Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: The contribution of T cell aging to skeletal muscle regenerative decline

Synopsis:

The application of regenerative medicine solutions to the treatment of skeletal muscle (SkM) diseases requires a deep understanding of the changes happening in the SkM regenerative niche throughout life, and their consequences to repair efficiency. Immune aging is emerging as a fundamental aspect of SkM dysfunction and regenerative decline in old age. In the SkM, profound alterations in the immune environment accompany the aging process and immune modulatory strategies have been shown to have a beneficial effect in regenerative capacity of old animals. However, our incomplete understanding of the cellular mechanisms linking age-related immune dysfunctions and regenerative impairments limits the development of efficient regenerative solutions to improve the health of the aged and diseased SkM.

T cell aging is a central driver of organ dysfunction and T cells play an important role in the regulation of SkM regeneration. Our recent work identified age-specific T cell populations in the SkM of old mice, displaying a phenotype of exhaustion, abnormal cytotoxicity and activated regulatory activity. Preliminary experiments involving the adoptive transfer of T cells from old to young mice suggest that aged T cells have a negative impact on the SkM regenerative process. We hypothesize an involvement of these newly identified aged T cell subsets in the decline of regenerative capacity of the SkM during aging.

In this project, we propose to test the causal nexus between aged T cells and SkM regenerative failure, defining the link between aged T cell subsets and alterations in other niche populations and muscle stem cell (MuSC) behavior.

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