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

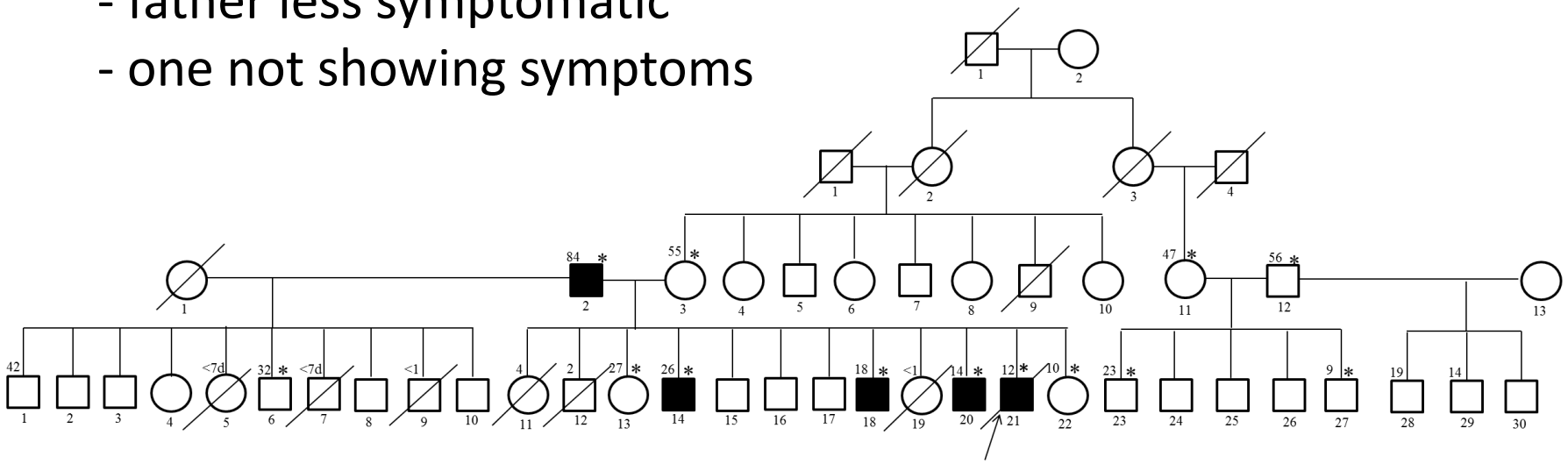
- Patients recruitment
  - patients from our neurology clinic or referred
  - field trips to enroll disabled patients and significant subjects
- Genetic analysis
  - clinically relevant genes will be tested in some families
  - exome sequencing + linkage analysis
  - variants in mapped regions will be 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

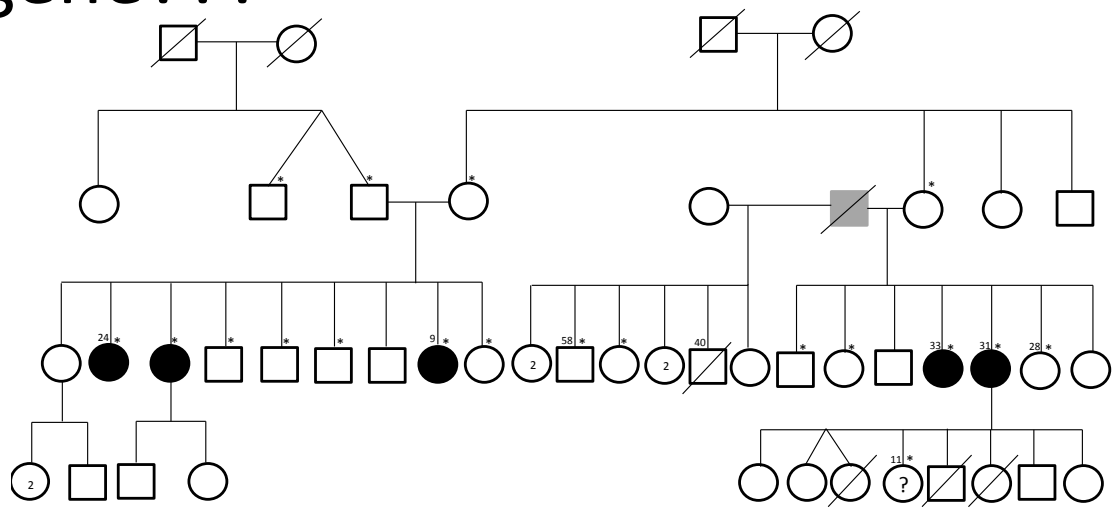
Spinocerebellar ataxia

- Autosomal dominant
- Ataxia, visual and hearing loss
- Psychiatric symptoms
- Challenging:
  - father less symptomatic
  - one not showing symptoms



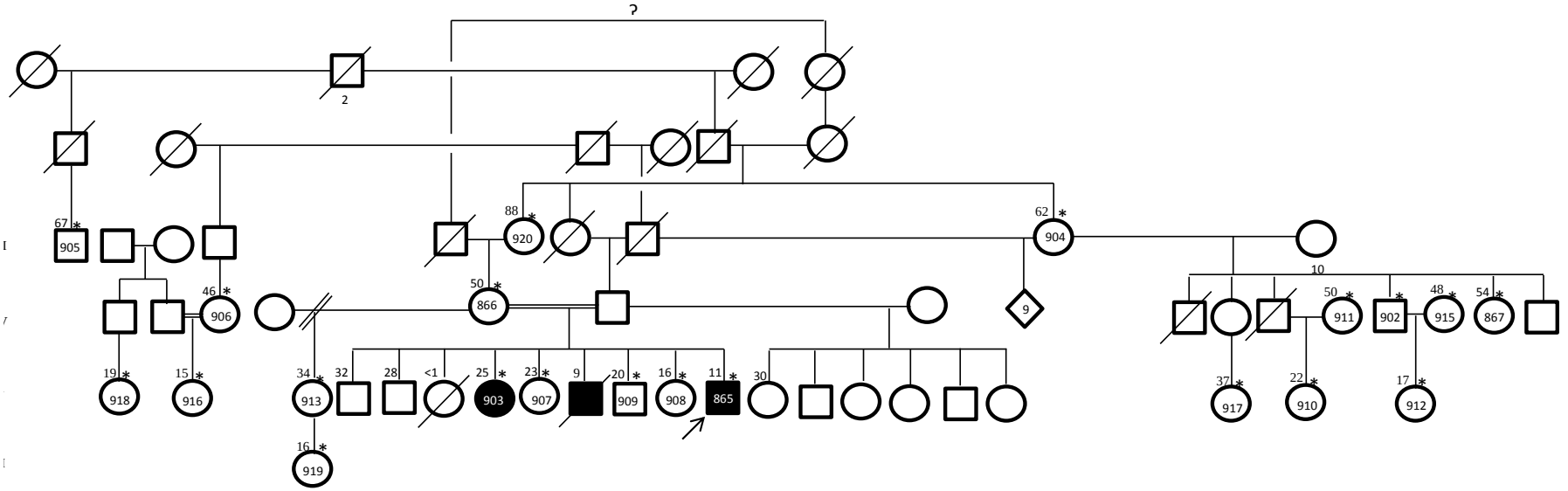
New Limb-Girdle-Muscular-Dystrophy?

- 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???



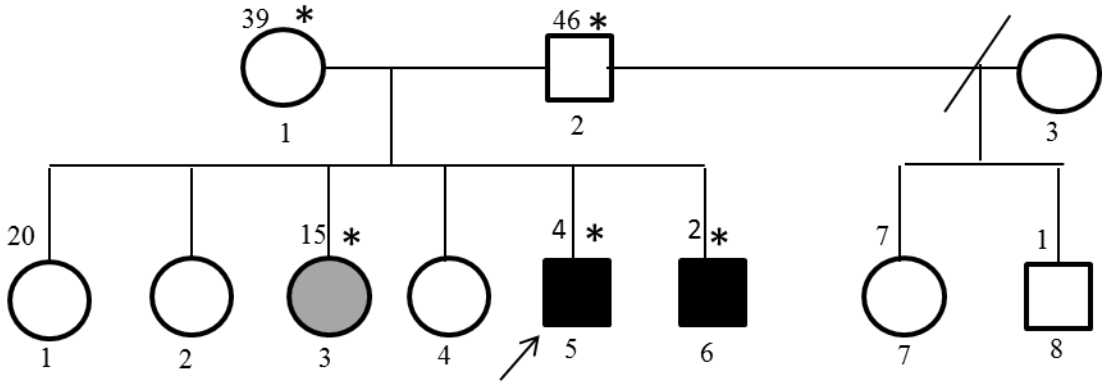
Hereditary spastic paraplegia

- 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

Acknowledgments

GOD and my parents
Participating families

- **Pr. Traoré M**
- **Dr. Fischbeck KH**

- **National Institutes of Health**
- **Grant#: U01HG007044**

Neurogenetics Branch/NINDS/NIH
- Kenneth Fischbeck
- Christopher Grunseich
- Alice Schindler
- Kelian Chen

University College London, London
- Robert Kleta
- Horia Stanescu

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- Pr. Guinto Cheick O.
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- Dr. Cissé Lassana
- Diarra Salimata
- Abdoulaye Yalcouyé
- Abdoulaye Tamega
- Kani Aghate Coulibaly
- Nouhoum Koita
- Soumaila Niaré