

Il cancro nell'era dell'RNA: risultati e prospettive dal Centro Nazionale CN3 – Spoke 2 “Cancer”

Alberto Boffi

*Full Professor of Molecular Biology, Sapienza University of Rome
Spoke Leader, CN3 Spoke 2 “Cancer”*

The development of RNA-based technologies is rapidly changing the landscape of cancer diagnosis and therapy, providing access to molecular targets and therapeutic strategies that were previously difficult to exploit pharmacologically. Within the PNRR National Center for Gene Therapy and Drugs based on RNA Technology (CN3), Spoke 2 “Cancer”, coordinated by Sapienza University of Rome, has brought together a large multidisciplinary network of universities, CNR institutes and industrial partners with the common objective of translating advances in RNA biology into new approaches to cancer treatment.

The activities of Spoke 2 have covered the entire translational pathway, from the identification of novel RNA biomarkers and therapeutic targets to their functional validation and preclinical development. Spatial transcriptomics and multi-omics approaches have provided new tools to dissect tumor heterogeneity and the interactions between cancer cells and their microenvironment. In parallel, different classes of RNA molecules—including miRNAs, siRNAs, antisense oligonucleotides and mRNAs—have been developed as therapeutic agents. Particular emphasis has been placed on mRNA-based cancer vaccines, non-coding RNA therapeutics and advanced delivery technologies.

A central challenge emerging from these activities is **RNA formulation and delivery**. Therapeutic activity requires not only the identification and engineering of the appropriate RNA molecule, but also its protection, formulation, cellular targeting and efficient intracellular delivery. To address this critical translational step, Sapienza has established the **RNA Formulation Lab**, the dedicated Spoke 2 Facility designed to support the development, optimization and characterization of RNA formulations and delivery platforms. The facility creates a direct connection between molecular discovery and preclinical translation, providing standardized workflows and technological support for the comparison and development of RNA formulations. Importantly, it is conceived as a shared infrastructure accessible not only to CN3 investigators but also to the broader academic community, research organizations and industrial partners. The

The scientific activities of Spoke 2 have also generated intellectual property, patent applications, startup and spin-off initiatives and collaborations with pharmaceutical and biotechnology companies. Together with the RNA Formulation Lab and the network of expertise established within CN3, these results provide the foundations for maintaining a national capability in RNA therapeutics beyond the formal duration of the PNRR.

The experience of CN3 Spoke 2 illustrates how a large research program can evolve from a collection of individual projects into an integrated ecosystem connecting RNA discovery, formulation and delivery, preclinical validation, technology transfer and entrepreneurship. The next challenge will be to consolidate this critical mass into a sustainable platform for the development of RNA-based precision oncology.