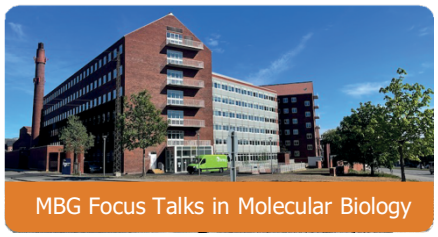
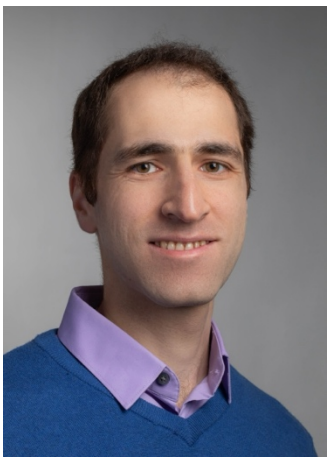
MBG FOCUS TALK

Hosted by Rune Hartmann



Wednesday 30 October 2024 @ 15:00

Online (*https://aarhusuniversity.zoom.us/j/66307084128*)



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Tissue adaptation to damage

Living organisms effectively manage a wide array of external and internal stressors to ensure their survival and optimal function. While a majority of research has focused on cellular stress responses, tissue-level stress responses remain poorly defined. Stressors can cause tissue damage resulting in infections, fibrosis, and cancer. Moreover, repeated exposure to damaging stressors can provide anticipatory strategies for improved resilience. Mechanisms behind these tissue adaptations to stress are not well understood. To shed light on these questions, we developed an experimental model where animals were exposed to the proteolytic toxin LasB in the lungs either once or three times. We discovered that single LasB exposure resulted in lung damage, red blood cell infiltration, and the release of heme, resulting in reduced lung function. Repeated exposure to LasB resulted in reduced damage and improved lung function and protected animals from subsequent bacterial and viral infections. Using genetic mouse models, sequencing, and pharmacological approaches, we determined that this adaptation is dependent on sensing of oxidative heme, comprising the tissue-level oxidative stress response. We found that lung alveolar macrophages are the main sensors of oxidative stress. Upon heme sensing, they activate nuclear factor erythroid 2-related factor 2 that induces expression of an antioxidant gene program, including heme oxygenase 1 (Hmox1). Hmox1 catabolizes heme, resulting in the accumulation of bilirubin that can relay cytoprotective responses to neighboring cells. This study provides a framework for understanding tissue remodeling and the development of memory to tissue damage.

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