Attitudes Regarding Prevention of mtDNA Diseases Through Mitochondrial Replacement Therapy

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Study Aims

1. “Oocyte Mitochondrial Replacement Therapy (MRT) Carrier Survey”
   • Assess the level of concern for transmitting mtDNA point mutations.
   • Assess support for the development of MRT, in the “at risk” mitochondrial community.
   • Assess personal interest in using MRT as a family planning option.

2. “Oocyte MRT Donor Survey”
   • Assess willingness to donate oocytes for research and for clinical use.
“Oocyte MRT Carrier Survey”

Eligibility Confirmation:

• Known or “at risk” carrier of mtDNA mutation
• Female
• ≥ 18 years of age
“Oocyte MRT Carrier Survey”

Questions for all female mtDNA mutation carriers:

1) Have you thought about not having a child because you were concerned about passing the mtDNA mutation to them? (yes/no)

2) Do you think that the project described above is important and worthwhile? (yes/no)

3) If you have stored eggs, would you be interested in donating them for basic laboratory research to develop this technique? No viable zygote would be produced. (yes/no)

4) Are you interested in becoming an egg donor? You would receive hormone injections then have an outpatient procedure to obtain the eggs. No viable zygote will be produced. (yes/no)
Questions 5-8 (Only for participants who are interested in having children)

5) Are you considering having children now or in the future? (yes/no)

6) How important is it that your children are your biological offspring? (not important, somewhat important, very important)

7) Would you be interested in using this technology to try to have a child? (yes/no)

8) Would you be interested in allowing your eggs to be used for basic laboratory research in the process of developing an implantable zygote? (yes/no)
“Oocyte MRT Donor Survey”

Questions

1) Would you be willing to donate your eggs for basic laboratory research in which a viable zygote would NOT be produced?

2) Would you be willing to donate your eggs for the production of an implantable zygote that has the father and the carrier mother’s nuclear DNA and your mtDNA?
Subject Recruitment

Carrier Females
- Private and clinic patients
- Matrilineal relatives of known patients
- Participants in previous studies
- Advertisement: NAMDC, UMDF, Mito-Action, patient support groups

Oocyte Donors
- Healthy oocyte donors at a local fertility clinic
Oocyte MRT Carrier Survey Results

Subjects:
N=92 test positive or “at risk” carriers
All >18 years of age

13 mtDNA mutations represented:
(m.3243A>G, m.3288A>G, m.8344 A>G, m.11778G>A,
m.12276G>A, m.3460G>A, m.8363G>A, m.10191T>C,
m.11484T>C, m.14484T>C, m.8993T>C, m.8993T>G,
m.9176T>C)
Oocyte MRT Carrier Survey Results

• 100% (92/92) of participants understood that they could transmit the mtDNA mutation to their offspring.

• 78% (35/45) of women of childbearing age had thought about not having children because of transmission risk.

• 73% (37/51) of women who had children prior to knowing they carried (or were “at risk” of carrying) a mtDNA mutation would have thought about not having children had they known of the risk.

• 95% (87/92) said the development of MRT was an important and worthwhile project.
Of women considering having children (n=21)

Having biological offspring was considered:
  52% - Very important
  43% - Somewhat important
  5% - Not important

90% are interested in using MRT to have a child

78% are interested in allowing their eggs to be used for basic laboratory research in the process of developing an implantable zygote.
“ONGT Donor Survey”
Results

N=112 Healthy oocyte donors

All at least 18 years of age

92% would donate for basic laboratory research in which viable zygotes are not produced

87% would donate for the production of implantable zygotes.
Conclusions

Among women who are known carriers, as well as for “at risk” individuals:
• There is widespread concern for transmitting mtDNA mutations.
• There is overwhelming support for the development and clinical use of MRT.
• There is widespread interest in MRT among women who are considering children.

Among healthy oocyte donors:
• The majority are willing to donate for research and development of MRT and for clinical use.
- Collaborative Clinical Research
- Public Resources and Education
- Centralized Data Coordination and Technology Development
- Training

DHHS-NIH
ORDR, NCATS, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIDCR, NIAID, NCI, NIMH, ODS

Inherited Neuropathies Consortium
Coalition of Patient Advocacy Groups (CPAG)
Primary Immune Deficiency Treatment Consortium
Rett Syndrome, MECP2 Duplications, and Rett-related Disorders Consortium

Lysosomal Disease Network

Urea Cycle Disorders Consortium

Brittle Bone Disorders Consortium

VASCUITIS CLINICAL RESEARCH CONSORTIUM

DYSTONIA COALITION

The Porphyrias Consortium

Rare Lung Diseases Consortium

cGVHD

RARE KIDNEY STONE CONSORTIUM

Nephrotic Syndrome Study Network

Frontotemporal Lobar Degeneration Clinical Research Consortium
Clinical Research in ALS and Related Disorders for Therapeutic Development

Autonomic Disorders Consortium

Developmental Synaptopathies Consortium
Genetic Disorders of Mucociliary Clearance Consortium

CEGiR
Consortium of Esophageal Gastrointestinal Disease Researchers

NAMDC
North American mitochondrial disease consortium

The Data Management and Coordinating Center
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United Mitochondrial Disease Foundation
Muscular Dystrophy Association
MitoAction
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<thead>
<tr>
<th>mtDNA mutation carrier questions</th>
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<td>2. For women who had children before knowing they carried or were at risk of carrying a mitochondrial DNA mutation: Would you have thought about NOT having children because you were concerned about passing a mtDNA mutation to them?</td>
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<td>3. Are you someone who did not/do not plan on having children anyway regardless of your mitochondrial DNA carrier status?</td>
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