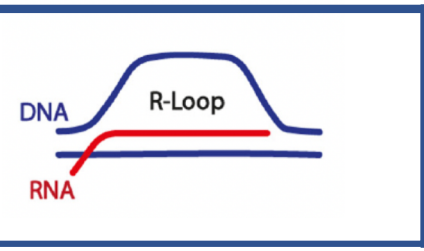

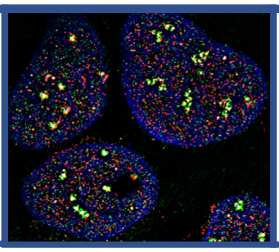

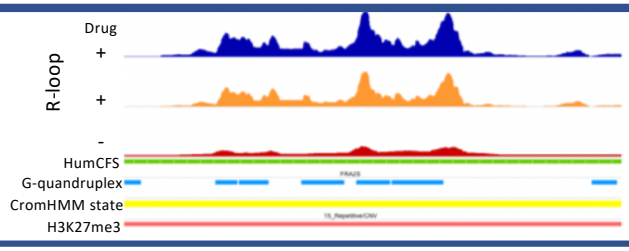

RESEARCH POSITION – ASSEGNO DI RICERCA:

The role of phase separation in the resolution of R-loops in repeated elements in cancer cells

(Il ruolo della separazione di fase nella risoluzione degli R-loop negli elementi ripetuti in cellule tumorali)

Laboratory for non-coding RNA and Genome Stability – Prof. Stefan Schoeftner
Department of Life Sciences, University of Trieste
https://dsv.units. it/it/research/researchareas/researchgroups/20382

Background:
R-loops are atypical, three-stranded nucleic acid structures that contain a 60-2000 nucleotide stretch of RNA:DNA hybrid sequences and an unpaired, single stranded DNA. R-loops are reported to encompass up to 5% of the human genome and control physiologically relevant processes. However, un-programmed or persistent R-loops represent a high risk for genome stability by mediating replication-transcription conflicts, interfering with DNA repair mechanism and becoming target for mutagenesis. R-loop mediated genome instability is reported to promote the formation of cytoplasmic DNA species leading to the activation of pathways of innate immunity.
Cancer cells use multiple mechanisms to prevent the formation of R-loops or resolve R-loops to suppress exacerbated levels of genome instability.
Preliminary data from the lab shows that induction of ectopic R-loops mediates the engagement of R-loop regulatory factors in phase separation. We hypothesize that phase separation may create subnuclear compartments that support R-loop resolution or eventually the repair of R-loop mediated DNA breaks. Remarkably, therapy resistant cancer cells show potentiation of phase separation processes, indicating clinical relevance.

Project activity:
R-loop management factors will be followed by time-lapse microscopy with particular focus on protein-shuttling and phase separation in the nucleolus, a subnuclear compartment prone to R-loop mediated genome instability. Past research discovered drugs that impair phase separation in our system. The impact of these compounds on nucleolar and genome stability, formation of rDNA containing cytoplasmatic DNA and innate immunity pathways will be investigated in normal and therapy resistant cancer cells. Functional tests will be flanked by molecular analysis such as mapping of R-loops and sites of DNA damage. Extensive research was carried out in the past year on this project. Depending on the training level of the candidate, we aim to submit scientific manuscript by the end of 2025.

Methods:
R-loop mapping, time lapse microscopy, immunoprecipitation (protein, chromatin), methods related to phase separation; immunofluorescence, DNA-FISH, RNA-FISH, cell culture

Contractual details:
Position is funded by a PRIN-PNRR project; € 27.000 (before all taxes; 12 months)
Ideal candidate hold a PhD title; however application of candidates with Master of Science title are welcome. Candidates should have experience in cancer cell biology, the use of classic cancer cell lines, immunofluorescence and molecular biology techniques. Experience in the analysis of genome stability, time-lapse microscopy or chromatin structure represents an advantage during the application procedure.
Duration of the research contract: 01.12.2024 – 29.11.2025 (negotiable)

For more project details, please contact: sschoeftner@units.it
For formal applications, please consult: https://amm.units.it/node/52080/assegno/pub

UNIVERSITÀ DEGLI STUDI DI TRIESTE
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