Department of Biomedical Sciences

presents a seminar

"Possible role of non-selective channels in the inflammatory response of chronic diseases"

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Date : **27 November 2017**
Time: **11:00am to 12:30pm**
Venue: **Meeting Room 2-130, 1/F, Block 2, To Yuen Building**

Abstract

Connexins and pannexins are protein subunits of non-selective membrane channels called hemichannels, which are activated in inflammatory responses by different mechanisms and in diverse tissues. Both hemichannel types release ATP to the extracellular milieu where it activates P2 receptors leading to an increase of intracellular free calcium ion concentration that activates pannexin1 and connexin hemichannels. Therefore, more ATP is released to the extracellular milieu. Since connexin hemichannels are permeable to calcium ion, a feedforward mechanism proper of inflammatory responses is generated. In the brain, we identified a cell-cell conversation mechanism mediated by a hemichannel-dependent release of proinflammatory cytokines and two neurotoxic gliotransmitters, glutamate and ATP. This mechanism involves cells of the innate immune system as well as parenchymal cells and operates in all neuroinflammatory diseases so far studied. On the other side, normal adult myofibers of skeletal muscles do not express connexins but upon denervation their inflammasome becomes activated in a hemichannel-dependent manner without participation of infiltrated inflammatory cells. This response is completely prevented in myofibers deficient in connexin expression or treated with D4, a potent and selective connexin hemichannel blocker recently discovered. Similarly, brain degeneration and dysfunction is prevented by D4 that preferentially blocks glial hemichannels in models of epilepsy and Alzheimer disease. Consequently, it is proposed that tissue dysfunction of chronic diseases is the consequence of the inflammatory response triggered by the disease and not by the disease itself.

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All are welcome!