Novel functions of Gasdermin D during NETosis and apoptosis

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Abstract
Apoptosis, NETosis and pyroptosis are different forms of cell death pathways that are important for the clearance of damaged, transformed or infected cells. Until recently, it was believed that these forms of cell death were independent of each other, however, emerging evidence from us and others are now challenging this concept. We found that Gasdermin D, a recently identified pore-forming protein that drives macrophage pyroptosis downstream of inflammasome activation, is also required for the execution of Neutrophil Extracellular Traps (NETosis), and to initiate inflammatory cell death during chemotherapy-induced apoptosis. Here, I will present a previously uncharacterised mechanism by which neutrophils defend against cytosolic Gram-negative bacterial infection. We found that cytoplasmic bacteria activate Gasdermin D to trigger neutrophil plasma and nuclear membrane rupture to induce the extrusion of antimicrobial NETs. In addition, I will highlight a novel mechanism of Gasdermin D activation during apoptosis and discuss the mechanisms by which effector caspase-3 and -7 suppress lytic cell death during apoptosis.

Kaiwen received his PhD in Immunology (2015) for his research on the characterisation of neutrophil inflammasomes, in the laboratory of Prof Kate Schroder at the University of Queensland, Australia. His subsequent postdoctoral training with Prof Schroder investigated cell death signalling in neutrophils, with a particular focus on necroptosis and NETosis. With the support of a Marie Skłodowska-Curie Individual Fellowship and a Swiss Government EKAS Excellence Postdoctoral Fellowship, Kaiwen moved to Switzerland and joined Prof Petr Broz’s laboratory in 2018. His current research focuses on the cross talk between cell death and innate immune signalling during development, infection and cancer chemotherapy.