

Preclinical Research Resources

FARA-funded research has facilitated the discovery and development of research resources such as animal models, cell models, antibodies, biorepositories etc. We are grateful to the discovery scientists who have worked hard to bring us these important assets and continue to give to the community by sharing their results, knowledge, expertise and resources. It is our goal to promote collaboration throughout the research community by communicating with the discovery, translational and clinical scientists and facilitating their access to such resources. For more information visit:

<http://www.curefa.org/researchresources>.

Frataxin:

Sequence and a summary of human frataxin features can be found at Uniprot:

<https://www.uniprot.org/uniprot/Q16595-3>

Biorepositories:

Plasma, serum, and fresh samples. Through the Collaborative Clinical Research Network (CCRN) in Friedreich's ataxia, biorepositories of DNA, RNA, plasma and serum from Friedreich's ataxia patients have been established. Additionally, investigators in the CCRN in Friedreich's ataxia are willing to collaborate with researchers who need fresh biological samples from Friedreich's ataxia patients for translational and clinical research studies. For more information contact David Lynch at lynchd@penncmedicine.upenn.edu

Tissue Bank. To make valuable tissues available to Friedreich's ataxia investigators everywhere, FARA supports an autopsy and tissue donation program at the VA Medical Center in Albany, New York. The program's principal investigator, Arnulf Koeppen, MD who is a neurologist and neuropathologist that has made significant contributions to our understanding of Friedreich's ataxia as well as other ataxias. This tissue bank has fixed and frozen tissues from brain, spinal cord, heart, sural nerve, and pancreas of 30 individuals with Friedreich's ataxia. Requests for tissues can be made to Dr. Koeppen (email: arnulf.koeppen@va.gov, phone: 518-626-6391 or 518-626-6377).

Cell Lines:

A repository of >80 **fibroblast lines** from Friedreich's ataxia patients, carriers and healthy individuals has been established at the University of Alabama at Birmingham. The repository is a collaboration between the laboratories of Dr. Marek Napierala, at UAB Dr. David Lynch at the Children's Hospital of Philadelphia. See the available cell lines here: <https://sites.uab.edu/thenapieralalab/frda-cell-line-repository> Send requests to mnapiera@uab.edu or lynchd@penncmedicine.upenn.edu

Reference:

- Li Y¹, Polak U², Clark AD¹, Bhalla AD¹, Chen YY¹, Li J¹, Farmer J³, Seyer L³, Lynch D³, Butler JS¹, Napierala M^{1,4}. (2016) Establishment and Maintenance of Primary Fibroblast Repositories for Rare Diseases-Friedreich's Ataxia Example. Biopreserv Biobank. 2016 Aug;14(4):324-9.

Friedreich's ataxia **lymphoblast and fibroblast** cell lines are available at the Coriell Cell Repository. Please note that several researchers have reported problems working with the fibroblast lines from Coriell (they have been passaged many times) and there are only a few lines available.

- <http://ccr.coriell.org/Sections/Search/Search.aspx?PgId=165&q=frda>.

Dr. Marek Napierala at the University of Alabama at Birmingham has established a repository of Friedreich's ataxia **induced pluripotent stem cells (iPSCs)**. The repository currently includes 20 FRDA and control iPSC lines including three sets of patient and isogenic, CRISPR/Cas9-edited paired lines. See the available lines here: <https://sites.uab.edu/thenapieralalab/frda-cell-line-repository> The price is \$1000 + shipping per vial but recipients of active FARA grants will only pay shipping costs. Send requests to mnapiera@uab.edu

FA iPSCs are also available at Coriell Cell Repository. These cell lines were established by the laboratory of Joel Gottesfeld, PhD at The Scripps Research Institute. Coriell provides a Certificate of Analysis.

- http://ccr.coriell.org/Sections/Search/Sample_Detail.aspx?PgId=166&Ref=GM23404
- http://ccr.coriell.org/Sections/Search/Sample_Detail.aspx?PgId=166&Ref=GM23913

References:

- Ku S, Soragni E, Campau E, Thomas E, Altun G, Laurent L, Loring J, Napierala M, Gottesfeld J. (2010) Friedreich's ataxia induced pluripotent stem cells model intergenerational GAA·TTC triplet repeat instability. *Cell Stem Cell*. **7**:631-7 2009. (PubMed ID: 21040903)

Expression Array Data:

FARA supported the development of a database of gene expression data from Friedreich's ataxia patients and from mouse models of the disease in collaboration with Dr. Giovanni Coppola and Dr. Brent Fogel at UCLA and the Collaborative Clinical Research Network (CCRN) and others. The database is available at <https://coppolalab.ucla.edu/account/login/>. You will need to register for a password to access the database. Array data is available for some patients who have taken part in natural history studies through the CCRN, so clinical data can be accessed. Additional data is still being added over time, and additional analyses are underway.

Mouse Models (see separate document for more details):

Friedreich's ataxia transgenic mouse models are now available through the Jackson Laboratory (JAX), and through collaborations with Brunel University (UK), Erasme University (Belgium), Murdoch Children's Research Institute (Australia), INSERM (France), and UCLA (California). These models include humanized mice that have a human gene with a repeat sequence inserted (Pook and Sarsero), models with a repeat sequence inserted into the frataxin mouse gene (Pandolfo KIKO), and models where frataxin is ablated (INSERM and Puccio conditional knockout, and UCLA inducible frataxin knockdown).

Cell Models & High-Throughput Assays:

FARA works closely with several investigators in the United States, Europe and Australia who are developing Friedreich's ataxia neuronal and cardiac cell models by differentiation of iPSCs derived from patient fibroblasts. Some of these models are available for sharing and some Friedreich's ataxia iPSCs are being banked for greater access to researchers worldwide.

For example, FARA funded efforts include:

- Liu J, Verma P, Evans-Galea M, Delatycki M, Michalska A, Leung J, Crombie D, Sarsero J, Williamson R, Dottori M, Pébay A. (2011) Generation of induced pluripotent stem cell lines from Friedreichataxia patients. *Stem Cell Rev.* 7: 703-13.
- Ku S, Soragni E, Campau E, Thomas E, Altun G, Laurent L, Loring J, Napierala M, Gottesfeld J. (2010) Friedreich's ataxia induced pluripotent stem cells model intergenerational GAA•TTC Triplet Repeat Instability. *Cell Stem Cell.* 7: 631-37.

Other cellular models have been developed from a variety of approaches, with different defining features. For example, Helene Puccio, PhD and colleagues developed murine cellular models for FA that have all the biochemical phenotypes associated with Friedreich's ataxia; making this model useful for drug discovery.

That work can be found here:

- Calmels N, Schmucker S, Wattenhofer-Donzé M, Martelli A, Vaucamps N, Reutenauer L, Messaddeq N, Bouton C, Koenig M, Puccio H. (2009) The first cellular models based on frataxin missense mutations that reproduce spontaneously the defects associated with Friedreich ataxia. *PlosOne.* 4: e6379.

Several other investigators have developed high throughput assays for drug discovery in Friedreich's ataxia. These assays vary significantly – some assays developed focus on readouts of mitochondrial function, some focus on direct measurements of frataxin (e.g., genetically-derived assays using cells that carry the expanded GAA repeats in the frataxin gene). If you would like to learn more about these cellular models or assays or to be connected directly to these discovery scientists please contact: Liz Soragni (liz.soragni@curefa.org), and see the associated informational sheet on frataxin-related assays.