S02-1 **NeuroImmunoMetabolic regulation of cardiac homeostasis and heart failure**

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Heart failure is a complex clinical syndrome characterized by cardiac function that is insufficient to meet systemic demand. In addition to abnormalities intrinsic to the heart, dysfunction in other organs and systemic factors greatly affect the development and consequences of HF. In particular, nearly half of chronic HF (CHF) patients also have chronic kidney disease (CKD), which increases their rate of cardiovascular mortality, suggesting cardiorenal linkage via mechanisms still poorly understood. We found that pressure overload in the heart activates renal collecting duct (CD) epithelial cells via sympathetic nerves. Within the kidneys, activated communication between CD cells, tissue macrophages and endothelial cells leads to secretion of CSF2, which in turn stimulates cardiac-resident macrophages essential for the myocardial adaptive response to pressure overload. We show that CD-specific deletion of the transcription factor *Klf5*, renal sympathetic denervation or adrenergic beta2 receptor blockade/deletion disrupts the renal response to cardiac pressure overload. Our results clearly demonstrate that dynamic interplay between the heart, brain and kidneys is necessary for proper adaptation to cardiac stress. In the heart resident macrophages control cardiac metabolism in the steady state, pointing to an immunometabolic crosstalk in the maintenance of cardiac homeostasis.