USF TECHNOLOGY TRANSFER

BIOPARTNERING

Investigator Highlight: Dr. Totary Jain RNA Biology Research

Dr. Hana Totary-Jain, Ph.D.

Associate Professor, Molecular Pharmacology and Physiology

Research Interests

Dr. Totary-Jain has a strong background in immunology, pharmacology and physiology and has worked in the RNA field for the past 23 years.

The goal of the Totary-Jain lab is the design and the delivery of cell-selective gene therapies to treat atherosclerotic cardiovascular disease, neurodegenerative disease, and infectious disease.

Since joining the Morsani College of Medicine at USF, her laboratory has focused on the development of a first of its kind cell-selective gene therapy that inhibits neointimal hyperplasia while preserving the integrity of endothelial cells following angioplasty.

In parallel, the Totary-Jain lab has uncovered the role of retrotransposons in the antiviral response. She has developed new methods to visualize and measure the expression levels of retrotransposons, and designed novel therapies for neurogenerative, cardiovascular and autoimmune diseases.

Interdisciplinary and Emerging Signature Programs

- Allergy, Immunology, Infectious Disease
- Biomedical Engineering & Nanomedicine
- Cardiovascular Sciences
- Women & Children's Health

Main Research Projects

- Develop site- and cell-selective anti-atherosclerotic nanotherapies that simultaneously inhibit infiltration and proliferation of inflammatory and vascular smooth muscle cells while preserving the integrity of endothelial cells.
- Investigate the role of LIN28B/let-7 switch in the pathogenesis of infantile hemangiomas (IHs)
- Elucidate the mechanism by which the microRNA cluster on chromosome 19 provides intrinsic protection against viral infections.

Seeking Collaborations, Sponsored Research and Licensing Opportunities.

Technologies

Retrotransposons Alu SINES of the mir-498(46) cistron mediate intrinsic interferon and antiviral response in human placenta

USF Tech ID# 18A080, 21A087, 23T070

Overview: Viral infections during pregnancy have often caused devastating effects on pregnancy outcome, fetal development, and maternal health. Since the defense against pathogens during pregnancy conflicts with the tolerance to the allogenic fetus, the placenta at the maternal-fetal interface has developed a unique antiviral defense mechanisms. Unlike somatic cells which require antiviral signals to mediate interferon (IFN) induction, human synctiotrophoblasts constitutively produce type III IFNs, even in the absence of a viral infection, by unknown mechanisms.

Researchers at USF investigate the protective role of Alu retrotransposons (RTs), which are constitutively transcribed with mir-498(46) cistron (known as C19MC) in the placenta, against viral infections during pregnancy. The inventors have developed a novel method of predicting the susceptibility or severity for viral infection during pregnancy by measuring and monitoring Alus. The inventors showed that transcriptional activation of miR-498(46) cistron increases Alu dsRNA that mediates the intrinsic type III IFNs production and antiviral protection and thus can be used as a therapeutic intervention.

Advantages:

- Predict susceptibility for infection or severity of infection in pregnant women
- Reduced viral infections during pregnancy
- Protection of both maternal and fetal health against infections
- Uses the placenta at the maternal-fetal interfaces for antiviral response

Preventing Alu SINEs-mediated Pathologies

USF Tech ID# 21A094

Overview: Retrotransposons (RTs) are the most abundant class of the transposable elements that comprise approximately 45% of the human genomic sequence, of which Alu repeats (Alus) are the most abundant and comprise 11% of the genomic sequence. Alus, named after the internal AluI restriction site found in these repeats, belong to the short interspersed nuclear elements (SINEs), which are non-autonomous RTs. Alu RTs are constitutively transcribed with mir-498(46) cistron (known as C19MC) in the placenta and are responsible for the viral resistance of the placenta.

USF researchers have shown that transcriptional activation of the mir-498(46) cistron in the placenta leads to an increased expression of antiviral type III interferon (IFN) and numerous IFN stimulated genes, in a miRNA independent manner and in the absence of viral infection. Now, the researchers are investigating the role of Alu double stranded (ds) RNA play to facilitate the intrinsic viral resistance of the placenta and the role of RNA-binding protein LIN28B plays to counterpoise the Alus dsRNA. Understanding this regulatory interplay between Alu dsRNA and LIN28B is essential to understand how alterations in this balance can lead to either excessive IFN-related pathologies and deleterious impacts on fetal and maternal health, or failure to restrict viral spread.

Targeting Alu RNA to Treat Atherosclerotic Cardiovascular Disease

USF Tech ID# 23T075

Overview: Atherosclerotic cardiovascular diseases continue to be the leading cause of death worldwide. Viral infections, such as SARS-CoV-2, accelerate atherosclerotic plaque progression and increase the incidence of myocardial infarction and strokes. Previous studies indicated that viral infections increase retrotransposon (RT) expression; however, their role in exacerbating the chronic inflammatory state of atherosclerosis has not been explored.

USF researchers discovered that increases in RT expression by viral infections exacerbate the inflammatory state of atherosclerosis and increase the risk of plaque rupture. They showed that human lungs and coronary arteries (hCA) isolated from SARS-CoV-2 positive patients exhibited increased expression of Alu RNA, RNA retrotransposons, as well as inflammasome-associated genes and pro-inflammatory cytokines.

These results indicate that Alu RNA plays an important role in inducing the sustained non-resolving inflammation in atherosclerosis and that targeting Alu RNA with antisense oligo or with siRNA represent a novel anti-atherosclerotic therapeutic strategy that targets the inflammatory pathway.

Method to visualize Alu RNA in Tissue

USF Tech ID# 23T072

Overview: Retrotransposons (RTs) are the most abundant class of the transposable elements that comprise approximately 45% of the human genomic sequence, of which Alu repeats (Alus) are the most abundant and comprise 11% of the genomic sequence. Alus, named after the internal AluI restriction site found in these repeats, belong to the short interspersed nuclear elements (SINEs), which are non-autonomous RTs.

USF researchers have discovered that following a viral infection transcribed Alu RNAs are expressed in human tissues and that these Alu RNAs can induce a sustained IFN mediated inflammatory response, which can be pathological. They have developed an in situ hybridization method to visualize Alu RNA in tissues.

Method for Measuring Alu RNA

USF Tech ID# 23T071

Overview: Retrotransposons (RTs) are the most abundant class of the transposable elements that comprise approximately 45% of the human genomic sequence, of which Alu repeats (Alus) are the most abundant and comprise 11% of the genomic sequence. Alus, named after the internal AluI restriction site found in these repeats, belong to the short interspersed nuclear elements (SINEs), which are non-autonomous RTs.

USF researchers have discovered that following a viral infection, transcribed Alu RNAs are expressed in human tissues and that these Alu RNAs can induce a sustained IFN-mediated inflammatory response, which can be pathological. Thus, sustained increased leveles of Alu RNA can be considered a biomarker for infections, autoimmune disease, preeclampsia, aging, neurological disease, and cancers. The researchers have developed a competitive RT-PCR method to measure Alu RNA.

Development of a novel messenger RNA therapeutic to treat atherosclerosis

USF Tech ID# 22A053

Overview: Atherosclerotic cardiovascular disease (CVD) continue to be the leading cause of death worldwide. Currently available treatment options increase the incidence of neo-atherosclerosis and in stent thrombosis. While the common therapy approach has been to treat the inflammation observed in atherosclerotic cardiovascular disease, site- and cell-selective therapies that target the atherosclerotic plaques, but not the endothelium are currently not available.

USF Researchers have combined miRNA-switch and siRNA technology to develop a novel vascular endothelial growth factor A (VEGF-A) mRNA therapeutic to selectively target atherosclerotic plaques while protecting the endothelium.

Cell-Selective Gene Editing

USF Tech ID# 15B161

Overview: Modified mRNA-based therapeutics hold great promise for numerous untreatable diseases. The potential advantages of modified mRNA biomolecules include reduced toxicity, decreased activation of the innate immune pathway, and improved translation in virtually all cell types, including non-dividing cells by circumventing nuclear localiza-tion. Additionally, modified mRNA provides enormous flexibility with respect to production and application, because any protein with a known sequence can be encoded and expressed. Lastly, modified mRNA can be produced rapidly in a cell-free, cost-effective manner. While modified mRNA presents an intriguing therapeutic option for drug delivery and disease treatment, its potential silencing by small interfering RNA or microRNA remains an issue.

Our inventors have discovered how microRNA target sequences could be added to guide RNA to selectively edit genes. This strategy is able to achieve cell-selective gene editing, gene activation, or gene sup-pression and it offers the capacity for multiple genes to be edited, activated or suppressed and multiple cell types to be selectively tar-geted simultaneously in a combination treatment to provide patient-specific therapy.

LIN28B as Biomarker for Propranolol Sensitive Tumors

USF Tech ID# 17B156

Overview:

The β-adrenergic receptor antagonist propranolol has been shown to have a therapeutic benefit in benign tumors, such as infantile hemangiomas (IHs). IHs are the most common benign vascular tumors of infancy. IH lesions are characterized by a rapid growth phase followed by a spontaneous involution, or triggered by propranolol treatment by poorly understood mechanisms.

The inventor has uncovered the role of the LIN28B/let-7 switch in infantile hemangioma pathogenesis and provides a novel mechanism by which propranolol induces IH involution. Specifically, it was discovered that the reprogramming factor LIN28B is highly expressed in the proliferative IH phase and is less expressed in the involuted IH phase and in IH tissues from propranolol-treated patients. The high LIN28B expression in proliferative IH correlates with the expression of the ESC-enriched mir-498(46)44–46 and is inversely correlated with the expression of let-7 miRNAs. Treatment of iPSCs with propranolol reduced the proliferation of iPSCs and reduced the expression of LIN28B and mir-498(46) while inducing the expression of let-7 family of miRNAs and EMT genes.

As a result, this research describes LIN28B as a novel therapeutic biomarker that can be used for detecting and treating tumors and cancers with propranolol in which the LIN28/let-7 pathway is imbalanced.

Methods of Measuring C19MC MicroRNA in a Post-natal Tissue

USF Tech ID# 22A088

Overview: Infantile hemangiomas (IHs) are common benign vascular tumors in childhood. Until recently, the role of miRNAs in the onset and progression of IH had never been investigated. Our scientists have recently shown a significant upregulation of the chromosome 19 miRNA cluster (C19MC) in IH specimens. Given the role of C19MC miRNAs in the regulation of cell proliferation, invasion, and differentiation, they hypothesize that temporal expression of C19MC plays a pivotal role in the onset of IH.

The C19MC miRNA is regulated by genomic imprinting with only the paternal allele expressed in the placenta. In addition, its expression is epigenetically regulated by DNA methylation of an upstream CpG rich promoter region. The inventors have developed a novel assays that can measure the expression and/or CpG methylation of the upstream C19MC promoter region in post-natal tissue. In addition to this, they have also developed a novel method to treat IHs via a modified CRISPR/Cas 9 Synergistic Activation Mediator system which incloves an upregulated actin gRNA (guide RNA) sequence that targets and inhibits the overexpressed C19MC promoter region commonly found in IHs.

In summary, the inventors provide a novel method of measuring increased C19MC microRNA found in IHs and a new approach for designing novel, targeted miRNA-based therapeutics for the treatment of IH and other vascular malformations.

Why Work With USF and the Technology Transfer Office?

USF Technology Transfer is committed to being the office of choice for our industry partners and envisions a future where every technology is given the opportunity to make a global impact.

- USF ranked 11th among American public universities and 23rd among all universities worldwide in generating new US Patents in CY 2021, according to the National Academy of Inventors (NAI) and Intellectual Property Owners Association (IPO). On a global scale, this is the 10th year USF has ranked in the top 25.
- USF facilitated the formation of 11 new startup companies in FY 2022 (ranking USF in the top 15 percent nationally for facilitating University startups).
- USF executed 99 options & licenses in FY 22 (ranking USF in the top 12 percent for executed agreements). These agreements represent companies that have contracted with USF to further develop research into commercial products and to help bring USF's innovation into the marketplace.
- USF Tampa was ranked #19 among the "Best Universities for Technology Transfer, 2017" by the prestigious Milken Institute.
- USF's innovation and economic development efforts generate more than $582 million in statewide impact.

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USF Technology Wheel

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USF Tech Transfer has over 250 technologies in the medical space. To learn more about how we can partner, please contact: ttoinfo@usf.edu

USF TECHNOLOGY TRANSFER
3702 SPECTRUM BLVD. STE. 165
TAMPA, FL 33612
813-974-0994 (OFFICE)

TTOinfo@usf.edu
www.usf.technologypublisher.com