RNA-Seq reveals distinct renal responses to murine trypanosomiasis in susceptible and tolerant mice

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Abstract

Host factors play a key role in the outcome of infection with African trypanosomes. Despite the well-documented anaemia characteristic of trypanosome infection, little is known about the response of the kidney; an organ that is important in the response to dwindling oxygen levels and blood volumes.

Using BALB/C (susceptible) and C57BL/6 (tolerant) mice infected with *T. brucei*, we profiled the transcriptional responses and tissue architecture of the mouse kidney at early (acute) and late (chronic) time points of infection. At a tissue level, early infection is characterised by tubular necrosis accompanied by mononuclear cell infiltration and vascular congestion in both strains. As the infection progresses, BALB/c mice displayed a worsening tubular necrosis whereas C57BL/6 mice showed signs of reparative tubular regeneration, correlating with a reduced parasite burden in these mice.

Bulk transcriptomics and gene ontology analysis of the mouse kidney detected both mouse strain- and time-dependent transcriptional responses upon infection. Common immune signatures were upregulated in both strains at early time points, (TNF, B cell receptor, and C-type lectin signalling pathways), with IL-17 signalling a significant feature in susceptible BALB/C, coinciding with the onset of an inflammatory response. The transcriptome of C57BL/6 was dominated by genes associated with cell cycle, DNA replication and JAK-STAT signalling pathways. During the chronic stage of the infection, gene pathways associated with complement and coagulation cascades were preferentially upregulated in BALB/C. Taken together, trypanosome infection induced similar lesions and responses in the kidneys of both strains early in the infection. However, reparative, and proliferative mechanisms were uniquely upregulated in tolerant C57BL/6 but not susceptible BALB/C, coinciding with the histological findings. The increased susceptibility of BALB/C may be related to increased parasite burden, a reduced ability to repair damaged organs or a combination of both features.