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Generation of Human Monocytic-Activating Leishmanial Parasites

Macrophages and other monocyte-derived cells are used by the immune system in response to environmental stimuli and the polarized effect of the response can have beneficial or detrimental outcomes in different settings. This project evaluates the efficiency of the specific transgenic *Leishmania tarentolae* to activate human macrophages and, if successful, the parasites could be used for macrophage-activating therapeutics for infected hosts. We hypothesize that nonpathogenic *L. tarentolae* expressing human cytokines from transgenes, will activate human macrophages in a consistent and controllable manner. DNA recombination methods were used to clone hIFNG and hGM-CSF into plasmid vectors capable of recombining with the highly repetitive ribosomal RNA locus of leishmanial parasites. In addition, fluorescent protein-coding genes were cloned into the plasmid vectors as a marker of successful genomic integration. Current efforts are focused on optimizing the efficiency of generating transgenic *L. tarentolae*. In addition to the potential of these transgenic parasites for use as macrophage-activating therapeutics, it is possible through cross protection for these parasites to be used as vaccines against the pathogenic forms of this neglected tropical disease.