RNA Horizons 2024
Therapeutics Symposium
Unlocking the RNA's Potential in Medicine
September 25-27, 2024
Alfandega Congress Centre, Porto, Portugal

A novel imaging-based R-loop screening platform

Robert M. Martin, Madalena R. de Almeida, and Sérgio F. de Almeida

Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da **Universidade de Lisboa**, Lisboa, Portugal

R-loops are non-canonical nucleic acid structures composed of an RNA:DNA hybrid and a displaced DNA strand, which play roles in numerous cellular processes, but are also an important source of genomic instability and play a role in several human conditions. Indeed, several studies have linked changes in R-loop frequency and stability to oncogene activation or loss of tumor-suppressor genes in cancer models. Such findings give rise to novel anti-cancer strategies, which exploit elevated R-loop levels to further exacerbate DNA replication stress. Moreover, R-loops have the potential to serve as biomarkers for therapy sensitivity or cancer type classification. We have developed RHINO, a genetically encoded sensor that selectively binds RNA:DNA hybrids enabling live-cell imaging of cellular R-loops. This tool allows the measurement of R-loop abundance and dynamics in live cells with high specificity and sensitivity. We are developing a screening platform based on microscopic high content imaging of RHINO aimed at identifying small molecules and drugs which affect cellular R-loop levels as well as novel cellular factors with important functions in R-loop metabolism as potential targets.