Summary provided by the Organizers.

The Adrenal Cortex/Molecular Steroidogenesis Meeting was delighted to receive generous support from the Office of Rare Diseases, and we feel that the program provided an outstanding forum to discuss cutting edge research directly relevant to the topic of Rare Genetic Diseases.

First, a number of talks focused specifically on rare genetic disorders that affected steroidogenesis or other endocrine processes causing significant phenotypes. Dr. Stephanie Seminara described mutations in the orphan G protein-coupled receptor GPR54 that are an important cause of autosomal inherited Kallman’s syndrome and delayed puberty. Dr. Simon Rhodes reviewed mutations that are associated with selective or combined deficiencies of pituitary hormones, genetic endocrine disorders that generally present in childhood. Dr. Adrian Clark discussed mutations in the melanocortin 2 receptor (mc2r) and in a mc2r accessory protein associated with the rare condition of familial glucocorticoid deficiency, type 2. This deficiency is associated with neonatal hypoglycemia or overwhelming infection due to the failure to synthesize cortisol. Dr. Clark’s findings have advanced our understanding of the basic mechanisms of ACTH signaling and have provided novel insights into the pathogenesis of familial glucocorticoid deficiency. Dr. Xianxin Hua described his studies with menin, a protein whose mutation is associated with a disease causing multiple tumors of the endocrine system including pituitary, pancreas, and parathyroids. These data provided new insights into how menin works that may translate into novel therapies for this disabling genetic disorder. Dr. Kenn Albrecht described a modifier gene that impacts on the severity of mutations in gonadal development and sex differentiation in genetically engineered mice. Ongoing studies are now examining the roles of these genes in human disorders of sex differentiation. The steroidogenic acute regulatory protein (StAR) is mutated in the rare genetic disorder congenital lipoid adrenal hyperplasia, the most severe congenital defect in steroid production. Talks on this protein by Dr. Walter Miller and Dr. Vassili Papadopolos described novel insights into the mechanisms by which this key mediator of steroidogenesis delivers cholesterol to the steroidogenic pathway. Dr. Perrrin White described the oxidative enzyme hexose-6-phosphate dehydrogenase (H6PD), which has been implicated in cortisone reductase deficiency, a rare genetic disorder that results from compound mutations in 11beta hydroxysteroid dehydrogenase and H6PD. Dr. Ed McCabe described his studies with DAX1, an atypical nuclear receptor whose mutation is associated with adrenal hypoplasia congenital and hypogonadotropic hypogonadism.

In addition to talks that directly dealt with examples of rare genetic disorders, other talks in the program described novel techniques that may uncover new mechanisms of genetic diseases. Dr. Myles Brown outlined his approach to define all of the sites in the genomic DNA that are bound by estrogen receptor in the cell. Given the emphasis on mutations in regulatory regions as causes of impaired gene expression in genetic disorders, this approach provides a model for defining relevant binding sites for transcription factors.
that may relate to human diseases. Similarly, Dr. Qing Fan described elegant molecular studies defining the structure of the gonadotropin receptors and their interaction with glycoprotein ligands. These studies provide novel insights into genetic diseases associated with aberrant gonadotropin signaling, such as the resistant ovary (FSH receptor) and familial precocious puberty (LH receptor).

In summary, the meeting brought together a diverse group of scientists and clinician scientists interested in important questions in molecular steroidogenesis and the adrenal cortex and their impact on human disease. One can anticipate that these studies will lead to better methods for early detection and diagnosis of these rare diseases and for rational strategies for therapeutic intervention targeted to affected genes. Attendance was excellent (125 participants), and included an impressive group of trainees (25 postdoctoral/graduate students). The meeting provided an excellent opportunity for the trainees to present their work to world-famous investigators in a poster session and to receive valuable feedback. The excellence of the presentations and the pivotal role that many of the speakers have played in defining the mechanisms of many rare genetic diseases ensured that this topic was at the forefront of this highly successful meeting.