Sympathetic stress and cardiac injuries

With the support by the National Natural Science Foundation of China, a study by the research groups led by Prof. Zhang YouYi (张幼怡) from Peking University Third Hospital demonstrates that inflammasome activated IL-18 triggers sympathetic stress-induced cardiac inflammatory injuries, which was published in *European Heart Journal* (2018, 39(1): 60—69, with editorial, IF 20.212).

Sympathetic overactivation triggers and exacerbates cardiovascular disorders such as coronary artery disease and stress cardiomyopathy. β-blockers are recommended for these cardiovascular diseases but are still contraindicated in some patients. Inflammatory responses caused by β-adrenergic stimulation play pivotal roles in myocardial damage and pathological remodeling resulted from sympathetic overactivation. However, molecular and cellular mechanisms by which β-adrenergic insults elicit inflammatory responses in the heart still remain unknown. This is a prevailing issue in understanding the pathogenesis of cardiovascular diseases that involve sympathetic overactivation and crucial for the identification of novel targets to inhibit cardiac inflammatory injury caused by acute β-adrenergic insults.

In order to bridge this gap, Zhang's group provided the profiling analysis characterizing the spatial and temporal changes of inflammatory activation upon acute β-adrenergic insult. They demonstrated that the activation of IL-18 by inflammasome specifically in the cardiomyocytes is a key trigger for the cytokine cascade and macrophage infiltration in the heart, which in turn leads to adverse cardiac remodeling. Moreover, they provided evidence using the acute coronary syndrome (ACS) patient sample, indicating an increased IL-18 level in patients with sympathetic overactivation. In addition, heart function was reduced in patients with higher IL-18 levels, and cardiac diastolic dysfunction was increased after β-adrenergic agonist administration in mice. In order to prove the clinical relevance of their findings, the authors utilized an IL-18-neutralizing antibody and found that an early administration of the antibody after β-adrenergic insult significantly reduced inflammatory responses and cardiac injuries.

By this work, Zhang's group provides novel insights into the molecular mechanism of β-adrenergic insult and identified IL-18 as a novel and selective therapeutic target against sympathetic stress-induced cardiac inflammatory injuries. As the editorial described, this study "perfectly demonstrate the translational chain from molecular—experimental approaches to the evaluation for novel immunomodulating therapeutic targets".