

HBRI Newsletter

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HBRI Celebrates Stem Cell Research at Open House

On May 21st, 2010, the Human Biomolecular Research Institute (HBRI) hosted an Open House to celebrate advancements in stem cell research. In collaboration with Professor Mark Mercola and Evan Snyder of the Sanford-Burnham Medical Research Institute, HBRI is developing small molecules to direct maturation of human stem cells and human induced pluripotent stem cells.

Duane Roth, the CEO and Board Member of CONNECT and Vice Chair of the California Institute for Regenerative Medicine, was the featured speaker. Mr. Roth spoke about why patients need to be involved in the advocacy process for drug development.

Along with a presentation by Mr. Roth, HBRI also honored two distinguished guests with Disease Advocate Awards.

These awards were presented to Joan Samuelson J.D., and David Serrano Sewell J.D., two Patient Advocates that have been particularly motivated and outspoken about patient causes including Parkinson's disease, Multiple Sclerosis and ALS (or Lou Gehrig's disease), and have worked tirelessly to make stem cell research for these diseases possible. Their

advocacy efforts will stimulate greater interest in research and eventually, clinical applications. Their dedication to support research is an inspiration to all.

HBRI welcomed over eighty members of the San Diego community to this event. Guests included local scientists from research institutes in the area, administrative personnel from local institutes and universities and six college and high school HBRI summer interns destined to be future stem cell chemists and stem cell biologists.

HBRI hosted this Open House to introduce people in the community to the research at HBRI, and to give them a chance to see the lab where the work is done. Guests had an opportunity to meet with scientists from the Institute in a casual, intimate environment and ask questions about HBRI's research.



Scientists Make Stem Cells to Heal Damaged Heart Tissue

Scientists at HBRI have been collaborating with scientists at the Sanford-Burnham Medical Research Institute (SBMRI) in La Jolla to identify stem cell approaches for regenerating heart muscle tissue after a heart attack.

Scientists have developed approaches that combine stem cell and chemical biology technologies to stimulate cardiogenesis in stem cells and eventually contribute to the development of drugs for regenerating heart muscle tissue.

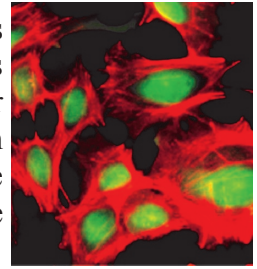
Currently, when someone has a heart attack some of the heart tissue is irreparably damaged, and scar tissue can form around the heart that may eventually lead to heart failure. The adult heart has

very limited abilities to regenerate itself.

If regenerative medicine could provide a way to re-generate damaged tissue, or provide a way to prevent heart tissue from sustaining such severe damage during a heart attack, it would be a significant benefit to millions of people who are currently living with heart disease.

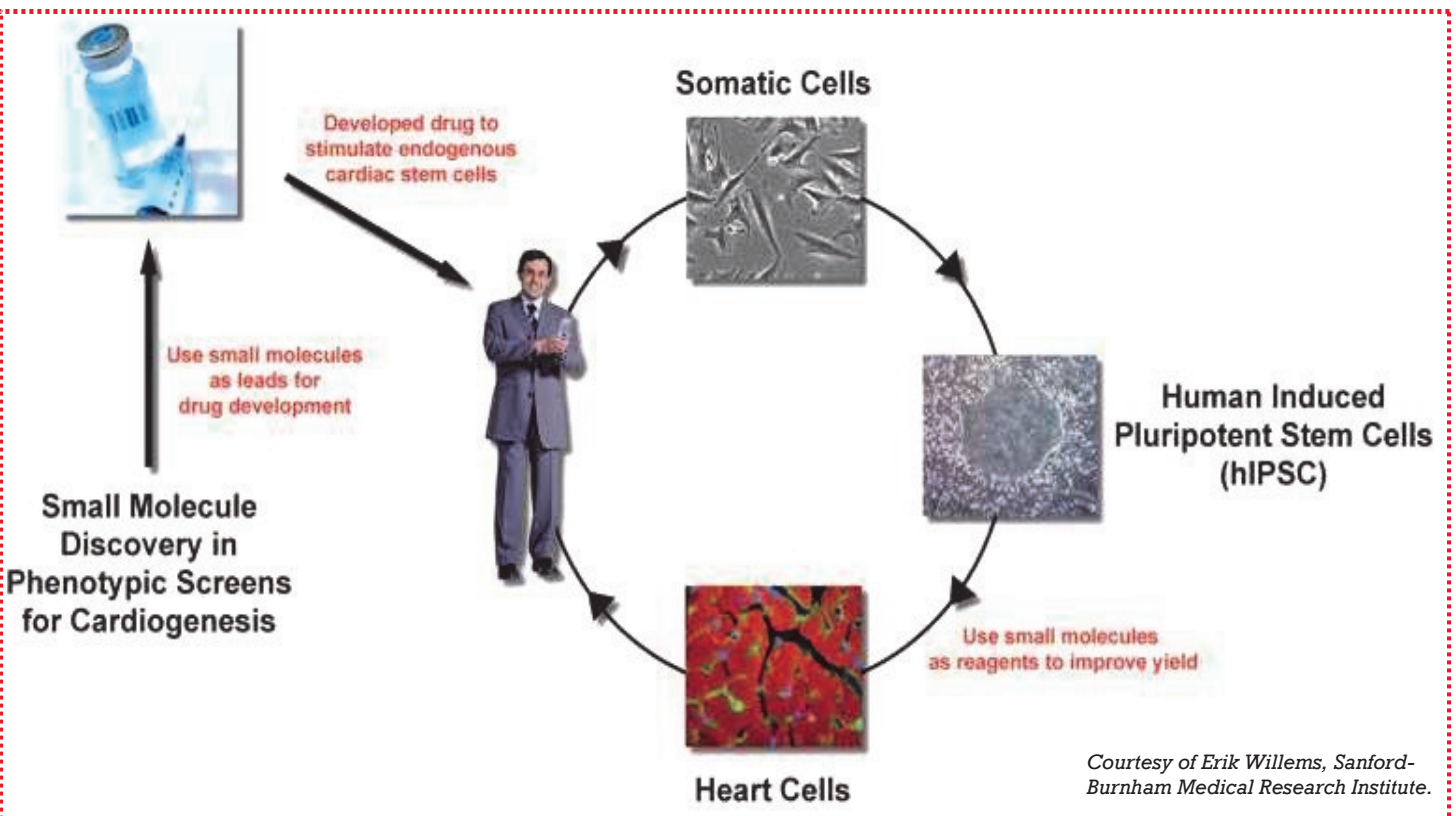
Scientists at HBRI and SBMRI have discovered a way to promote cardiogenesis in human embryonic stem cells (hESCs) or human induced pluripotent stem cells (hiPSCs) using small molecules. These small molecules could eventually lead to drugs and be used to regenerate critical tissue in

the heart. This approach is one of four research strategies the scientists are working on.



Human Heart Cells

The combination of medicinal chemical and stem cell biology is unprecedented in the field of cardiovascular disease research, and represents an exciting new approach to discover therapies for a disease that is the number one killer of adults in the United States, and one that affects millions of people worldwide.



Courtesy of Erik Willems, Sanford-Burnham Medical Research Institute.

2010 HBRI Summer Interns!

In 2010 HBRI welcomed six summer interns to the labs on Eastgate Mall.



Claire Johns

The Biology department welcomed three interns this year: Tara Alpert, Claire Johns and Brittney Nguyen. Tara graduated from Francis Parker School in San Diego. She is a sophomore at Washington University in St. Louis, MO.



Tara Alpert

Claire Johns, a graduate of Point Loma High School, is also a sophomore in college and attends The University of



Brittney Nguyen

California, Berkeley. A third biology intern, Brittney Nguyen, is a recent graduate of High Tech High School and is in her freshman year at Stanford.

The Chemistry department welcomed three interns as well. Isaac Tian is a senior at Westview High School and is a drum major with the marching band. Alyssa Morgosh is a senior at Bishop's School, and is on the cross country and soccer teams. Torrey Czech, the third chemistry intern, is a senior at La Jolla High School and is the President of the California Scholarship Federation at La Jolla High School, among other activities.

This bright group of students spent 8-10 weeks being mentored in the lab by HBRI scientists participating in

actual experiments, learning hands-on about the research done at HBRI, and what life is like working in a lab environment.



Isaac Tian

Some of these students are majoring or plan to major in the sciences in college, and



Isaac & Alyssa Morgosh

will be able to use this internship to further their education toward a future degree in science or medicine.



Torrey Czech

2011 Summer Internship Program

HBRI offers summer internships in Biology (Molecular and Cell Biology), Chemistry and Analytical Chemistry. This is a tremendous educational opportunity and an extension of a students' science education. Students gain hands-on laboratory experience and are mentored by well-renowned scientists in their field of study.

This is a highly coveted program year after year. The internship program is open to highly motivated high school juniors and

seniors and college students interested in developing scientific expertise. Applicants must be currently attending or have graduated from a high school in San Diego County, and must complete AP Biology and/or AP Chemistry prior to applying for the internship program.

The online application will be available February 1st, 2011. No applications will be accepted prior to Feb. 15th. **2011 applications will be due on April 1st.** Late applications will not be accepted.

Applicants are encouraged to request recommendation letters from their teachers as soon as possible. Please submit all application forms, including recommendation letters, at the same time.

For more information, students are encouraged to visit the website at www.hbri.org.

Because gathering information is part of the learning experience we will not entertain calls or e-mails from parents.



Scientists Discover New Medications for Depression

Scientists at the Human BioMolecular Research Institute (HBRI) in San Diego, CA, in collaboration with West Virginia University Health Sciences Center in Morgantown, WV, Oregon Health and Science University and The Methamphetamine Abuse Research Center in Portland, OR, have been studying new approaches to serotonin and norepinephrine re-uptake inhibitors as novel medications development for depression and have published three papers on the subject*. Research showed that combining compounds that have complimentary functional activity into the same molecules may be effective in treating diseases such as depression.

Numerous clinical studies suggest that serotonin is involved in depression, and that elevating

serotonin by administration of serotonin re-uptake inhibitors may be useful in treating depression. Certain antidepressants work by inhibiting the re-uptake of serotonin and norepinephrine in the brain. It was also known that inhibition of phosphodiesterase is also associated with antidepressant function. In separate studies, HBRI scientists took serotonin and norepinephrine re-uptake inhibitors, linked them to an inhibitor of phosphodiesterase using a five-carbon chain, and found that the dual inhibitors worked effectively to inhibit phosphodiesterase as well as serotonin and norepinephrine re-uptake, respectively.

To test these agents in small animals, scientists used mice to study the effects of inhibiting phosphodiesterase and serotonin

or norepinephrine re-uptake on depressive behavior. The new multi-target compounds synthesized by linking a serotonin re-uptake inhibitor to a phosphodiesterase inhibitor showed promise. It may be that the combination of two functional activities in the same molecule may expedite the antidepressant activity shown by the re-uptake inhibitor alone.

The dual function of serotonin re-uptake inhibition and phosphodiesterase inhibition linked together in the same molecule may be effective in treating depression more rapidly and efficiently than current serotonin re-uptake agents alone.



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*Cashman JR, Ghirmai S (2009) Inhibition of serotonin and norepinephrine re-uptake and inhibition of phosphodiesterase by multi-target inhibitors as potential agents for depression. *Bioorg Med Chem* 17:6890-6897.

*Cashman JR, Voelker T, Zhang H-T, O'Donnell JM (2009) Dual inhibitors of phosphodiesterase-4 and Serotonin re-uptake. *J Med Chem* 52:1530-1539.

*Cashman JR, Voelker T, Johnson R, Janowsky A (2009) Stereoselective Inhibition of Serotonin Re-uptake and Phosphodiesterase by Dual Inhibitors as Potential Agents for Depression. *Bioorg Med Chem* 17:337-343.

Our Mission

To conduct basic research related to disorders of the central nervous system and help develop new therapeutic agents that address these disorders and promote scientific learning through community service and public access.