, that classically depends on the Th profile, suggesting the participation of GATA-3 also in events prior to the acquired immunity.

We demonstrated the association of the *GATA3* gene to leprosy in Brazilian. Besides, we verified an influence of the associated variant on the expression of this transcription factor. No data regarding the *GATA3* gene and infectious diseases is available in the literature. Thus, here we presented a new gene associated to leprosy and a new fact to the better understanding of the pathways involving GATA-3 in infectious diseases.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.meegid.2016.01.015.

Acknowledgments

We thank all the individuals who participated in this study. This study was supported by FAPESP Grant 2009/16873-8, CNPq/DECIT Grant 576051/2008-0 and Fundação Paulista Contra a Hanseníase. PM received a master fellowship from CAPES-DS and BBOG received a graduation fellowship from FAPESP (Grant 2014/04143-3).

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