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CHALLENGES FOR LABORATORY DIAGNOSIS OF LEPROSY

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The maintenance of high leprosy prevalence in developing countries in spite of the efficacy of multidrug therapy suggests that there still are undiagnosed cases keeping the leprosy endemy. Early diagnosis and regular treatment have been recommended by WHO as strategies for the leprosy control. However, the complexity of the clinical manifestations becomes very difficult the diagnostic in primary health care services. Thus, the development of laboratory tests with high sensitivity, easy implementation and low cost can have a great value for the disease control.

The histopathological analysis of biopsies from skin lesions and slit skin smears are the main tools for laboratory diagnosis of leprosy. However, the success of both depends on the correct choice of the site and the proper procedure for collecting, as well as careful processing and analysis of these materials by trained professionals. In this scenario, laboratory tests based on blood or serum samples with fast and standardized results can minimize such difficulties improving the field diagnosis.

The discovery of the phenolic glycolipid (PGL-I), specific antigen from *Mycobacterium leprae* (1), allowed the development of enzyme immunoassays (ELISA) for detection of anti-PGL-I IgM antibodies which are very effective for the diagnosis of multibacillary patients and monitoring of contacts, as well. However, they are ineffective to paucibacillary patients diagnosis (2), which present predominantly cell mediated immune response that results in low levels of antibodies against the bacillus. Besides, the dosage of anti-PGL-I requires adequate facilities. The creation of immunochromatographic devices, including the ML-Flow, simplified the detection of anti-PGL-I antibodies, allowing its use in the field. However, ML-Flow has not been produced on large scale.

The complete sequencing of the *M. leprae* genome (3) in 2001 allowed the study of unknown protein sequences from the bacillus. Thus, recombinant proteins were synthesized and tested in order to assess the cellular and humoral immune response of leprosy patients aiming the standardization of new methods of diagnosis. Several studies have demonstrated the presence of IgG antibodies against these proteins, in particular directed against ML0405 and ML2331 proteins, which were combined giving rise to a fusion protein called LID- 1 (4). The latter has been shown to be recognized by multibacillar patients from different parts of the world; however no great advantage in the diagnosis of paucibacillar patients was achieved if compared with tests based on the detection of anti-PGL-I antibodies.

Among tuberculoid leprosy patients, which are often affected by neuropathy and leprosy reactions, the cell mediated immune response predominates

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and antibody titers are low. For these individuals, new approaches based on the evaluation of cytokine production against bacillus antigens are interesting promises for laboratory diagnosis. For this purpose, it is necessary to standardize simple methods for *in vitro* stimulation of cells with *M. leprae* antigens. Besides, the distinction between the response manifested by patients and healthy individuals naturally resistant to leprosy that cohabit in endemic areas should be understood.

The development of new assays combining quick detection of antibodies against specific components of *M. leprae*, either proteins or lipids, and measurement of cytokines produced in response to bacillary antigens using accurate devices with easy interpretation is the ideal scenario for early laboratory diagnosis of leprosy aiming to interrupt the transmission and prevent disabilities.

REFERENCES

1 Hunter SW, Brennan PJ. A novel phenolic glycolipid from Mycobacterium leprae possibly involved in immunogenicity and pathogenicity. J Bacteriol [Internet]. 1981/09/01 ed. 1981;147(3):728–35. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7024248

2 Oskam L, Slim E, Buhrer-Sekula S. Serology: recent developments, strengths, limitations and prospects: a state of the art overview. Lepr Rev [Internet]. 2003/10/28 ed. 2003;74(3):196–205. Available from: http://www.ncbi.nlm.nih.gov/pubmed/14577464

3 Cole ST, Eiglmeier K, Parkhill J, James KD, Thomson NR, Wheeler PR, et al. Massive gene decay in the leprosy bacillus. Nature [Internet]. 2001/03/10 ed. 2001;409(6823):1007–11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11234002

4 Duthie MS, Goto W, Ireton GC, Reece ST, Cardoso LP, Martelli CM, et al. Use of protein antigens for early serological diagnosis of leprosy. Clin Vaccine Immunol [Internet]. 2007/09/28 ed. 2007;14(11):1400–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17898185