

The SMART Library Now Available for Research

Researchers who study Rett syndrome are increasingly identifying new underlying biological pathways that contribute to the cause of and to the symptoms of the disease. The researchers believe that a chemical or biological compound that influences such a biological pathway (or disease mechanism) that they are studying may have an important effect on Rett syndrome. Thus, understanding these disease mechanisms is a starting point for drug discovery.

Traditionally, biological experiments are designed to discover compounds that impact the particular disease mechanism that is believed important. A large number of compounds can be tested in these experiments in a quest to find that rare chemical compound that can selectively and potentially influence the disease mechanism that may cause or contribute to Rett syndrome. This is a lengthy and expensive process. Fortunately, many of the emerging biological pathways that may be involved in Rett syndrome have been the subject of other investigations that were not relating to Rett syndrome research. Researchers can take advantage of these other studies and shortcut the time and expense that are both part of traditional drug discovery.

Dr. Irina Gaisina and Dr. Alan Kozikowski from the University of Illinois at Chicago have decided to aggressively pursue a process of repurposing established compounds for Rett syndrome research. Many of these compounds have been developed for other purposes and are in advanced stages where they have already been used in human medicine or close to human clinical trial studies. The IRSF is supporting the collection of known compounds called the SMART library. SMART stands for Selected Molecular Agents for Rett Therapy. The SMART library is not a traditional chemical library. Each compound in this library is known to address a specific biological pathway that may be important to either the cause of Rett syndrome or to the symptoms that the disease produces. Therefore, each compound is a potential key that can help unlock new knowledge. Altogether, the SMART library may shorten the path to actual treatments by linking an advanced therapeutic to Rett syndrome.

The SMART library of compounds is well vetted by modern day bioinformatics methods, tightly focused on Rett syndrome and its biological causes. The IRSF Science Advisory Board has also recommended a number of compounds that have been either purchased or prepared and are now included in the library. With the goals in mind to save both time and resources and accelerate drug discovery for Rett syndrome, the compounds in the SMART library will be readily available to investigators working on Rett syndrome research.

The SMART library is currently housed at the University of Illinois-Chicago where it is administered by Dr. Kozikowski and Dr. Gaisina. They have acquired 150 compounds to date. They intend to continue growing the collection while making it available to researchers in the field.

This is a low cost strategy when compared to the cost of developing a single drug from the biological target to the clinic (generally over \$20M). However, the library construction is not cheap. A few milligrams of the more complex compounds can cost \$50 to \$200. Researchers

will need to prepare milligram quantities of some compounds that cannot be purchased or acquired from a pharmaceutical company as a gift. In order to support animal research using Rett mouse models, multi-gram quantities of interesting compounds will need to be synthesized. All of these activities are essential if they are going to move compounds quickly from the bench to the individuals who suffer from Rett syndrome.

The SMART Library Initiative has been highly supported by the lay and medical leadership of IRSF, together with the funds from IRSF's win in the Pepsi Refresh Project. For more information on this library, please contact Dr. Janice Ascano at jascano@rettsyndrome.org.

For researchers who wish to obtain compounds, please contact Dr. Irina Gaisina at igaysina@uic.edu.

