

## RIGENERATIVE ORTHOPEDICS

### **Project title**

"Role of the adipokine visfatin in inflammation and metabolic syndromes"

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### **Abstract**

Population ageing represents the largest risk factor for chronic diseases, which impose enormous burdens on societies and economies. Ageing determines pathophysiological changes and metabolic complications, which establish a sub-clinical syndrome of "homeostatic frailty" that predisposes to chronic and degenerative diseases. The system composed by the adipokine visfatin (a.k.a. NAMPT) and the NAD-dependent protein deacetylase SIRT1 plays a key role in maintaining and enhancing the robustness of physiological processes. We recently identified NAMPT as a critical modulator of both immunometabolism and differentiation of anti-inflammatory myeloid cells under stress conditions. We aim to investigate the relevance of the NAMPT system in the "homeostatic frailty" of the elderly population. We will focus on osteoarthritis (OA), the third most common chronic condition in the elderly, a disease associated with metabolic dysfunctions causing significant disability and decreased quality of life.

### **Main technical approaches**

Expression of NAMPT, evaluation of energy metabolism and role of NAMPT system in myeloid cell

differentiation and polarization; description of methylation patterns in human and murine OA settings; adipokine circulating levels in OA and control mouse sera; publication of a manuscript about role of NAMPT system in myeloid differentiation and polarization. Month 18-36: Identification of the inflammatory circuits and epigenetic events promoting age-related NAMPT downregulation; study of the impact of NAMPT system and adipokine cluster in experimental model of OA and in OA patients; publication of manuscript on the role of age-related NAMPT system impairment and its involvement in the pathogenic mechanisms of human and murine OA settings.

1-Expression of M1/M2 markers in mono/macrophages from HD and OA patients; correlation with NAMPT, SIRT1 and NAD and ATP levels

2-Recovery of the homeostatic capacity of macrophages from elderly by pharmacological supplementation

3-Role of NAMPT on MDSC differentiation

4-Description of methylation patterns in the NAMPT gene in HD and OA patients



5-NAMPT expression in the myeloid compartment, joint tissue and sera of OA and control mice

6-Adipokine levels in sera of OA and control mice

**Scientific references**

- 1 Gomes AP et al (2013) Cell 155, 1624-1638.
- 2 Yoshino J et al (2011) Cell Metab 14, 528- 536.
- 3 Imai S and Guarente L (2014) Trends Cell Biol 24, 464-471.
- 4 Brunet, A et al (2004) Science 303, 2011-2015.
- 5 Sica A and Mantovani A (2012) J Clin Invest 122, 787-795.