Neurogenetic diseases in Mali: case presentation

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Introduction

• Neurogenetic diseases are neglected
  - incurable and debilitating
  - social factors and limited resources increase this burden
  - raising awareness may lessen the burden

• Previous studies in Mali
  - Malians favor genetic testing
  - Malians gain knowledge with genetic counseling
  - Novel mutations and gene in 27 families
Questions

• Are there new hereditary neurological diseases entities or variants in Mali?
• Are these variants due to novel genetic defects or other genetic or environmental factors?
• Premises
  - Malian have specific phenotypic variants
  - mutations in novel genes or novel mutations in known genes
Specific aims

• Specific aim 1
  - Characterize families with hereditary neurological disorders

• Specific aim 2
  - Identify mutations causing these diseases and explore their effect in cell culture models

• Specific aim 3
  - Train faculty members and students in genetics and molecular biology
Methods

• **Patients recruitment**
  - patients from our neurology clinic or referred
  - field trips to enroll disabled patients and significant subjects

• **Genetic analysis**
  - clinically relevant genes will be tested in some families
  - exome sequencing + linkage analysis
  - variants in mapped regions will be first assessed

• **Cell culture studies and animal models**
Summary

• 141 families with 486 subjects
• 485 DNA were collected
• 224 patients (150 expected for the year)
• 22 have other diseases
• Main diseases
  - 29 Spinocerebellar ataxia: SCA2, SCA3, SCA7, unknown
  - 26 Muscular disease
  - 13 Spastic paraplegia
Spinocerebellar ataxia

- Autosomal dominant
- Ataxia, visual and hearing loss
- Psychiatric symptoms
- Challenging:
  - father less symptomatic
  - one not showing symptoms
New Limb-Girdle-Muscular-Dystrophy?

• Very slow progressive proximal weakness
  - childhood onset but ambulatory at 33 years
  - CK levels normal
  - slight bone deformity in older patients

• Negative for all muscle genes, SMA, Pompe

• New gene???
Hereditary spastic paraplegia

- Targeted NextGen panel (all 58 SPG genes)
- 3 families with novel mutations
  - SPG42: one Chinese family
  - SPG10 and SPG11
- 4 negative families
Spinal muscular atrophy

- Autosomal recessive and most common severe inherited disorder of childhood
- Low carrier frequency in population with African ancestry: Mali 1/209 (1/25-1/50)
- Genetic analysis: 0 copies SMN1, 3 copies SMN2
Challenges

• Long consent process: low literacy, translation
• Blood chemistries expensive or unavailable
• Access to patients in the countryside difficult
Conclusion/Perspectives

• Genetic heterogeneity of Malian population
• Opportunity to consolidate previous finding and find new genes relevant to other populations
• Whole exome sequencing and cell studies
• Reach out to other countries
• Center for training in neuro- or genetics
• West African neurogenetic disease survey
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