Cellular, genetic and molecular aspects associated with the differential clinical evolution of human Chagas disease.

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Chagas disease, caused by the infection with *Trypanosoma cruzi*, is endemic in all Latin America. Due to the increase in population migration, Chagas disease has spread worldwide and is now considered a health issue not only in endemic countries. While most chronically infected individuals remain asymptomatic, approximately 30% of the patients develop a potentially deadly cardiomyopathy. The exact mechanisms that underlie the establishment and maintenance of the cardiac pathology are not clear. However, there is consistent evidence that immunoregulatory cytokines are critical for orchestrating the immune response and, thus, influence disease development or control. While the asymptomatic (indeterminate) form represents a state of balance between the host and the parasite, the establishment of the cardiac form represents the loss of this balance. Analysis of data obtained from several studies have led to the hypothesis that the indeterminate form is associated with an anti-inflammatory cytokine profile, represented by high expression of IL-10, while cardiac form is associated with a high production of IFN-gamma and TNF-alpha in relation to IL-

10, leading to an inflammatory profile. Recent data have shown that the production of the different cytokines is associated with gene polymorphisms and also with differential gene regulatory mechanisms, such as microRNA expression, pointing to the use of these characteristics as markers of disease susceptibility. Interestingly, we have recently observed that interference with the antigen presentation and subsequent activation of major cell populations involved with the expression of inflammatory cytokines leads to the control of the inflammatory response in patients with the cardiac form of disease, suggesting a promising path to immunological control of disease progression.