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**The role of mitochondrial dysfunction in inflammatory crosstalk between immune cells and non-myeloid cells such as fibroblasts and myoblasts****Katarzyna Swist-Szulik**

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**Introduction:** Mitochondria are double-membrane-bound organelles and primary source of cellular energy adenosine triphosphate (ATP). Mitochondria are also involved in innate responses and are necessary for NLRP3 inflammasome activation and maturation of IL-1 $\beta$  in immune cells. Research project investigates the role of mitochondrial dysfunction in cell to cell cytokine crosstalk.

**Aims:** To characterise the nature of cytokine crosstalk between fibroblasts and myoblasts with induced mitochondrial dysfunction and inflammatory cells such as monocytes and THP1 cells.

**Methods:** Stimulation with LPS (lipopolysaccharide) and benzylated ATP were used to cleave NLRP3 inflammasome and release IL-1 $\beta$  in monocytes and THP1 cells. Supernatants containing IL-1 $\beta$  from treated for inflammasomes THP1 cells as well as recombinant IL-1 $\beta$  were applied on fibroblasts and myoblasts with induced by Rotenone (Complex I inhibitor) mitochondrial dysfunction. Blocking experiment using anti-IL-1 $\beta$ , anti-IL-1 $\alpha$  antibodies as well as IL-1 receptor antagonist characterized the interactions between IL-1 $\beta$  and IL-6 cytokines. ELISA tests were used to measure the content of IL-1 $\beta$  and IL-6 in supernatants. Seahorse was used to assess the changes in bioenergetics profile of the treated cells.

**Results:** Fibroblasts and myoblasts release IL-6 in the presence of supernatants containing IL-1 $\beta$  from THP1 cells and monocytes in the dose dependent manner. Cells with induced mitochondrial dysfunction produce high levels of IL-6 level in close correlation with the degree of mitochondrial dysfunction and dose of recombinant IL-1 $\beta$ . IL-6 released by fibroblasts is inhibited 90% by adding IL-1 receptor antagonist (IL-Ra) and anti-IL-1 $\beta$  antibodies what would suggest single cytokine crosstalk between IL-1 $\beta$  and IL-6.

**Conclusions:** The data indicate the presence of crosstalk between monocytes and fibroblasts or myoblasts on the cytokine level characterized by IL-1 $\beta$  and IL-6 relationship. Ability to produce high levels of IL-6 by fibroblasts or myoblasts is amplified by degree of mitochondrial dysfunction and presence of IL-1 $\beta$  in dose dependent manner.

**Biography**

Katarzyna Swist-Szulik is working as a Consultant in Paediatric Intensive Care and has her passion in research on the role of mitochondria in inflammatory signalling. She is pursuing her PhD on the role of mitochondrial dysfunction in intercellular crosstalk between myeloid and non-myeloid cells. There are building evidences that mitochondria-inflammatory interactions are relevant to many disease processes such as inflammatory myopathies, neurodegenerative diseases, autoimmune diseases as well as multi-organ failure and drug induced sterile inflammation. She is working on developing the translation research investigating mitochondria-inflammatory relationship.

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