USING NEUTROPHIL PHENOTYPE AS A MARKER OF TB DISEASE AND TREATMENT RESPONSE

Lerato Ndlovu, Shepherd Nhamoyebonde, Alasdair Leslie

Africa Health Research Institute, University of Kwa-Zulu Natal, Durban, South Africa.

Background

Efforts to control the global tuberculosis (TB) epidemic would be transformed by shortening the length of drug treatment to less than 6 months. However, improved methods for monitoring treatment responses are needed first, as the current options, such as sputum culture conversion at 2 months, are not a predictive of treatment success. Host-mediated biomarkers offer an attractive alternative approach to bacterial culture, as they potential offer a more systemic view of treatment success with the host. Neutrophils are the most abundant immune cell type in circulation, they are rapidly recruited to the infection site and are short lived, and thus provide a potentially strong and universal disease signature that rapidly resolves, as imprinted neutrophils are quickly replaced.

Aim

Using flow cytometry and RNA sequencing, we are investigating the potential of blood neutrophil phenotypic and genetic signatures as biomarkers for TB disease and treatment response in a longitudinal TB-treatment study.

Methods

Blood samples are collected from TB patients at the time they are diagnosed and serially until treatment completion at 6 months. We are measuring neutrophil expression levels of key markers including HLA-DR, CD15, CD16, CXCR4 and CD177 by FACs. These will be correlated with treatment success at 6 months and relapse rate over 2 years. Sample collection and analysis is on-going.

Results

Preliminary data suggest CD15 expression levels change in a predictable manner over the course of treatment. Importantly, these changes are not impacted by HIV co-infection. In addition, sorted neutrophil populations are being RNA sequenced to seek potential gene signatures for future study.

Conclusion

We anticipate that the generated data from this novel approach could lead to the development of a new paradigm for monitoring TB treatment response and may also demonstrate use as a TB diagnostic tool.

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