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A TSPO ligand Ro5-4864 as an inhibitor of NLRP3 inflammasome

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Translocator protein 18 kDa (TSPO) is a protein located on the outer membrane of mitochondria. TSPO is expressed mainly in glial cells in the central nervous system and its expression level is highly up-regulated during neuronal injury and neuroinflammation. We previously reported that TSPO acts as a negative regulator of microglia activation. However, it is not known yet whether TSPO is involved in inflammasome signaling. Inflammasomes are multiprotein complexes for caspase-1 activation and IL-1 β processing and implicated in many inflammatory diseases. In this talk, I present the evidence that the prototypical TSPO ligand, Ro5-4864 (Ro5) inhibits NLRP3 inflammasome signaling in THP-1 cells using the canonical LPS-primed/ATP-induced NLRP3 inflammasome model. Ro5 efficiently blocked release of IL-1 β and caspase-1, and reduced ASC speck formation and NLRP3 translocation to mitochondria. Ro5 also attenuated LPS/ATP-induced perturbation of mitochondrial function by preventing generation of mitochondrial superoxide and depolarization of mitochondrial membrane potential. These results indicate that the immune modulatory effect of the TSPO ligand Ro5 is through inhibition of NLRP3 inflammasome signaling, suggesting Ro5 as a promising agent with efficacy for NLRP3 inflammasome-associated diseases.

Biography

Seong-Woon Yu has completed his PhD from Seoul National University, Korea and postdoctoral studies from Johns Hopkins University School of Medicine. He was assistant professor at the Departments of Neurology, Pharmacology and Toxicology in Michigan State University and now is associate professor of the Department of Brain and Cognitive Sciences, DGIST, Daegu, Korea. His research efforts are focused on the mechanisms of cell death of neurons and neural stem cells during neurodegeneration. The molecular mechanisms regulating neuroinflammation is also his main research interest.

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