Impact of PGL-1 seropositivity on the immune response to *Mycobacterium leprae* antigens

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Factors associated with acquiring the disease:

1. Not receiving the BCG vaccine;
2. A negative Mitsuda Reaction;
3. Contact with a patient with multibacillary form of the disease.

Source: Sarno et al., 2012.
Factors associated with infection:

1. Seropositive reaction for anti-phenolic glycolipid 1 IgM;
2. Young age (< 20 years);
3. Low measured Mitsuda reaction (< 5 mm);
4. Contact with an index patient who had a high bacilloscopic index.

Source: Sarno et al., 2012.
Contact Surveillance

• The detection of antibodies to PGL-1 antigen of *M. leprae* has been used to understand the epidemiology of subclinical infection, as opposed to active disease. However, this technique has not been proven for the early diagnosis of clinical cases and for predicting who will develop leprosy in the future.

• Seropositivity has been reported to be higher in contacts of leprosy patients than among the general population and has been associated with the development of leprosy (Düppre et al., 2012; Sales et al., 2011; Douglas et al., 2004).
It is possible that the combination of IgM antibodies and cell-mediated immune markers can distinguish active disease from sub-clinical infection. The aim of this study was to evaluate the immune response in PGL-1 seropositive contacts.
The present study included 149 contacts (97 from multibacillary index case and 52 from paucibacillary index case). 91 contacts were female (mean age= 38.3, SD=16.6) and 58 were male (mean age=39.5, SD=17.7). The rate of seropositivity to PGL-1 was 18.12% among contacts.
VDR and FOXP3 gene expression are increased in whole blood from PGL-1(+) leprosy contacts

No significant changes were observed in IDO and IFNγ gene expression in the different groups tested, although the median was higher in PGL-1(-) group.
Decreased CD69 expression in CD4 T cells from PGL-1(+) leprosy contacts
Differences in Naive e TEMRA phenotypes in PGL-1(-) and PGL-1(+) leprosy contact cells

Naive

TEMRA

CM

EM
Increased FoxP3+ frequencies in PGL-1(+) leprosy contact cells stimulated with *M. leprae* antigens

![Graph showing increased FoxP3+ frequencies in PGL-1(+) leprosy contact cells stimulated with *M. leprae* antigens.](image)
Mycobacterium leprae-induced interferon-gamma production by household contacts of leprosy patients: association with the development of active disease

Immunologic response to M. leprae

Risk of developing disease

2 year follow up: Five contacts (6.41%) developed leprosy during follow-up and, as predicted, belonged to the group of individuals who were negative or showed reduced levels of IFN-γ in response to the antigen.
ML0840 discriminates PGL-1(+) and PGL-1(-) contacts independently of the clinical form of the index case
PBMC from PGL-1(-) contacts produce increased IFN-γ levels in response to *M. leprae* antigens
The decrease on IFN-γ production in ML0840-stimulated PGL-1(+) contact cells was not associated with increased IL-10 or IL-4 levels.
IL-1β levels in response to both ML and ML2478 are increased in PGL-1(-) when compared with PGL-1(+) contacts and leprosy patients.

# = p<0.05 when compared to other tested groups.
PGL-1(+) contact cells produce less TNF and IL-17 in response to ML0840 when compared to PGL-1(-) cells.
Conclusion

Our data demonstrated ML0840 antigen can discriminate PGL-1(-) and PGL-1(+) contacts. PGL-1(+) contacts presented reduced levels of IFN-γ, TNF, IL-6 and IL-17 in response to ML0840 when compared with PGL-1(-) contacts.

In addition, ML2478 decreases both TNF and IL-1β levels in supernatants from PGL-1(+) contact cells when compared to PGL-1(-) which can suggest a capacity of this antigen to stimulate innate responses.
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