Effector CD4⁺ T cells recognize intravascular antigen presented by patrolling monocytes

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In recent years advances in imaging technology has brought attention to the concept of immune patrolling of the vasculature.¹ Classically, monocytes were viewed as being abundant in blood but then readily extravasating to inflammatory sites in target tissues. "Non-classical" monocytes (also known as patrolling monocytes) remain in the vascular system and will engage in long-term migration along the endothelium either with or against blood flow. Recognition of "non-classical" monocyte migration along the endothelium has been made possible due to advances in multi-photon intravital imaging platforms and this process has been described in numerous tissues and several small animal models.

Last month Westhorpe and colleagues published an impressive manuscript in *Nature Communications*² that provides exciting new details on how the immune system interacts with the glomerulus in glomerulonephritis. Using intravital multiphoton imaging of the kidney, the authors examined immune cell interactions with the glomerulus. First they established that CD4⁺T-cells migrate constitutively to an uninfamed glomerulus with increased retention in antigen-bearing glomerular capillaries. The authors subsequently showed that MHCII⁺monocytes also migrate to glomerular capillaries, that T-cells interact with these monocytes, and (most importantly) that MHCII⁺ monocytes were required for T-cell induced neutrophil activation and glomerular inflammation in a mouse model of ovalbumin-induced glomerulonephritis.

While the role of T-cells in glomerulonephritis has been described previously³, this study provides convincing evidence that MHCII⁺"patrolling" macrophages play a critical role in at least one form of experimental

glomerulonephritis. In my opinion, the methodology used is sound and, indeed, at the very leading edge of this field. The multiphoton images in the main body of the document are clear and the videos in the data supplement strongly support the authors' conclusions. It is important, however, to acknowledge that the process of immune surveillance is far more completely understood in mice than it is in humans where many of the labeling techniques employed for visualization of immune cell-endothelial interactions are not possible. In addition, this is a single animal model of glomerulonephritis and whether this is conserved across other forms of glomerulonephritis is unclear. It is worth noting that the authors observed immune patrolling in the non-diseased state which is at least suggestive of the process being conserved across multiple pathological states. Regardless, the results must be corroborated by other groups in other experimental models and ultimately in human glomerulonephritis. If this process proves true however, patrolling macrophages may represent a novel target to interfere with intraglomerular antigen presentation and ultimately, T-cell-mediated glomerular inflammation.

REFERENCES:

1. Buscher et al.(2017)*Front Cardiovasc Med* 4:80. dx.doi.org/10.3389/fcvm.2017.00080
2. Westhorpe CLV et al.(2018) *Nat Comm* 9:747. dx.doi.org/10.1038/s41467-018-03181-4
3. Summers SA et al.(2009)*J AM Soc Nephrol* 20:2518-2524. dx.doi.org/10.1681/ASN.2009030337

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