&\WRNLQHV LQ DWKHURVFOHURVLV GLVHDVH SURJUHVVLRQ therapeutic approaches

'LSDN 3 5DPML 7KRPDV 6 'DYLHV -RH : (0RVV -HVVLFD :LOOLDPV)ÀRQ +DUULV $OH[-RV
Cardiff University UK

Atherosclerosis, the underlying cause of heart attack and stroke, is an in ammatory disorder of the vasculature regulated by both the innate and adaptive immune systems. Cytokines play a pivotal role in controlling the in ammatory response in atherosclerosis and regulate all the di erent stages in disease progression. Current approaches to target pro-in ammatory cytokines include neutralization using blocking antibodies or soluble decoy receptors and the use of speci c inhibitors against key components of intracellular signaling pathways. In contrast, approaches for anti-atherogenic cytokines include their local delivery and the use of agents that augment their expression/actions. Numerous cytokines are expressed in atherosclerot lesions and it is therefore essential that their actions in disease progression are fully understood to validate their therapeuti potential and to identify potentially new targets or approaches for therapeutic intervention. My laboratory has recently been investigating cytokine signaling in atherosclerosis, particularly in macrophages that play key roles in all stages of diseas progression, using a combination of in vitro and vivo approaches. Novel insights have been obtained on the actions of the cytokines interferon-gamma, transforming growth factor-beta, interleukin-33 and tumor necrosis factor-like protein 1A on key macrophage processes in atherosclerosis (e.g. foam cell formation, regulation of in ammation). For example, we have identi ed a key role for extracellular signal-regulated kinase: signal transducer and activator of transcription-1 serine 727 phosphorylation axis in the control of macrophage foam cell formation and the regulation of pro-in ammatory gene expression by interferon-gamma. e outcome of our studies on di erent cy1_0 1 Tf 0.118 Tw [(a)1av.9 cf e id9 (n)4 (d)c15.9 (

Notes: