Rett Syndrome (RTT)

Presented by Khristy Nicholas
Dr. Andreas Rett (1960s)
- Neurodevelopmental disorder
- Females vs. Males
  - 1 in 10,000 females
- Sporadic cases
- Penetrance of RTT difficult to assess because it is so variable
**Symptoms**

- Different forms of RTT
  - Preserved Speech Variant (PSV)/ Zappella variant (recover some speech and hand use)
- It is distinguished by:
  - arrested development (6-18 months)
  - regression of acquired skills
  - loss of speech
  - Stereotypical movements
  - microcephaly
  - seizures
  - mental retardation
  - Breathing difficulty
  - Scoliosis

- [http://www.youtube.com/watch?v=53k1EsP5D8k&feature=related](http://www.youtube.com/watch?v=53k1EsP5D8k&feature=related)
Diagnostic criteria/ symptoms:
- partial or complete loss of acquired purposeful hand skills or spoken language, repetitive hand movements, and gait abnormalities (including toe-walking or an unsteady, wide-based, stiff-legged walk)

2 gene model

Normal development/ normal neonatal head circumference
Methyl CpG binding protein 2 (MECP2) gene located on long arm of X chromosome (1999)
- MeCP2 protein
- Atypical (<10 % of RTT cases)
  - CDKL5
  - FOXG1
- Since MECP2 is not solely responsible for RTT, scientists are still looking for other causes
Dr. Uta Francke

- Professor at Stanford University
  - Department of Genetics
- RTT gene co-discoverer
- “The hope for a cure for Rett Syndrome is not unreasonable because the damage to the brain appears to happen in later stages of development, after birth…”
Novel Diagnosis and Understanding

- De-novo
- Emphasis on it remaining a clinical diagnosis
- Deceleration of head growth no longer necessary for diagnosis
- Epigenetic regulation
  - Early diagnosis and prenatal detection.
- Reactivation of inactive X chromosome
- Genetic blood tests
Current Treatment

1) Management of gastrointestinal issues
2) Surveillance of scoliosis
3) Communication skills
4) Parental counseling
5) Modifying social medications
6) Sleep aids
7) Selective serotonin reuptake inhibitors (SSRIs)
8) Anti-psychotics
9) Occupational/speech/physical therapy
Hope for the future...

- Reactivation of MeCP2 protein (mice)
  - Phenotypic reversal
- Treatment of syndrome or symptoms?
- Aminoglycosides
- Environmental enrichment (mice)
- Experimenting on mutation in sperm
- Locus coeruleus
Why does a mutation in a widely expressed protein produce a syndrome with a predominantly neurological phenotype?
References