ImmunoTools *special* Award 2018

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Neutrophil associated Signatures in Tuberculosis

Tuberculosis (TB) is the prime bacterial infectious disease in humans worldwide and caused by members of the *Mycobacterium tuberculosis* (*M. tuberculosis*) complex. Active TB patients develop lung granulomas associated with exacerbated pathology ultimately facilitating mycobacterial aerosol transmission. Despite successful cure following standard antibiotic therapy, a significant number of patients fail to regain sufficient lung function and suffer from long-term sequelae.

We hypothesize I) that lung-sequelae are associated with exacerbated inflammation and tissue destruction prior to initiation of treatment, and II) that neutrophil granulocytes play an important role in disease exacerbation, as they represent the predominant phagocyte population in active pulmonary TB *(Eum et al. 2010)*. To investigate the underlying pathways leading to TB exacerbation, we use protein-biochemistry, flow cytometry, multiplex, and microscopy to analyze sputum samples from active TB patients before, during and after treatment. Previous studies revealed a decrease of matrix metalloproteinases in sputum during anti-TB drug treatment *(Ugarte-Gil et al. 2013)*. Furthermore, sputum of active TB patients showed a decrease of cytokines such as interferon-γ, interleukins and granulocyte colony stimulating factor compared to patients with other respiratory diseases *(Ota et al. 2014)*. These data indicate that sputum represents a promising sample material, which originates from the site of infection and therefore carries factors generated during the neutrophil driven inflammatory process. These factors are putative signatures for point-of-care (POC) diagnostic during treatment, for predicting the risk of disease exacerbation and long-term sequelae as well as, ultimately, targets for host-directed therapy (HDT) to support antibiotic treatment and to limit immunopathology.

Initial analyses of sputum form acute TB patients indicate correlation of neutrophil associated proteins with neutrophil cell counts and therapy progress. Mass spectrometry based proteomics of *M. tuberculosis* infected and non-infected human neutrophils revealed several protein candidates as potential signatures and HDT targets. These potential signatures are now under investigation in patient sputum.

Ultimately, we will establish neutrophil-based signatures in sputum, which can indicate disease state and treatment efficacy as well as early detection of exacerbated pathology to initiate neutrophil specific HDT. Our goal is to develop a “low tech” field ready POC diagnostic method to support monitor drug treatment.

This study is part of the TB-Sequel consortium to improve collaboration and build up TB research capacity in high incidence countries of Africa.

ImmunoTools *special* AWARD for **Christoph Leschczyk** includes 20 reagents

human ELISA-set (for one 96 plate): human IFN-gamma, human TNF-a, human sCD147 (sEMMPRIN), IP-10 (CXCL10), human IL-10