POST-WEBINAR SUMMARY

Exposing Hidden Targets Within the mRNA Regulation Space

AnimaBiotech ENDPOINTSNEWS

Exposing Hidden Targets Within the mRNA Regulation Space

In a webinar hosted by *Endpoints News*, the co-founder and chief scientific officer of Anima Biotech, a leading drug discovery platform company in the field of mRNA biology, joins a world-renowned cancer biologist from Memorial Sloan Kettering Cancer Center to unpack the latest advancements in mRNA regulation research and the impact of these findings on drug discovery. This webinar is the first in a series on mRNA regulation.

- mRNA regulation is a highly complex and tightly controlled process that plays a fundamental role in protein synthesis. It directly responds to external and internal cues. It encompasses several general and highly target mRNA specific steps, including RNA processing, nuclear and cytoplasmic export, translation, and degradation. Gaining a comprehensive understanding of these intricate processes and developing the ability to manipulate them can have significant implications for disease treatment and the discovery of novel drugs.

- RNA processing is a critical phase in mRNA regulation, encompassing modifications such as alternative splicing and alternative polyadenylation. These modifications allow the mRNA molecule to adapt to the specific needs of the cell. Key participants in this process are RNA binding proteins which selectively bind to recognition sequences encoded in the untranslated regions (UTRs) of the mRNA transcript. RNA binding proteins selectively bind to specific splice sites, inhibiting the utilization of certain splice donors or acceptors. This process results in mRNAs with different exon structures, leading to potential functional diversity. Another aspect of RNA processing is cleavage and polyadenylation, which determines the length of the 3' UTR of the mRNA molecule and contributes to its steady state levels.

- Anima Biotech has developed advanced single cell, high-content, modalities that specifically focus on mRNA regulation. These modalities employ state-of-the-art RNA detection technologies in a high-throughput screening format, enabling the simultaneous assessment of the impact of compounds on both protein and mRNA levels. Through the screening of a diverse small molecule library of over 200,000 compounds, Anima discovers molecules that can modulate mRNA splicing and translation, thus discovering novel targets for unmet needs.

- Translation, the process by which proteins are synthesized, involves distinct stages: initiation, elongation, and termination. During initiation, ribosomes recognize specific structural features of the mRNA molecule and assemble to initiate translation. Translation terminates when a stop codon is encountered. The rate of translation is influenced by various factors, including the availability of transfer RNA (tRNA) which carries amino acids to the ribosomes, the presence of secondary structures in RNA or protein binding to mRNA. Proper regulation of translation rate is crucial to ensure accurate protein folding.

- Targeting the regulatory program of RNA holds immense promise for cancer treatment. RNA-binding proteins play critical roles in cancer progression, and their activity can be perturbed to disrupt cancer cell programs. For instance, Musashi-2 (MSI2), an RNA-binding protein, is indispensable for the function of leukemia stem cells. By inhibiting the binding of MSI2 to its RNA targets, it is possible to impair the leukemia stem cell program, potentially mitigating disease progression.

- Dr. Michael Kharas and his laboratory at Memorial Sloan Kettering Cancer Center focus on unraveling the dysregulation of RNA regulation in blood cancers, particularly acute myeloid leukemia (AML). Through their research, they have identified small molecules that can block the binding of MSI2 to its RNA targets, resulting in reduced tumor burden in animal models. Additionally, they investigate the role of PRMT5, which modified arginines residues in proteins by methylation, in cancer and have discovered a correlation between PRMT5 expression and MSI2 levels. Simultaneous inhibition of both PRMT5 and MSI2 has shown significant effects on oncogenes gene expression. Dr. Kharas' lab has also developed innovative strategies to map and measure the activity of RNA-binding proteins on their targets, thereby facilitating the screening of potential drug candidates.

WATCH THE WEBINAR

Stay tuned for upcoming Anima webinars in this series featuring renowned scientists from leading academia and institutions sharing their knowledge and insights. The series will explore the complex and dynamic world of mRNA regulation, with a focus on targeting regulatory events such as splicing, nuclear export, intracellular localization, degradation, stabilization, and translation for therapeutic purposes.

IRIS ALROY

Co-Founder and Chief Scientific Officer,
Anima Biotech

Iris Alroy, Ph.D., has over 25 years of experience in drug discovery, preclinical and early clinical development. Dr. Alroy has served as co-founder and CSO of Anima since 2015, supervising drug discovery and pipeline development in the emerging field of mRNA translation regulation. Prior to Anima, she acted as VP of Discovery at Proteologics and Pharmos Corp. and CEO of several startup biotech companies, including Fusimab, Ltd. and ProMining Therapeutics Ltd. Dr. Alroy earned her doctorate in Cell Biology from Cornell University and completed a post-doctoral fellowship at the Weizmann Institute. She has authored more than 20 scientific articles in peer-reviewed journals.

MICHAEL G. KHARAS

Member with Tenure, Molecular Pharmacology Program,
Memorial Sloan Kettering Cancer Center

Dr. Michael G. Kharas is an Investigator that leads a laboratory in the Molecular Pharmacology Program at the Memorial Sloan Kettering Cancer Center (New York, NY, USA) and Professor at Weill Cornell Pharmacology Graduate Program. Dr. Kharas finished his postdoctoral training at Brigham and Women's Hospital and studied how signaling pathways alters stem cell regulation. In 2011 he started his laboratory at MSK and focused on the controllers of cellular fate in the blood. His laboratory has uncovered new RNA regulators and how they modulate self-renewal, cell-fate decisions, and differentiation in both normal blood development and in myeloid leukemia. Also, his laboratory is developing inhibitors that block the function of RNA regulators as a new therapeutic strategy in cancer. Dr. Kharas has received recognition including the Leukemia Lymphoma Society Scholar Award and American Society of Hematology Scholar Award.

About Anima Biotech

Anima Biotech is advancing mRNA Lightning, a novel platform for the discovery of small molecule mRNA drugs and their mechanisms of action. The company's differentiated approach combines high-scale phenotypic screening that automates millions of experiments in live mRNA biology with MOAi technology using AI to elucidate the mechanism of action of active molecules. This approach has been validated by collaborations with Lilly, Takeda Pharmaceuticals and AbbVie and a broad pipeline across 20 different discovery programs in various therapeutic areas.

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