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A unique mode of interleukin-6 signalling in non-immune cells of the lung

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Interleukin-6 (IL-6) is a cytokine characterized by its pleiotropic actions. It regulates many cellular functions (e.g. inflammation, survival, proliferation) on a vast array of cells in many organ systems. IL-6 signals via two distinct types of cellular receptors; IL-6 receptor α subunit (IL-6R), and glycoprotein 130 (gp130). Upon IL-6 binding, the IL-6/IL-6R complex associates with gp130 which leads to activation of numerous downstream pathways to modulate cellular functions. While the expression of IL-6R is limited to certain immune cells, gp130 is expressed on almost all cells of the body. This leads to the notion that IL-6 acts on a broad range of non-IL-6R expressing cell types via an alternate signalling mode. In this regard, IL-6 signals via 2 distinct modes;

(i) "classical" signalling via its cell membrane-bound IL-6R, which orchestrates both innate and adaptive arms of the immune response against bacterial, fungal and viral pathogens.

(ii) IL-6 can signal by an alternate mode called trans signalling (TS) via a naturally-occurring soluble (s) IL-6R, which forms an IL-6/sIL-6R complex. It has demonstrated that IL-6TS can alter several cellular and molecular processes in different tissues, such as bowel, peritoneum and cartilage, though the predominant mode of IL-6 signalling in the lung has not been studied. We have discovered that the increased expression of IL-6 in a genetic mouse model with a knock-in mutation in gp130, causes a disruption to lung architecture leading to emphysema. Accordingly, we have employed these mice in an innovative and novel experimental approach based on the targeted inhibition of IL-6 signalling to determine which signalling mode preferentially contributes to emphysema development.

Biography

Saleela Ruwanpura is an outstanding young scientist who completed PhD in 2008 from Monash University, Australia. She has excelled in the cytokine field and has been successful in obtaining competitive funding such as Monash Faculty Bridging Postdoctoral Fellowship in 2009 and a prestigious NHMRC Training Postdoctoral Fellowship in 2010-2014. She has an excellent publication record relative to experience and opportunity (16.2 months of career interruption), which includes 12 publications in reputed journals, 1 further manuscript in preparation for the publication in *Science*. In addition, she has presented her research in the premier international/national meetings and has received several awards.

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