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Further Characterisation of NLRP10 Functions in Human Cell Lines

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Members of the nucleotide-binding oligomerization domain (NOD)-like receptors (NLR) are intracellular pattern recognition receptors (PRR) and recognize a broad spectrum of damage- or pathogen-associated molecular patterns (DAMP and PAMP). One group of NLR proteins (NLRPs) are characterised by an N-terminal pyrin domain (PYD), typically responsible for inflammasome formation by associating to the adaptor ASC. This leads to maturation of caspase-1, subsequent interleukin-1?-processing, gasdermin-D cleavage and pyroptotic cell death. All human NLRPs except for NLRP10 contain leucine-rich repeats (LRR), that can serve as PAMP sensor domains. This, raised the question whether NLRP10 is directly engaged in pathogen recognition.
In response to bacterial challenge (e.g. Shigella flexneri), we showed before that NLRP10 can contribute to pro-inflammatory responses and recently identified Abin-1, a negative regulator of NF-?B, as a direct interaction partner of NLRP10 leading to destabilisation of Abin-1 and subsequent enhanced proinflammatory signalling. Recent work from Próchnicki et al. showed that NLRP10 can form an inflammasome in epithelial cells and suggested mitochondrial stress as one key activator. To further understand the function of NLRP10 we generated and characterised stable HeLa cell lines, which allow doxycycline-inducible eGFP-NLRP10 expression as well as CRIPR ko cell lines. With these cell lines we aim to understand how NLRP10 contributes to cell death and inflammatory signalling in response to bacterial infection and cellular stress. First results provide evidence that the NLRP10 interactome dramatically changes upon induction of mitochondrial stress by m-3M3FBS. Analysis of the differentially bound proteins and their functional link to NLRP10 will help to better understand NLRP10 in the context of inflammation, cellular homeostasis and innate immunity.