ImmunoTools IT-Box-Cy55M-Award 2013

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Malaria – Tuberculosis Co-Infection: Dissecting the immunological interactions during concurrent *Plasmodium* and *Mycobacterium* infection

Malaria and tuberculosis are two of the three leading causes of death from infectious diseases globally. The infectious agents, *Plasmodium* parasites and *Mycobacterium tuberculosis*, are co-endemic in tropical regions of the world, and large numbers of individuals are at risk of co-infection. Altered immune responses through coinciding infections can not only affect the outcome of disease but may also interfere with anti-infective interventions. Therefore, a comprehensive picture of the immunomodulation during malaria-tuberculosis co-infection is needed to appreciate how co-infection can affect vaccination, immunodiagnostics and therapy.

Our lab has established an experimental mouse model that allows us to dissect the elicited immune responses to both pathogens in the co-infected host (Mueller *et al.*, 2012). Our studies demonstrate striking changes in the immune regulation by co-infection with *Plasmodium* and *Mycobacterium* and thus emphasize that a detailed understanding of the immunomodulation during malaria-tuberculosis co-infection is of pivotal importance.

Different rodent malaria parasites do closely resemble certain aspects of naturally acquired human malaria infection in different mouse strains. Of particular interest during my PhD project will be the influence of *M. tuberculosis* co-infection on malaria infection in the *Pb*ANKA model of experimental cerebral malaria (ECM). Cerebral malaria is the most severe complication of human infection with *Plasmodium falciparum*. The underlying mechanisms which lead to cerebral malaria are incompletely resolved. However, the pathology of severe malaria is thought to be at least partially immune-mediated. Pro-inflammatory (Th1-like) cytokines are required for parasite clearance but, in excess, also contribute to immunopathology. *M. tuberculosis* is a potent inducer of type 1 immunity, and the mycobacteria-elicited pro-inflammatory immune response might affect the course of malaria by exacerbating immunopathology. Our preliminary analysis indicates that the *M. tuberculosis* induced immune response indeed exacerbates the course of ECM. We are in the process of identifying cyto- and chemokines which are differentially regulated during co-infection and single infection. The administration of individual cytokines/chemokines will reveal their function and immunoregulatory properties in the context of co-infection both on the level of the whole organism (*in vivo*) and individual cell populations (*in vitro*).

Therefore, the ImmunoTools *IT-Box Cy55M* offers the great chance to study the role of a whole bunch of different cyto- and chemokines and their impact on disease outcome in the co-infected host.

Müller, A.-K. et al. Natural Transmission of Plasmodium berghei exacerbates chronic tuberculosis in an experimental co-infection model. PLOS One 2012; 7(10): e48110.

ImmunoTools *IT-Box-Cy55M* for **Jannike Blank**
includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS