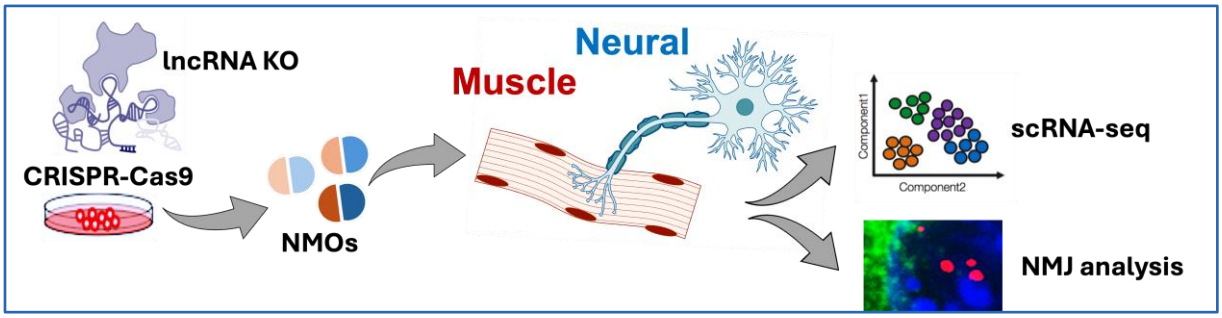
Finanziato dall'Unione europea NextGenerationEU | Ministero dell'Università e della Ricerca | Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA | Consiglio Nazionale delle Ricerche

Project title: Study of noncoding RNAs in organoids for muscle-nerve development



Acronym: NOMeN

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Description:

The neuromuscular junction (NMJ) is a specialized synapse where the motoneuron (MN) nerve terminal and the skeletal muscle fibre (SMF) convert electrochemical signals into muscle contraction. As a critical site for controlling movement, the NMJ is targeted by numerous diseases and pharmacological drugs, making it one of the most studied synapses. Despite the extensive expression/activity of the noncoding transcriptome, its contribution to NMJ development, structure, and function is still poorly described. This regulatory layer may offer insights into the biology of such a crucial anatomical junction.

Aims:

To fill this gap, NOMeN will shed light on NM differentiation and NMJ organisation through the lens of noncoding RNAs (ncRNAs). We will focus on tissue-specific long ncRNAs (lncRNAs) we previously identified as key players in MN or SMF maturation and function. This will be combined with the generation human NM organoids (NMOs) recapitulating the simultaneous, positionally precise, and interactive development of nerve and muscle lineages from a common pool of neuromesodermal progenitors.

Expected results:

This model will be analysed by a cutting-edge experimental package integrating lncRNA CRISPR-Cas9 knockout, single-cell RNA-seq, NMJ confocal imaging, and electrophysiology. We will delve into the:
- Cell type-specific gene contributions to NM differentiation/interfaces;
- Impact of lncRNAs on NM gene pathways;
- Non-cell-autonomous effects resulting from tissue-specific noncoding defects.

These aspects are relevant in NM disorders, where muscle-nerve crosstalk is a critical paradigm (denervation/muscle atrophy) or a challenging hypothesis (the "dying back" model).

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