Setting standards for research into Rett syndrome

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There is an urgent need for new drugs to treat Rett syndrome, a rare and severe neurological disease mainly affecting girls. A bottleneck in drug development for this syndrome is a lack of clarity at the level of preclinical research. Key researchers in this field now tackle this issue, proposing standards and guidelines for Rett syndrome research, in an Open Access review article published on Oct. 31, 2012 in *Disease Models & Mechanisms* (DMM) at http://dmm.biologists.org/. This "state of the science" assessment serves as a comprehensive resource of all findings and citations related to Rett syndrome.

Rett syndrome is a rare neurological disease that affects girls almost exclusively. Affected children appear to grow and develop normally for the first 6-12 months of life, but then begin to show symptoms including slow development, problems crawling or walking, and diminished eye contact. As the syndrome progresses, affected children show a regression of many skills, with loss of purposeful hand use, speech and basic motor function. Severe cases can experience problems with heart, respiratory and gastrointestinal function. Rett syndrome is extremely difficult on affected girls and their families. Although the disease-causing gene (called MECP2) has been identified, there is no cure, and only limited symptomatic treatments are available. A key to developing new treatments for this devastating disorder is to improve systems and standards at the preclinical research level.

The new review article reports on outcomes from a workshop held in September of 2011 focused on the state of the art in animal studies of

Rett syndrome. The workshop was convened by important funders of Rett syndrome research, including the National Institute of Neurological Disorders and Stroke (NINDS), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the International Rett Syndrome Foundation (IRSF) and the Rett Syndrome Research Trust (RSRT). Workshop participants included key members of the Rett syndrome research community, including basic scientists, clinicians, and representatives from the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the pharmaceutical industry and private foundations. Several workshop participants contributed to the article, and the corresponding authors are Dr. David Katz (Case Western Reserve University School of Medicine), Dr. Laura Mamounas (National Institute of Neurological Disorders and Stroke) and Dr. Huda Zoghbi (Baylor College of Medicine).

The main aim of the workshop was to identify crucial knowledge gaps in Rett syndrome research at the preclinical level, and to suggest scientific priorities and best practices for the use of animal models in preclinical evaluation of potential new therapeutics. As explained in the new review article, the combination of an urgent need for effective treatments for Rett syndrome, coupled with the availability of good mouse models, is a driving force for studies that can identify and test new drugs. The outcome of the workshop included a set of recommended guidelines for animal studies of Rett syndrome, to ensure that decisions to initiate costly clinical trials will be founded on reliable data that is produced using standardized study design and transparent reporting. Ultimately, the increased level of rigor in animal studies should shorten the time to effective treatments.

More information: Katz, D. M., Berger-Sweeney, J. E., Eubanks, J. H., Justice, M. J., Neul, J. L., Pozzo-Miller, L., Blue, M. E., Christian, D., Crawley, J. N., Giustetto, M. et al. (2012). Preclinical research in Rett syndrome: setting the foundation for translational success. Dis.

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