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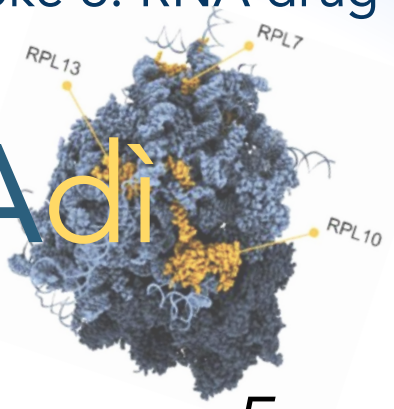
Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA
spoke.6

MUR PNRR National Center for Gene Therapy and Drugs based on RNA Technology

Spoke 6: RNA drug development

veRNAdì



A webinar series about RNA

to share projects and competences,
increase networking, discuss issues
and new ideas, and disseminate results

Every last Friday of the month

https://rb.gy/y40y6

7th veRNAdì: Friday 31 May 2024, 15:00

A deep dive into ribosome heterogeneity: insights from spinal muscular atrophy and opportunities for biomarker and drug discovery

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For decades ribosomes have been considered as static and homogeneous particles composed of highly conserved rRNAs and ribosomal proteins. Recent evidence suggests that they are more dynamic and heterogeneous machines, actively involved in translation regulation. This heterogeneity arises from many molecular interactors and epi-transcriptional and translational layers of modification, including for instance ribosomal associated proteins (RAPs), and rRNA/ribosomal protein variants and modifications. Ribosome heterogeneity is largely unexplored, and, in the context of diseases, it is a potential gold mine of innovative targets for drug and biomarker discovery. Focusing on the neuromuscular disorder spinal muscular atrophy (SMA) as a case study, our lab gathered evidence supporting the hypothesis that the survival motor neuron (SMN) protein, loss of which causes SMA, plays a key role in determining ribosome heterogeneity. Over the past years, we demonstrated that SMN interacts with ribosomes (SMN-primed ribosomes) orchestrating a platform modulating the translation of a specific set of mRNAs and, consequently, the cellular proteome. Recent data suggest that the methyltransferase fibrillarin – which is responsible for the deposition of 2'-O-methylations (2'Ome) on rRNA – interacts with the SMN-ribosome platform, suggesting that SMN might play a role in the modulation of epitranscriptional modifications of ribosomal RNA. Indeed, investigating the 2'Ome landscape both in vivo and in vitro in primary, patient-derived cultures, we identified alterations in SMA. Overall, our data indicate that the SMN-ribosome platform can be leveraged to identify novel biomarkers for SMA, including 2'Ome, an innovative target for biomarker discovery.