**Andersen-Tawil Syndrome: Genotype-Phenotype Correlation and Longitudinal Study**

**Characteristics of Andersen-Tawil Syndrome**

Andersen-Tawil Syndrome (ATS) is a rare, genetic disorder that causes episodes of muscle weakness, potentially life-threatening changes in heart rhythm, and developmental abnormalities. Disease symptoms can vary.
the cause of some ATS cases remains unknown, and no specific treatment has been identified. The purpose of this multi-site study is to better characterize ATS, establish whether symptoms change over time, and determine if symptoms are related to a mutation in the KCNJ2 gene.

**Detailed Description:**

ATS is an ion channel disorder that causes episodes of muscle weakness and potentially life-threatening heart arrhythmias for which no treatment has been identified. The majority of ATS cases are caused by a mutation in the KCNJ2 gene; other cases result from unknown causes. The KCNJ2 gene mutation alters potassium channels in such a way that it disrupts the flow of potassium ions in skeletal and heart muscle. This can lead to the characteristic periodic paralysis and irregular heart rhythms. The purpose of this study is to better define the genetic basis, clinical features, and disease progression of ATS. The study will also establish clinically relevant endpoints for use in future clinical studies.

This observational study will last 2 years and will involve three study visits. The first visit will entail a 1.5- to 3.5-day inpatient stay; the length of stay will depend on whether a participant has been taking medications for their symptoms of weakness. Participants will be asked to discontinue use of such medications during the inpatient stay. Participants will not be asked to stop any medications they may be taking for heart symptoms. This first study visit will include a medical history, a quality of life questionnaire, a physical exam, and muscle strength testing. Nerve, muscle, and heart activity will also be measured, and blood will be drawn for laboratory tests and optional DNA analysis. The second and third study visits will take place 1 and 2 years after the initial study visit and will include the same evaluations. During the 8 weeks following
Each study visit, participants will record in a telephone diary any muscle and heart symptoms that they experience. During the 1 week after both yearly visits, participants will also undergo an outpatient heart rhythm evaluation. A study coordinator will contact participants once a month by phone over the course of the study to review symptoms.

**Record Verification Date:** August 2007  
**Overall Status:** Not yet recruiting  
**Study Start Date:** August 2007  
**Last Follow-Up Date:**  
†NOTE: Last Follow-Up Date not entered.

**Study Characteristics:**  
Primary Purpose: Natural History  
Duration: Longitudinal  
Selection: Defined Population  
Timing: Prospective Study  
Enrollment: 50 [Anticipated]

**Conditions:**  
Andersen-Tawil Syndrome  
Andersen Syndrome

**Keywords:**  
Arrhythmia  
Muscle Weakness  
Periodic Paralysis  
Channelopathy

**Groups:**  

**Interventions:**  

** Eligibility Criteria:**  
Inclusion Criteria:  
- Clinically confirmed diagnosis of ATS as defined by at least two of the following three criteria:  
  1. Presence of clear-cut episodes of transient muscle weakness
with or without a fixed deficit, typically following exertion or prolonged rest OR atypical history with otherwise typical exam findings (absent reflexes with normal sensation during an episode) OR unexplained hypokalemia between episodes OR abnormal long-exercise nerve conduction study

2. Heart conduction defects: prolonged QTc interval on 12-lead electrocardiogram OR ventricular ectopy, including uniform or multifocal PVCs, polymorphic VT, or bidirectional VT

3. Presence of two or more of the following physical features: low set ears, hypertelorism, small mandible, clinodactyly, syndactyly, micromelia of hands or feet --OR--
   - Meets one of the above three criteria and has at least one family member with two of the criteria --OR--
   - Does not meet the above three criteria, but possesses a mutation in the KCNJ2 gene

Exclusion Criteria:

- Age < 10 years
- Pregnancy

**NOTE:** Preferred format includes lists of inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Gender:</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum Age:</td>
<td>10 Years</td>
</tr>
<tr>
<td>Maximum Age:</td>
<td></td>
</tr>
<tr>
<td>Accepts Healthy Volunteers?</td>
<td>No</td>
</tr>
</tbody>
</table>
### Central Contact:

Kimberly Hart, MA  
Telephone: 585-275-3767  
Email: [Kim_Hart@URMC.Rochester.edu](mailto:Kim_Hart@URMC.Rochester.edu)

### Study Officials/Investigators:

- **Rabi Tawil, MD**  
  Study Chair  
  University of Rochester School of Medicine

- **Robert C. Griggs, MD**  
  Study Principal Investigator  
  University of Rochester School of Medicine

### Locations:

- **Facility:** University of California, San Francisco  
  San Francisco, California, United States  
  **Contact:** Kristin Wong  
  **Investigator:** Jeffrey W. Ralph, MD  
  **Role:** Principal Investigator  
  **Recruitment Status:** Not yet recruiting

- **Facility:** University of Kansas Medical Center  
  Kansas City, Kansas, United States  
  **Contact:** Laura Herbelin  
  **Investigator:** Richard Barohn, MD  
  **Role:** Principal Investigator  
  **Recruitment Status:** Not yet recruiting

- **Facility:** Brigham and Women's Hospital  
  Boston, Massachusetts, United States  
  **Contact:** Kristen Whiteside  
  **Investigator:** Anthony Amato, MD  
  **Role:** Principal Investigator  
  **Recruitment Status:** Not yet recruiting

- **Facility:** University of Rochester School of Medicine and Dentistry  
  Rochester, New York, United States  
  **Contact:** Kimberly Hart  
  **Telephone:** 585-275-3767  
  **Email:** [Kim_Hart@urmc.rochester.edu](mailto:Kim_Hart@urmc.rochester.edu)  
  **Investigator:** Robert C. Griggs, MD  
  **Role:** Principal Investigator  
  **Investigator:** Rabi Tawil, MD
<table>
<thead>
<tr>
<th>Facility</th>
<th>Contact</th>
<th>Investigator</th>
<th>Role</th>
<th>Recruitment Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Texas Southwestern Medical Center</td>
<td>Nina Gorham</td>
<td>Jaya Trivedi, MD</td>
<td>Principal Investigator</td>
<td>Not yet recruiting</td>
</tr>
<tr>
<td>Institute of Neurology and National Hospital for Neurology</td>
<td>Doreen Fialho, MD</td>
<td>Michael Hanna, MD</td>
<td>Principal Investigator</td>
<td>Not yet recruiting</td>
</tr>
<tr>
<td>London Health Sciences Centre</td>
<td>Kori LaDonna</td>
<td>Angelika Hahn, MD</td>
<td>Principal Investigator</td>
<td>Not yet recruiting</td>
</tr>
</tbody>
</table>

**Citations:**

