

NCGG SEMINAR

“Immune signaling in aging: Targets to reverse immunosenescence”

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**Room: The 2nd floor Conference Hall Small
in the 1st Research building, NCGG**

<Reference for Seminar>

Aging is accompanied by many physiological changes and the immune system is not escaping this. This effect of time is affecting most cells of the immune system. Numerous changes have been described but most of them are phenomenological, a typical example is the change of phenotypes in T cells. We are interested since years to uncover the intracellular signaling associated with phenotypic and functional changes of various immune cells. We identified several signaling alterations starting from the early to the most downstream events in several cells like neutrophils, monocytes and T lymphocytes. We not only were interested in the forward signaling driven by kinases but also by the feedback or regulatory signaling mediated by phosphatases. We found profound alterations of regulatory phosphatases activity and phosphorylation (eg. SHP-1). The question was always whether these changes are occurring also uniformly in T cell or there are differences between the various subpopulations (naive to the continuum of memory T cells). Our studies clearly indicate that there are no changes according to the subpopulations and that basal hyper-phosphorylation status we observe may be explained by other signaling crosstalks. Immune cells in elderly individuals are likely to adopt a differential metabolism suggested by the altered membrane composition (cholesterol, lipid rafts). The question rose whether by modulating some of these modulators of signaling we could improve functionality of cells. We used high-density lipoproteins (cholesterol transport), SHP-1 inhibitor and C4-GSH (Th1/Th2 regulator) and found that these are able to improve the functionality of cells, while Vitamin E was not. In conclusion, alterations of early events of signaling cascades may be corrected. A better understanding of the changed signaling crosstalks induced by the modulation is necessary.

1. A Page, C Fortin, H Garneau, N Allard, K Tsvetkova, A Larbi, G Dupuis, T Fülöp. SRC homology 2 domain-containing phosphatase-1 (SHP-1) is a negative T cell regulator of T lymphocyte responses associated with aging. *Cell Commun Signal*. 2014;12(1):2.
2. CF Fortin, A Larbi, N Douziech, O Lesur, T Fülöp. Impairment of SHP-1 down regulation in lipid rafts under GM-CSF stimulation contributes to the age-related altered human PMN functionality. 2006, *J. Leuk. Biol.* 79(5): 1061-1072.
3. T Fülöp, A Le Page, C Fortin, JM Witkowski, G Dupuis, A Larbi. Cellular signaling in the aging immune system. *Curr Opin Immunol*. 2014 ;29C:105-111.

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