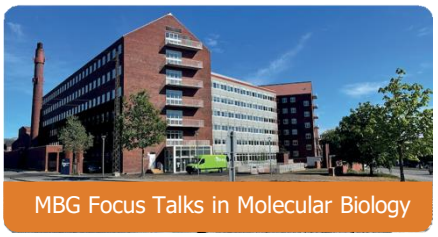
MBG FOCUS TALK

Hosted by Rune Hartmann



Thursday 3 October 2024 @ 09:00-09:45
Faculty Club (1870-816)

Tim Willinger

Center for Infectious Medicine (CIM)

Karolinska Institute

Stockholm, Sweden

Metabolic Signals Regulating Macrophage Differentiation in Lung Injury

Monocytes occupy niches in damaged tissues where they differentiate into macrophages. Monocyte-derived macrophages play an important role in the outcome of lung injury, yet the signals regulating the injury-induced differentiation of monocytes into macrophages are poorly understood. Tissue damage induces the local production of metabolites, and we found that cholesterol is metabolized during lung injury. Moreover, using single-cell RNA-sequencing, we discovered that disease-associated human lung monocytes sense inflammatory cholesterol metabolites that are induced by lung injury. Genetic loss-of-function studies in mice revealed that damage-induced cholesterol metabolites promote the differentiation of monocyte-derived macrophages in the inflamed lung. We confirmed these results using new genetic tools for the specific depletion of distinct populations of lung macrophages. Using multiplexed immunofluorescence microscopy, we found that cholesterol metabolites guide monocytes to specific macrophage niches in the lung. Furthermore, we defined how cholesterol metabolite sensing shapes the molecular program of monocyte-derived lung macrophages. Overall, our study shows how immune sensing of injury-induced metabolic signals stimulates the differentiation of monocyte-derived macrophages in the inflamed lung. In the future, targeting cholesterol metabolism could represent a new way to treat inflammatory lung diseases.

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