Our True North: Family & Patient Impact on Research & Development
Speaker: Dr. Wendy Chung, Chung Lab, Columbia University
August 16, 2019

Visit kif1a.org/2019Conference to watch a recording of this presentation.
Research Strategy

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Wendy Chung, MD, PhD
**KIF1A motors**

- Cargo
- Cargo binding domain
- Motor domain
The $KIF1A$ problem

- Trains can run slower than they should (reduced cargo transport)
- Trains can get stalled at the station (no cargo transport)
- Trains can break down on the tracks and cause a traffic jam, preventing other trains from passing (no cargo transport, likely accumulation)
TREATMENT

TARGETED RESEARCH AND EXPLORATION ADVANCING TRIAL MODELS, EDITING, AND NEXT-GENERATION THERAPIES

1. CASE FINDING
2. NATURAL HISTORY
3. OUTCOME MEASURES/BIOMARKER
4. REAGENTS
   - Induced pluripotential stem cells, differentiated cells, organoids, mouse models
5. DETERMINE DISEASE MECHANISM
6. IDENTIFY BEST THERAPEUTIC OPTION
   - Small molecular, biologics, stem cells, gene therapy, gene editing
7. PRECLINICAL TRIALS
   - Rodent studies, large mammal, nonhuman primate
8. CLINICAL TRIALS

TARGETED RESEARCH AND EXPLORATION ADVANCING TRIAL MODELS, EDITING, AND NEXT-GENERATION THERAPIES
1. **Disease Characterization**
   - Longitudinal natural history project
   - Genotype/phenotype studies
   - KAND patient biobank (including postmortem)
   - Collect neuroimaging/raw EEG
   - Additional seizure & medication questionnaire
   - Meaningful difference to families
   - Biomarkers

2. **Disease Modeling**
   - In silico & in vitro analyses of motor function
   - Patient-derived iPSC lines
   - Differentiate PSCs into neurons
   - Determine disease mechanism, genotype/phenotype correlation
   - Generate patient-specific KI mouse models (*Jackson Labs*)

3. **Model Characterization**
   - Behavioral & histological phenotype of mice
   - Cellular morphology, electrophysiology
   - Identify cellular assay amenable to high throughput screening

4. **Therapy Development**
   - Small molecules
   - Oligonucleotides
   - Vectors for delivery
KIF1A Genetic Tags
What families can do

• Natural history study
  • Information from the past, present, and future
  • Genetic lab result
  • Caregiver report
  • Define meaningful difference
  • Medical records/therapists’ evaluations/educators’ evaluations
  • Assessments at the family meeting (height, weight, head circumference)
  • MRIs and EEGs
  • Priority is to determine what is working and what is harmful

• Samples, preferably blood
  • To determine if mutation is de novo or inherited
  • To know what other variants there are in KIF1A
  • To determine if there are other genes beyond KIF1A
  • To determine common genetic variants in KIF1A to target for oligonucleotides
  • Biomarker development
  • To provide a cell based model to ensure your family is represented

• Increase awareness: Rare Disease Day
• Partners/funders (call your senator/representative about NIH grant R01 NS114636-01)
Questions?

Looking forward

KAND Family & Scientific Engagement Conference
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Thank you