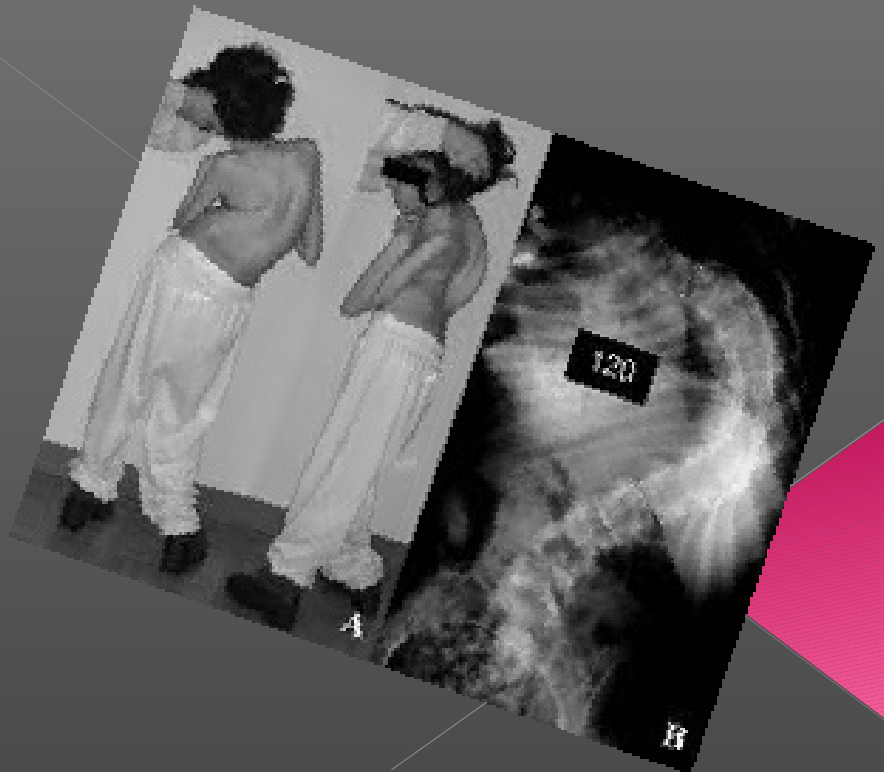
Rett Syndrome (RTT)

Presented by Khristy Nicholas



Background Information

- 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

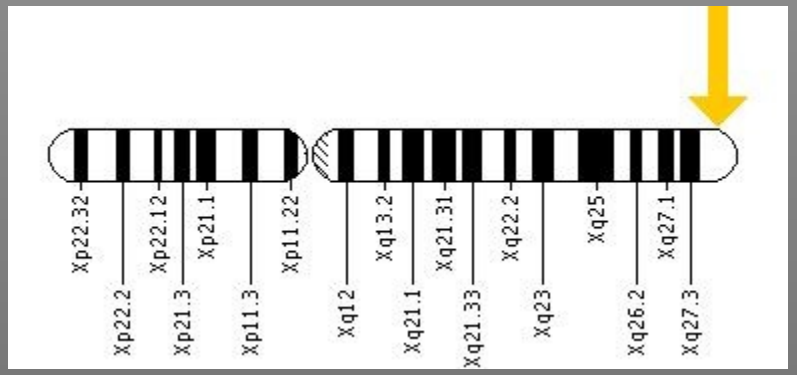
- Different forms of RTT
  - Preserved Speech Variant (PSV)/ Zappella variant (recover some speech and hand use)
- It is distinguished by:
  - **arrested development (6-18 months)**
  - regression of acquired skills
  - loss of speech
  - **Stereotypical movements**
  - **microcephaly**
  - seizures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

- http://www.youtube.com/watch?v=53k1EsP5D8k&feature=related

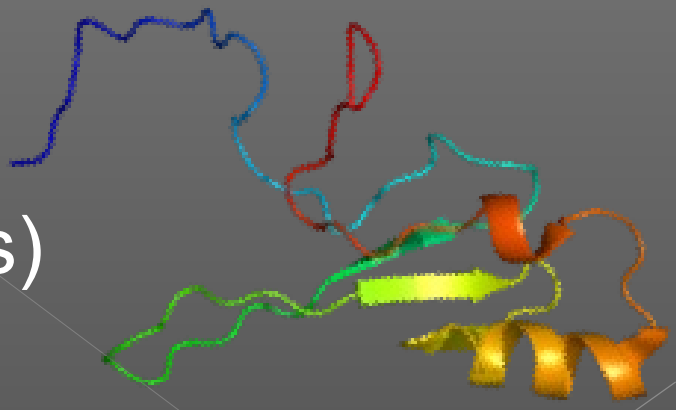
Classical Diagnosis and Treatment

- 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

Gene Knowledge



- **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

Big Question Remains…

- Why does a mutation in a widely expressed protein produce a syndrome with a predominantly neurological phenotype?

References

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