Modelling syndromic autism caused by mutations in the ADNP gene, (AUTISYN)

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Autism, perhaps best characterized by a lack of social skills, is a poorly understood disorder. We know little about the different types of the disorder. Though is clear that genetics plays an important role in the occurrence of the disorder, of very few forms of autism the cause is known. In this project, we will study a form of autism that is caused by mutations in a single gene called ADNP. Mutations in this gene lead to autism in almost all patients known to date. Using an established mouse model of Adnpautism,
which mimics the disorder allows us to study the disorder in vivo, and to test drugs for possible later use in humans. It is known that a specific part of the ADNP protein called NAP can replace many of the functions of the entire protein, thereby indicating that NAP can be a primary drug candidate for testing in the Adnp-autism mouse model. In addition, as we know little of the consequences of the mutation in human cells, we will produce neuron-specific cell types generated from patient-derived skin biopsies, using the technique of induced-pluripotent stem cells. Thus, we will be able to study the processes that are disturbed in patient brain cells. By applying a variety of state of the art technologies, our network will detect novel pathways in cells disturbed in ADNP, and in related forms of autism. Once we characterized those pathways, we can then try to modify them for clinical benefit, using novel drugs. Finally, since many unrelated patients share the very same ADNP mutation, we will determine the mechanism of how these mutations arise. Knowledge of the mutational mechanism may be another way of detecting or preventing the disease in the future.