Identification of Biomarkers of IGF1's related drugs in Rett Syndrome

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During the last few years there has been intense activity in the field of translational research in Rett syndrome (RTT). This has led to some positive early phase trials and the promise of a first RTT-specific drug. The success of these recent trials has been the result of testing therapies in genetic animal models of RTT and other neurobiologically based experimental approaches. While this is good news for the RTT field, the success of subsequent pivotal clinical trials that will determine the regulatory approval (FDA, EMA) of the drugs will depend on refining their study design. Outcome measures with strong measurement properties, and biomarkers that can identify potential responders to drugs, will ensure appropriate cohort selection and detection of clinical improvement of functional significance. In order to accelerate the achievement of these goals, the establishment of working groups bringing together top experts in each modality of outcome measures and biomarkers will be a significant step. Here, we report the establishment of a working group focused on molecular biomarkers for RTT clinical trials: the RTT Molecular Biomarkers Working Group. The three investigators in the group have long track records in the development and application of novel treatments to RTT. Moreover, they have been working together on the development of biomarkers for these intervention studies and have a common interest in two of the successful drugs in RTT early phase trials: the IGF1-related drugs mecasermin and trofinetide. Dr. Walter Kaufmann, a neuroscientist and child neurologist who has led the design and implementation of novel drug trials for RTT and other neurogenetic disorders, will represent and coordinate the group's activities and interact with Rettsyndrome.org, drug companies, regulatory agencies, and other entities. He will also oversee the metabolomics analyses performed by the group. Most of the molecular studies carried out by the group will be conducted at the laboratories of Dr. Mriganka Sur, a leading neuroscientist who has studied many aspects of the neurobiology of RTT and led the development of IGF1-based therapies, and Dr. Daniela Tropea, who conducted pioneer experimental trials in Dr. Sur's laboratory and since then has become a leader in the study of the neurobiology of IGF1.
The proposed application entitled Identification of Biomarkers of Response to IGF1-related Drugs in Rett Syndrome, based on blood samples from two recent successful drug trials, represents the first comprehensive project of the RTT Molecular Biomarkers Working Group aiming at identifying biomarkers of positive response to IGF1-related drugs in RTT. The project is presented as single entity. However, because of logistics and following Rettsyndrome.org's advice, each aim will be carried out as an independent project under the coordination of Dr. Kaufmann. Thus, separate budgets will be submitted by Drs. Tropea and Sur for aims 1 and 2, respectively.