Frontotemporal dementia

Frontotemporal dementia (FTD) represents only 10-20% of all dementias, but remains important because of its earlier age of onset compared to Alzheimer's disease (AD), and its characteristic attack on core human qualities such as compassion, insight and verbal communication. Treatment of FTD is more likely to succeed when given in the early stages than in later stages, when symptoms appear and worsen. Detection of brain alterations is needed prior to these symptoms in order to develop new treatments.

The National Institute on Aging has funded a research project to use magnetic resonance imaging (MRI) to detect brain alterations in persons without dementia symptoms, but who may later develop FTD. FTD can occur in persons with mutations in the valosin-containing protein (VCP). The VCP gene is located on chromosome 9, and is associated with FTD, Paget's disease of bone, and inclusion-body myopathy (IBMPFD).

In this research, volunteers in families with IBMPFD will be tested to insure the absence of symptoms typical of FTD. Those with mutations will be compared to members of the same families without mutations. Functional MRI studies to measure frontal and parietal activation during tasks often performed poorly in persons with early symptoms of FTD. These images will be analyzed using advanced analytical and statistical techniques. The research will also compare brain anatomy between VCP mutation carriers and non-carriers.

The hope for the research is to combine the imaging measurements with cognitive test results to develop a predictive model for dementia. These fundamental studies are expected to allow prediction of FTD in IBMPFD members, to allow treatments to be developed to prevent dementia.

The principal investigator is Dr. Charles Smith. Volunteers will travel to Lexington, Kentucky for one full day to undergo cognitive testing, examination and MRI scanning. Travel costs and other expenses will be paid by the study. This is an important investment confirming the importance the National Institutes of Health places on IBMPFD and the need to develop treatment for this condition. The investigators will be contacting eligible families, and we hope to have enthusiastic participation by many family members.

To find out more information please call Dr. Charles Smith at (859)323-1113 or the Research Coordinator, Barbara Martin, RN at (859)323-0494, bjpatt@email.uky.edu

Pre-Implantation Genetic Diagnosis

In addition to genetic testing for IBMPFD, Preimplantation Genetic Diagnosis (PGD) is a valuable option available for those who have been identified as carriers of the mutation. For those who have IBMPFD, it means that they carry the gene that can be passed on to their children. Each pregnancy/child has a 50% chance of being a carrier for the gene that causes the disease. The advantage of having PGD is that we can test for the disease in the baby *before* the woman is pregnant.

The process is similar to IVF, in-vitro fertilization, with the PGD testing added in. The couple donates eggs and sperm, which become embryos. When this single cell starts to multiply to about 8 cells, one cell is removed, and the rest is left to grow into an embryo. Research has not shown that removing one cell from the embryo hurts the baby's development.

That one cell is tested for the gene mutation that causes the disease, IBMPFD. The embryos that do not have the mutation are implanted into the mother, and hopefully grow into a healthy baby or babies.

PGD does not test for every gene mutation, only for IBMPFD, or other specific mutations that are requested. It is also not a guarantee for a baby without any birth defects; all pregnancies, regardless of testing, age and family history, are at a 3-5% risk for birth defects, including those that are not genetic. However, PGD is able to give parents peace of mind that their children will not inherit IBMPFD.

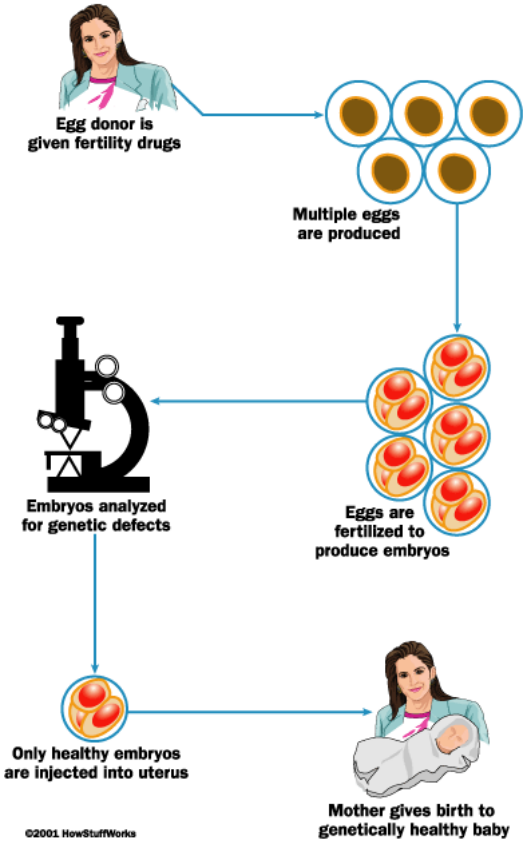
Single cell being removed

For More Information about PGD:

•University of Chicago Hospitals:
http://babies.bsd.uchicago.edu/endo/artLaboratories.htm
To set up an appointment: 773-702-6642

•Genesis Genetics Institute Detroit, MI:
Director: Mark Hughes, M.D., PhD
Genetic Counselor: Shannon K Wiltse, MS, CGC
E-mail: pgd@genesisgenetics.com
E-mail: counselor@genesisgenetics.org
Phone: 313-544-4006

Overview of the General Techniques Used in PGD:



CLIA testing

In order to give results of DNA tests to patients who may have mutations, the testing must be done in a CLIA (Clinical Laboratory Improvement Amendments) laboratory. This is done because CLIA labs are certified for accuracy, reliability and timeliness of test results, and are specialized in providing information for the diagnosis, prevention, or treatment of disease, and for the assessment of health.

We have worked with the Mitomed laboratory at the University of California, Irvine in developing testing for VCP mutations. Individuals from families with known mutations can learn of their status by testing in the CLIA laboratory. At 2014 Hewitt Hall ,Irvine, CA 92697-3940. If you would like more information please contact the lab at 949-824-1886 , email at mdl.lab@uci.edu or the Kimonis laboratory at 949-824-0571.