FLORIDA STATE UNIVERSITY
COLLEGE *OF* MEDICINE
DEPARTMENT OF BIOMEDICAL SCIENCES
NEWSLETTER

January 6, 2017

Announcements

The next BMS Seminar is Wednesday, January 18th from noon-1:00PM in COM 1306. The speaker will be Dr. Hong Liu, Assistant Professor at Tulane University. He will be hosted by **Dr. Yanchang Wang**.

The Life Sciences Symposium, hosted by the BMS Department, will be February 9th and 10th here at the COM. This year's theme is, "Fighting Invisible Enemies: Host-Pathogen Interactions in Infectious Disease." Registration is now open on the website. For more information and to register for the event, visit our website.

The 13th Annual Research Fair, sponsored by the Division of Research, Graduate and Undergraduate Programs, will be held on Monday, February 6th in the COM Atrium from Noon to 1:30pm. Please register here.

Accomplishments

Dr. Akash Gunjan (Associate Professor) has recently received a $456,000 grant from the National Institute of Health for his research project titled, "Developing Therapeutic Strategies for Histone H3.3 Mutant Tumors via Rational Targeting." Congratulations, Gunjan Lab!

Trefoil Therapeutics Inc., a company co-founded by BMS Professor, **Dr. Michael Blaber**, has some exciting news. Below is a press release about the company's new collaboration with the National Institutes of Health's National Center for Advancing Translational Sciences.

Trefoil Therapeutics announced it will collaborate with the National Institutes of Health's (NIH) National Center for Advancing Translational Sciences (NCATS) to complete the investigational new drug enabling activities for their lead compound, TTHX1114, toward a treatment for Fuchs endothelial corneal dystrophy (FECD). Applicants to the TRND program are selected through a competitive process from an evaluation of the most promising proposals for these prestigious public-private partnerships. Once chosen for the program, the company and NCATS enter into a Collaborative Research and Development Agreement (CRADA) to set forth the activities that NCATS researchers will undertake to move the compound forward through the preclinical phase, including development of plans for clinical trials and submission of an IND application to the FDA. TTHX1114 is an engineered FGF-1 (eFGF-1) developed by Trefoil co-founder Dr. Michael Blaber, Professor of Biomedical Sciences at the Florida State University College of Medicine. The eFGF-1 platform represents an innovative approach to improving the properties of FGFs as drugs, yielding novel FGF-1s, which have demonstrated superior pharmacodynamic and pharmaceutical properties compared to the naturally occurring FGF-1s in animal models of tissue healing.

Additionally, Trefoil Therapeutics released the following press release regarding their recent successes in funding lead by Hatteras Venture Partners.

Trefoil Therapeutics Inc., an early stage biopharmaceutical company focused on developing a regenerative approach to corneal endothelial dystrophies and other diseases based on novel engineered derivatives of fibroblast growth factor-1 (eFGF-1), announced today the closing of an oversubscribed $5.2 million Series 1 financing lead by Hatteras Venture Partners. In addition to Hatteras Venture Partners, the syndicate included four other firms with significant experience investing in the

ophthalmic sector: AJU IB Investment, Correlation Ventures, ExSight Capital and InFocus Capital.

This financing, in conjunction with the recently announced National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS) Therapeutics for Rare and Neglected Diseases (TRND) collaborative research agreement, provides funding and research support that will allow the firm to progress toward an Investigational New Drug (IND) filing.

Trefoil is developing TTHX1114 as the first therapeutic application for the treatment of Fuchs endothelial corneal dystrophy (FECD), the most common cause of corneal transplantation. FECD can lead to severe visual loss for which there is currently no approved pharmaceutical therapy.

"With the closing of this round of financing and the TRND collaboration, we will be able to complete the necessary studies for an IND filing," noted Trefoil CEO David Eveleth, Ph.D. "We are gratified to have Hatteras Venture Partners as our lead investor along with the other members of the financing syndicate who understand ophthalmology and the unmet medical need that TTHX1114 will address."

"Hatteras Ventures has followed the progress of Trefoil, and we have been impressed with their accomplishments over the past year, including the recent TRND collaborative research agreement," said Christy Shaffer, Ph.D., General Partner, Hatteras Ventures Partners. "The Trefoil team has significant experience in the development and commercialization of ophthalmic products, and I am looking forward to serving on the board of directors. Hatteras is pleased to be leading the investment in this underserved market segment where today patients with endothelial deficiencies often require cornea transplantation surgery."

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Congratulations to Dr. Blaber and Trefoil Therapeutics!

Publications

The **Kaplan Lab** recently had a paper published in *Genes* titled, "Origin DNA Melting—an essential process with divergent mechanisms." Authors on the paper include **Matthew Martinez** (Undergraduate research member), **John Jones** (Undergraduate research member), **Irina Bruck** (Assistant Scholar Scientist), and **Dr. Daniel Kaplan** (Associate Professor).

The **Dr. Yanchang Wang** Lab has had two recent publications.

The first publication titled, "Identification of a novel Polo-like kinase 1 inhibitor that specifically blocks the functions of Polo-Box domain," was published in *Oncotarget*. Authors: Chen Y, Zhang J, Li D, Jiang J, **Wang Y** (Professor), Si S. A brief summary of their work is below:

> Polo-like kinase 1 (Plk1) is a promising target for cancer therapy due to its essential role in cell division. In addition to a highly conserved kinase domain, Plk1 also contains a Polo-Box domain (PBD), which is essential for Plk1's subcellular localization and mitotic functions. We adopted a fluorescence polarization assay and identified a new Plk1 PBD inhibitor T521 from a small-molecule compound library. T521 specifically inhibits the PBD of Plk1, but not those of Plk2-3. T521 exhibits covalent binding to some lysine residues of Plk1 PBD, which causes significant changes in the secondary structure of Plk1 PBD. Using a cell-based assay, we showed that T521 impedes the interaction between Plk1 and Bub1, a mitotic checkpoint protein. Moreover, HeLa cells treated with T521 exhibited dramatic mitotic defects. Importantly, T521 suppresses the growth of A549 cells in xenograft nude mice. Taken together, we have identified a novel Plk1 inhibitor that specifically disrupts the functions of Plk1 PBD and shows anticancer activity.

The second publication titled, "Premature Silencing of the Spindle Assembly Checkpoint Is Prevented by the Bub1-H2A-Sgo1-PP2A Axis in Saccharomyces cerevisiae" was published in *Genetics.* Authors: **Jin F** (Research Scholar Scientist), **Bokros M** (BMS Graduate

Student), **Wang Y.** A brief summary of their work is below:

The spindle assembly checkpoint (SAC) monitors mistakes in kinetochore-microtubule interaction and its activation prevents anaphase entry. The SAC remains active until all chromosomes have achieved bipolar attachment that applies tension on kinetochores. Our previous data in budding yeast Saccharomyces cerevisiae show that Ipl1/Aurora B kinase and a centromere-associated protein Sgo1 are required to prevent SAC silencing prior to tension generation, but we believe that this regulatory network is incomplete. Bub1 kinase is one of the SAC components, and Bub1-dependent H2A phosphorylation triggers centromere recruitment of Sgo1 by H2A in yeast and human cells. Although yeast cells lacking the kinase domain of Bub1 show competent SAC activation, we found that the mutant cells fail to maintain a prolonged checkpoint arrest in the presence of tensionless attachment. Mutation of the Bub1 phosphorylation site in H2A also results in premature SAC silencing in yeast cells. Previous data indicate that Sgo1 protein binds to PP2ARts1, and we found that rts1Δ mutants exhibited premature SAC silencing as well. We further revealed that sgo1 mutants with abolished binding to H2A or PP2ARts1 displayed premature SAC silencing. Together, our results suggest that, in budding yeast S. cerevisiae, the Bub1-H2A-Sgo1-PP2ARts1 axis prevents SAC silencing and helps prolonged checkpoint arrest prior to tension establishment at kinetochores.

BMS Graduates

Dr. Xue Xia (Susie), PhD Biomedical Sciences Class of 2015 and a former graduate student in the **Blaber Lab**, has obtained a position as a Senior Specialist, Engineering in the drug manufacture and technical operations division at Merck. Merck is one of the largest and most admired pharmaceutical companies in the world. Her job responsibilities are to support downstream process development, including purification, analytical, and quality assays for biological therapeutics in the production pipeline. Dr. Xia's PhD thesis on "Engineering Fibroblast Growth Factor-1 (FGF-1) as a Human Therapeutic" while in the FSU College of Medicine provided her with the skills needed to successfully compete for this position. Congratulations Susie!

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