

NIH RDCRC Natural History Study

Shedding New Light

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NATURAL HISTORY STUDY

- Goal: Enroll 1000 girls or women with RS
- 900 typical and 100 atypical
- Must meet consensus criteria or have *MECP2* mutation
- Purpose: expand phenotype-genotype studies and set stage for clinical trials
- Principal sites: Baylor, Greenwood Genetic Center, and UAB

The Team

- **Baylor College of Medicine**

- Daniel Glaze
- Kay Motil
- Jeff Neul
- Judy Barrish
- Carmel Lusk

- **Greenwood Genetic Center**

- Steve Skinner
- Fran Annese
- Joy Graham
- Lauren McNair

- **UAB**

- Alan Percy
- Jane Lane
- Suzie Geerts
- Jerry Childers
- Russell Kirby

- **NIH/NCRR/NICHD**

- **DTCC – Hye-Seung Lee**

- **Girls and women with RS and their families**

IRSF Clinics

Natural History Clinics

- Chicago - Marie Kral
- Oakland - Paige Nues
- New Jersey - Leslie Greenfield
- Florida - Henry Perez

Rare Disease CRC

- RDCRC natural history study of Angelman, Rett, and Prader-Willi syndromes to develop critical data necessary for initiation of clinical trials
- UAB is lead site for Rett consortium and lead site for competitive renewal (PI: A. Percy); review in 2/2009
- Consortium sites: Baylor, Greenwood Genetic Center, Harvard, KU, UAB, UCI, UCSD, Univ of Florida, and Vanderbilt
- More than 1132 enrolled to date
- More than 756 enrolled in RTT study

Seizures in Rett syndrome

- Seizures are common: 59% noted 1 or more by 1st visit
- No significant difference in Typical vs. Atypical RTT
- No significant difference by ethnicity/ race
- Significant age difference: unlikely < age 3 years; rarely begin after age 20; noted in 50-70% from age 5-20
- Occurrence varies by mutation: most frequent for T158M (74%) and R106W (78%); less frequent for R255X (48%) and R306C (44%)
- Age-adjusted clinical severity, poor walking, and poor hand skills, but not FOC greater in those with seizures
- For those reporting seizures: none in 36% at time of visit; only 17% with daily seizures

Scoliosis in Rett syndrome

- Scoliosis in 50% of 586 with classic RTT
- Mean age with scoliosis: 15 yr
- Mean age without scoliosis: 6 yr
- >80% with scoliosis by age 16
- MBA score, delayed or absent walking, and constipation correlate with scoliosis
- Reduced risk with R294X and R306C
- Surgery in 12%; >90% with delayed or absent walking

Longevity in Rett Syndrome

- Normal survival until age 10
- > 50% survival to age 50 versus > 95% in all females and 27% in persons with profound motor and cognitive impairments

Family: *MECP2*+ Non-Rett Males and Rett Female

