Genetic Research in the Aka Pygmy people

Background

- CCCH tandem zinc fingers are critical to the stability of some mRNA.

- 4 proteins have been isolated in this family
  - TTP
  - 11B
  - 11D
  - One found in frogs and fish

Background

- TTP is the best studied zinc protein and has been shown critical to destabilizing the mRNA of GM-CSF and TNF alpha.

- Deficiency of TTP is linked to systemic inflammatory disease.

Background

- In Environmental Genome Project, researchers are studying the stability of certain types of messenger RNA.

- DNA was examined from the stored samples of 72 individuals in the Coriell repository :
  - 24 Caucasians
  - 24 Asians
  - 24 Africans

Background

- Of these 72 genomes, one genome had a null mutation in one allele of the gene for 11B, a zinc finger protein of interest

- This genome came from a female Aka Pygmy from the Central African Republic.

Background

- “We presume, but cannot prove, that these other members of the CCCH tandem zinc finger family will play a role in the turnover of some mRNA species…[and that] both the hemizygous and putative homozygous states might be associated with clinical disease.”

Current Study--Objectives

- To obtain larger number of DNA samples from Aka Pygmies to determine
  - Frequency of the 11B mutation in the population
  - Phenotypic expression of such a mutation in terms of human disease.
- This might lead to knowledge of the function of these proteins and insights into the cause of a human disease.

Current Study--Procedures

- Work with a US anthropologist who has conducted research with the Aka Pygmies for 20 years.
- Contact individuals and families on the road (nomadic)
- Oral process of consent

Current Study--Procedures

- Use tooth brush to scrape inner buccal membranes and spit into a cup.
- Treat the cup with alcohol to preserve DNA for up to 30 days without refrigeration.
- The toothbrush will be washed with distilled water and given to the individual Aka Pygmy as remuneration
- The whole procedure takes 30 seconds.

Current Study--Procedures

- Estimate obtaining DNA samples from 1,000 Aka Pygmies.
- Samples will be obtained from both children and adults.
- Samples will be labeled with the person's name, location, and age to facilitate re-contact if mutations are found and warrant further study.

Current Study

- Transport all the samples to the USA.
- In USA, extract DNA from cells and test for mutations and polymorphisms in 11B genes.

Current Study

- Discussions about the proposed study:
  - Ministers of Health and Scientific Research of CAR
  - Mayor of Bagandu
  - Town meetings in Bagandu
  - Spread word among Aka acquaintances
  - Individual family groups on forest trails
  - Oral consent of individuals obtained

Current Study

- Buccal brushing is harmless.
- Each participant gets a new toothbrush
- Funds will be provided for the completion of the floor of their proposed school and for hiring a teacher for the school.

Current Study

- No physical examination or treatment of infectious or other diseases will be provided.

- More clinical interaction will be built into a subsequent study if we do return to study the link between health status and phenotype with the DNA findings.

- You are the IRB asked to review and approve this study

- What issues should be considered?

8 Ethical Principles

1) Collaborative Partnership
2) Social Value
3) Scientific Validity
4) Fair Subject Selection
5) Favorable Risk-Benefit Ratio
6) Independent Review
7) Informed Consent
8) Respect for Enrolled Participants