EpiMyco : EPIGENETIC PROGRAMMING OF MACROPHAGES UPON EXPOSURE TO MYCOBACTERIUM LIGAND

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Lesions caused by exposure of human skin to *Mycobacterium ulcerans* can naturally heal or evolve into damaging Buruli ulcer. Previously the Marion's lab uncovered two mouse strains exhibiting differential response to secondary exposure to this pathogen: either dampening or exacerbation of the macrophage response. This differential behaviour mimics response in human and provides us with an ideal platform to identify chromatin alteration tracking with tolerization *versus* training. First using RNA-seq analysis, we will describe macrophage's transcriptional response to repeated pathogen exposure and identify set of genes that exhibit strain-specific training or tolerization. Second, using calibrated ChIP-seq analysis we will first evaluate genomic changes to the distribution of modified histones following exposure to Mycobacterium ligands in macrophages from the two mouse strains. Lastly, gene expression analysis in nuclei from trained or tolerized macrophages transplanted to oocytes will identify genes whose transcriptional programming by *M. ulcerans* is chromatin-based. By integrating these epigenomic and transcriptomic data, we will identify epigenetic features that have the credentials to epigenetically reprogram macrophage response to repeated pathogen exposure. Such candidate epigenetic feature will be functionally tested by interference with epigenetic pathway in cultured macrophages or nuclear transfer assay. Altogether this proposal will thoroughly evaluate the extent to which innate cell programming by *M. ulcerans* is encoded in chromatin.