DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO

40th CYCLE
Project proposal for a Sapienza PhD scholarship

Main research line

Title: 3D chromatin organization in multipotent stromal cells: devising new reprogramming strategies to promote skeletal muscle regeneration

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Summary

Aging invariably causes deterioration of tissue homeostasis and regeneration, which is accompanied by functional decline in stem cell activity and disrupted niche interactions. Age-related alterations in stem and niche cells are caused by substantial epigenetic changes in gene expression patterns, with progressive loss of constitutive heterochromatin and disruption of nuclear lamina (NL) organization being the major epigenetic hallmarks of aging. Skeletal muscle is one of the main tissues compromised during aging that can culminate in sarcopenia, an accelerated form of muscle wasting. Age-related decline in muscle function is caused by both intrinsic and extrinsic changes in muscle stem cells (MuSCs) and its niche. Among the different MuSCs' niche cellular components, mesenchymal cells known as Fibro-Adipogenic Progenitors (FAPs) are emerging as crucial regulators of niche environment, having a considerable impact on the regenerative failure of sarcopenic skeletal muscles. Thus, understanding the epigenetic mechanisms behind FAPs fate and activity is key to devise preventive therapeutic strategies to restore or maintain an healthy niche.
We have recently demonstrated that genome-nuclear lamina interactions critically modulate FAPs identity and activity. However, whether their disruption underlies alterations in FAPs' fate, abundance and activity that cause the declined regenerative capacity of aged/sarcopenic muscles is still unknown. Thus, we aim to fill this gap of knowledge and to reveal how genome-NL interactions dynamically shape the fate of FAPs along the different phases of skeletal muscle regeneration and aging with the ultimate goal to identify molecular targets exploitable to reprogram FAPs towards therapeutically relevant fates.

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