Computational RNA Biologist - Building an isoform-resolved structural atlas of cancer proteoforms

Are you fascinated by the AlphaFold revolution and by what it can reveal about the largely invisible layer of protein diversity in cancer?

We are looking for a postdoctoral researcher to lead the computational discovery pipeline connecting RNA isoform diversity to protein structure prediction, within the Molecular Machines in Signalling Pathways group led by Prof. Simona Polo at IFOM, The AIRC Institute of Molecular Oncology in Milan, Italy.

This is not a generic bioinformatics role. We want someone who who can reason about protein structure as fluently as about RNA sequence data and is excited about applying structural reasoning to one of the most dynamic and least explored frontiers in cancer biology: the proteoforms that alternative splicing creates.

The Challenge

Alternative splicing is pervasive in cancer, yet its structural consequences remain largely uncharted. You will:

- Integrate long-read (Iso-Seq/Nanopore) and short-read RNA-seq data from colorectal cancer cohorts to curate full-length transcript variants and define translationally supported open reading frames, combining transcript-level and ribosome profiling (Ribo-seq) evidence to distinguish real, translated isoforms from noise.
- Develop systematic workflows for investigating the structural consequences of alternative splicing (AlphaFold2/3, AlphaFold-Multimer, or equivalent): how exon inclusion or skipping events reshape domain architecture, interaction interfaces in cancer-relevant isoforms.
- Use the resulting atlas to generate concrete, testable mechanistic hypotheses: which isoforms lose or gain functional motifs, which show tumor-biased expression shifts, and which are worth prioritizing for experimental validation by the lab's wet-lab team.

Who You Are

You hold a PhD in structural bioinformatics, computational chemistry, or a closely related field, and you are drawn to biological questions rather than purely methodological ones. You bring:

- A track record of independent research (e.g. first-author publications) in genomics, RNA biology, computational structural biology, or a closely related field.
- Expertise integrating multi-omic sequencing data (long-read and short-read RNA-seq; ribosome profiling is a strong plus) to define transcript and ORF models.
- Genuine hands-on experience with AlphaFold2/3 or equivalent structure prediction tools, including at scale; you understand their confidence metrics and failure modes, especially for non-canonical or disordered proteoforms.
- Programming proficiency in Python. Working knowledge of container technologies (e.g. Singularity) and workflow managers (e.g. Nextflow) is a plus; experience with distributed/HPC computing (e.g. SLURM) is welcome but not required.
- A solid grounding in alternative splicing: understanding how isoform diversity translates into changes in protein fold, interaction surface, or disordered region composition.

- Comfort with protein biochemistry: you can reason about domain architecture, binding interfaces, allostery, and the structural consequences of post-translational modifications.
- Ability to work across multiple concurrent projects and communicate clearly to experimental colleagues.

Prior experience with colorectal cancer biology, RNA-protein interactions or cancer genomics is a plus, not a requirement. Curiosity, rigour, and ability to ask the right biological question matter most.

🌟 Why IFOM, Why Now

The lab has just uncovered a widespread alternative splicing reprogramming affecting hundreds of cytoskeletal and adhesion genes in colorectal cancer, a dataset now under active analysis, and the reason this is an exceptional moment to join. This builds on our track record in the functional and structural impact of alternative splicing (*Cell Rep.* 2023; *EMBO Rep.* 2022; *Nat Commun.* 2019; *Cell Rep.* 2016; *Nat Struct Mol Biol.* 2016). IFOM is one of Europe's leading molecular oncology institutes, supported by the Italian Association for Cancer Research (AIRC) and embedded in the Milan biomedical campus alongside the European Institute of Oncology (IEO) and the Italian Institute of Technology (IIT). This position is part of the five-year PI research programme supported by AIRC, with additional internal funding from IFOM, giving you the resources and the time horizon to build something ambitious from the ground up.

You will work across the full breadth of the lab's projects, collaborating directly with wet-lab researchers spanning cancer cell biology, patient-derived organoids, and biochemistry, contributing to high-impact publications and gaining broad exposure to cutting-edge experimental approaches.

Position Details

- Contract: 3-year postdoctoral position, in line with the AIRC-funded programme.
- Salary: up to €40,000 gross/year, depending on the candidate's seniority.
- Start date: as soon as possible, by mutual agreement.
- Location: IFOM, Milan, Italy (on-site).

📩 How to Apply

Send a single PDF to **simona.polo@ifom.eu** containing:

- Your CV, highlighting any independent research contributions (computational or experimental).
- A short cover letter (max one page) describing what draws you to apply and why the intersection of RNA biology and protein structure interests you.
- Contact details for two references.

Applications will be reviewed on a rolling basis until Sunday, 18 October 2026. Incomplete applications will not be considered. OnlineOnline interviews will follow shortly after the deadline. Informal enquiries about the position are very welcome and can be directed to Prof. Simona Polo at the address above.