

Macrophage engulfment of apoptotic neutrophils controls their decision making during inflammation and its resolution

Amiram Ariel

**Department of Human Biology, University of Haifa, Israel*

The engulfment of apoptotic leukocytes (efferocytosis) by macrophages during the resolution of inflammation is essential for tissue homeostasis and results in macrophage reprogramming to anti-inflammatory and reparative phenotypes. However, a distinct subset of resolution phase macrophages lose their phagocytic potential, and hence were termed satiated macrophages. Here, we asked whether the loss of phagocytic capacity shapes macrophage phenotype at the molecular and functional levels, and whether novel mediators of resolution can be identified in these cells. We show, using an unbiased RNA-Seq analysis, that satiated macrophages express distinct gene profiles in comparison to phagocytic resolution phase macrophages that can be assigned to differential functions. Particularly, satiated macrophages expressed a distinct IFN β -related gene signature. Consequently, we determined IFN β is produced during the resolution of inflammation and facilitated resolution indices, such as PMN apoptosis, macrophage efferocytosis of apoptotic cells and reprogramming to pro-resolving phenotypes. These findings indicate for the first time that IFN β is a key effector cytokine in resolving inflammation.

Related research questions

Do macrophages govern inflammatory, fibrotic and metabolic disorders through different phenotypes?

Does the loss of phagocytic capacity change the phenotype and function of macrophages during inflammation and its resolution?

Can satiated macrophages serve as a source for resolution promoting mediators?

Suggested reading

New lives given by cell death: macrophage differentiation following their encounter with apoptotic leukocytes during the resolution of inflammation. Ariel, A., and Serhan, C. N. 2012. *Frontiers in Immunology*, 3:4. doi: 10.3389/fimmu.2012.00004.

Anti-inflammatory Mechanisms Triggered by Apoptotic Cells during Their Clearance. Szondy, Z., Sarang, Z., Kiss, B., Garabuczi, E., and Köröskényi, K., 2017. *Frontiers in Immunology*. doi.org/10.3389/fimmu.2017.00909

DELining resolution of inflammation, Fredman, G., 2019. *Nature Immunology* 20, 2-3.