Inflammasomes and mesothelial to fibroblast transition (MFT): is there a connection?

Joyce K. Thompson[1], Stacie Beuschel[1], Maximillian B. MacPherson Arti Shukla[1]
University of Vermont, College of Medicine, Department of Pathology

Asbestos exposure has been shown to activate the NLRP3 inflammasome in immortalized human peritoneal mesothelial cells (LP9/hTERT) leading to the activation of caspase-1 and mature IL-1β secretion by mechanisms that are not completely understood. Additionally, IL-1β has been shown to promote mesothelial cell proliferation as well as mesothelial to fibroblastic transition (MFT, a form of epithelial to mesenchymal transition (EMT)) upon exposure of mesothelial cells to erionite. This implies that MFT/EMT may be regulated in part by the inflammasome. We therefore hypothesize that the asbestos-induced MFT may in part be regulated by the inflammasome. The study of the MFT process and its regulation by the inflammasome will lend a better understanding of initiating processes leading to mesothelioma. We have generated data to indicate that exposure of LP9 cells (as well as primary human pleural mesothelial cells) to asbestos leads to the differential expression of genes involved in the MFT pathway after 24 and 48 h. Studies are also underway to assess inflammation, MFT related gene expression and morphological changes in wild type and NLRP3 knockout mice exposed to asbestos for 5 and 60 days. Understanding these acute and chronic changes will subsequently help identify targets in the MFT pathway and their regulation by the inflammasome and how they can be used as drug targets. This work is supported by NIH grant RO1 ES021110.