

Friedreich Ataxia -Omic Datasets

FARA is grateful to the research community for continued characterization and subsequent data sharing of datasets from Friedreich ataxia patient samples and animal and cell-based models.

An overview of published transcriptomic, proteomic and metabolomic studies using different FA models is shown below:

Published Transcriptomic FA Studies		
Reference	Method	Sample
Yeast		
Moreno-Cermeño A, Alsina D, Cabiscol E, Tamarit J, Ros J (2013) "Metabolic remodeling in frataxin-deficient yeast is mediated by Cth2 and Adr1." <i>Biochim Biophys Acta</i> . 1833: 3326-37.	Transcriptome profiling by microarray	Conditional yeast frataxin homologue (Yfh1) depletion mutant.
shRNA FXNKD Mouse Model		
Chandran V, Gao K, Swarup V, Versano R, Dong H, Jordan MC, Geschwind DH. (2017) "Inducible and reversible phenotypes in a novel mouse model of Friedreich's Ataxia." <i>Elife</i> . 6: e30054.	Transcriptome profiling by microarray	Heart, cerebellum and DRG neurons from shRNA FXNKD mouse, WT, and rescue mice.
KIKO Mouse Model		
Coppola G, Choi S, Santos MM, Miranda CJ, Tontier D, Wexler EM, Pandolfo M, Geschwind DH. (2006) "Gene expression profiling in frataxin deficient mice: Microarray evidence for significant expression changes without detectable neurodegeneration." <i>Neurobiol Dis</i> . 22:302-11.	Transcriptome profiling by microarray	3 CNS regions (spinal cord, brainstem, cerebellum).
Rai M, Soragni E, Jenssen K, Burnett R, Herman D, Coppola G, Geschwind DH Gottesfeld JM, Pandolfo M. (2008) "HDAC inhibitors correct frataxin deficiency in a Friedreich ataxia mouse	Transcriptome profiling by microarray	Brain (cerebral hemispheres), cerebellum, and heart.

model." <i>PLoS One</i> . 3 : e1958.		
Coppola G, Marmolino D, Lu D, Wang Q, Cnop M, Rai M, Acquaviva F, Coccozza S, Pandolfo M, Geschwind DH. (2009) "Functional genomic analysis of frataxin deficiency reveals tissue-specific alterations and identifies the PPARgamma pathway as a therapeutic target in Friedreich's ataxia." <i>Hum. Mol. Genet.</i> 18 :2452-2461.	Transcriptome profiling by microarray	Heart, liver, and skeletal muscle.
YG8R Mouse Model		
Shan Y, Schoenfeld RA, Hayashi G, Napoli E, Akiyama T, Carstens MI, Carstens EE, Pook MA, Cortopassi GA. (2013) "Frataxin Deficiency Leads to Defects in Expression of Antioxidants and Nrf2 Expression in Dorsal Root Ganglia of the Friedreich's Ataxia YG8R Mouse Model." <i>Antioxid Redox Signal.</i> 19 :1481-93.	Transcriptome profiling by microarray	DRG tissue.
MCK-FXNKO Mouse		
Seznec H, Simon D, Bouton C, Reuenaier L, Hertzog A, Golik P, Procaccio V, Patel M, Drapier JC, Koenig M, Puccio H. (2004) "Friedreich ataxia: the oxidative stress paradox." <i>Hum. Mol. Genet.</i> 14 :463-74.	Mitochondrial transcriptome profiling by microarray (Mitochip, MAMMAG)	Heart of MCK-FXNKO mouse (i.e., heart and skeletal muscle FXN knockout).
Martin AS, Abraham DM, Hershberger KA, Bhatt DP, Mao L, Cui H, Liu J, Liu X, Muehlbauer MJ, Grimsrud PA, Locasale JW, Payne RM, Hirschey MD. (2017) "Nicotinamide mononucleotide requires SIRT3 to improve cardiac function and bioenergetics in a Friedreich's ataxia cardiomyopathy model." <i>JCI Insight.</i> 2 : e93885.	nanoLC-MS/MS	Heart of MCK-FXNKO mouse (i.e., heart and skeletal muscle FXN knockout).
FA Cell Culture Models; FA Fibroblasts; FA Lymphocytes; FA-Patient iPSC-Derived Cells		
Tan G, Napoli E, Taroni F, Cortopassi G. (2003) "Decreased expression of genes involved in sulfur amino acid metabolism in frataxin-deficient cells." <i>Hum. Mol. Genet.</i> 12 :1699-711.	Transcriptome profiling by microarray	Lymphoblasts, fibroblasts, and N-tera2/D1 (NT2) cells (with siRNA against frataxin).

<p>Tan G, Napoli E, Taroni F, Cortopassi G. (2003) "Decreased expression of genes involved in sulfur amino acid metabolism in frataxin-deficient cells." <i>Hum. Mol. Genet.</i> 12:1699-711.</p>	<p>Transcriptome profiling by microarray</p>	<p>Lymphoblasts, fibroblasts, and N-tera2/D1 (NT2) cells (with siRNA against frataxin).</p>
<p>Burnett R, Melander C, Puckett JW, Son LS, Wells RD, Dervan PB, Gottesfeld JM. (2006) "DNA sequence-specific polyamides alleviate transcription inhibition associated with long GAA.TTC repeats in Friedreich's ataxia." <i>Proc. Natl. Acad. Sci.</i> 103:11497-502.</p>	<p>Transcriptome profiling by microarray</p>	<p>FA and control lymphoid cells.</p>
<p>Ku S, Soragni E, Campau E, Thomas EA, Altun G, Laurent LC, Loring JF, Napierala M, Gottesfeld JM. (2010) "Friedreich's ataxia induced pluripotent stem cells model intergenerational GAA·TTC triplet repeat instability." <i>Cell Stem Cell.</i> 7:631-7.</p>	<p>Transcriptome profiling by microarray</p>	<p>FA patient fibroblast-derived iPSCs.</p>
<p>Chan PK, Torres R, Yandim C, Law PP, Khadayate S, Mauri M, Grosan C, Chapman-Rothe N, Giunti P, Pook M, Festenstein R. (2013) "Heterochromatinization induced by GAA-repeat hyperexpansion in Friedreich's ataxia can be reduced upon HDAC inhibition by vitamin B3." <i>Hum. Mol. Genet.</i> 22:2662-75.</p>	<p>High-throughput RNA sequencing treated with nicotinamide</p>	<p>Patient primary lymphoblasts</p>
<p>Soragni E, Miao W, Iudicello M, Jacoby D et al. (2014). "Epigenetic therapy for Friedreich ataxia." <i>Ann Neurol</i> 76(4):489-508. PMID: 25159818.</p>	<p>BeadArray of cells treated with HDAC109</p>	<p>Patient iPSC neurons</p>
<p>Napierala JS, Li Y, Lu Y, Lin K, Hauser LA, Lynch DR, Napierala M. (2017) "Comprehensive analysis of gene expression patterns in Friedreich's ataxia fibroblasts by RNA sequencing reveals altered levels of protein synthesis factors and solute carriers." <i>Dis Model Mech.</i> 10(11):1353-1369.</p>	<p>RNAseq</p>	<p>FA and control fibroblasts</p>

Erwin GS, Grieshop MP, Ali A, Qi J et al. (2017) "Synthetic transcription elongation factors license transcription across repressive chromatin". <i>Science</i> 358(6370):1617-1622	RNAseq of cells treated with synthetic transcription elongation factors	FA lymphocytes
Cotticelli MG, Xia S, Kaur A, Lin D, Wang Y, Ruff E, Tobias JW, Wilson RB. (2018) "Identification of p38 MAPK as a novel therapeutic target for Friedreich's ataxia." <i>Scientific Reports</i> . 8:5007.	Transcriptome profiling by microarray	FA fibroblast lines (growth defect and cytokine secretion defect).
FA Patient Peripheral Blood		
Haugen AC, Prospero NA, Parker JS, Fannin RD, Chou J, Meyer JN, Halweg C, Collins JB, Durr A, Fischbeck K, Van Houten B. (2010) "Altered gene expression and DNA damage in peripheral blood cells from Friedreich's ataxia patients: cellular model of pathology." <i>PLoS One</i> . 6: e1000812.	Transcriptome profiling by microarray	Peripheral blood.
Coppola G, Burnett R, Perlman S, Versano R, Gao F, Pasterer H, Rai M, Sacca F, Filla A, Lynch DR, Rusche JR, Gottesfeld JM, Pandolfo M, Geschwind DH. (2011) "A gene expression phenotype in lymphocytes from Friedreich ataxia patients." <i>Ann Neurol</i> . 70:790-804.	Transcriptome profiling by microarray	Peripheral blood mononuclear cells.
Salehi MH, Kamalidehghan B, Houshmand M, Yong Meng G, Sadeghizadeh M, Aryani O, et al. (2014) "Gene Expression Profiling of Mitochondrial Oxidative Phosphorylation (OXPHOS) Complex I in Friedreich Ataxia (FRDA) Patients." <i>PLoS ONE</i> . 9: e94069."	Gene expression profiling (RT-PCR) of mitochondrial and nuclear DNA genes that encode for OXPHOS.	Blood.
Steinkellner H, Singh HN, Mcekenthaler MU, Golderberg H, Moganty RR, Scheiber-Mojdehkar B, Sturm B. (2017) "No changes in heme synthesis in human Friedreich's ataxia erythroid progenitor cells." <i>Gene</i> . 621:5-11.	"cDNA-microarray analysis ("IronChip"; the Chip measures the expression of 536 genes with a special focus on genes which are involved in iron/copper metabolism)."	Erythroid progenitor cells.

Seco-Cervera M González-Rodríguez D, Ibáñez-Cabellos JS, Peiró-Chova L, González-Cabo P, García-López E, Vilchez JJ, Sanz-Gallego I, Pallardó FV García-Giménez JL (2017) "Circulating miR-323-3p is a biomarker for cardiomyopathy and an indicator of phenotypic variability in Friedreich's ataxia patients". <i>Sci Rep.</i> 7(1):5237.	RNAseq for miRNA	Plasma
Dantham S, Srivastava AK, Gulati S, Rajeswari MR. (2018) "Differentially Regulated Cell-Free MicroRNAs in the Plasma of Friedreich's Ataxia Patients and Their Association with Disease Pathology". <i>Neuropediatrics.</i> 49(1):35-43.	Agilent microarray platform for miRNA	Plasma
Nachun D, Gao F, Isaacs C, Strawser C, Yang Z, Dokuru D, Van Berlo V, Sears R, Farmer J, Perlman S, Lynch DR, Coppola G. (2018) "Peripheral blood gene expression reveals an inflammatory transcriptomic signature in Friedreich's ataxia patients." <i>Hum. Mol. Genet.</i> ddy198. *	Transcriptome profiling by microarray	Peripheral blood.

* FARA is working with Giovanni Coppola, PhD at UCLA and the Collaborative Clinical Research Network (CCRN) and others to develop a database of gene expression data from Friedreich's ataxia patients and from mouse models of the disease. The database is available from Dr. Coppola's website 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. For more information, please contact Giovanni Coppola: gcoppola@ucla.edu

Published Large Scale Methylation FA Studies			
Reference	Method	Sample	PubMed link
FA-Patient iPSC-Derived Cells			
Evans-Galea MV, Carrodus N, Rowley SM, Corben LA, Tai G, Saffery R, Galati JC, Wong NC, Craig JM, Lynch DR, Regner SR, Brocht AF, Perlman SL, Bushara KO, Gomez CM, Wilmot GR, Li L, Varley E, Delatycki MB, Sarsero JP (2012) "FXN methylation predicts expression and clinical outcome in Friedreich ataxia." <i>Ann Neurol.</i> 71(4):487-97.	EpiTYPER MassARRAY platform to determine C methylation upstream and downstream of the GAA	FA Lymphocytes	https://www.ncbi.nlm.nih.gov/pubmed/22522441

Published Proteomic FA Studies		
Reference	Method	PubMed link
Yeast		
Alsina D, Ros J, and Tamarit J. (2018) "Nitric oxide prevents Aft1 activation and metabolic remodeling in frataxin-deficient yeast." <i>Redox Biol.</i> 14 : 131-41.	Proteomics (MRM: Multiple Reaction Monitoring; targeted mass spectrometry)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5602528/
Moreno-Cermeño A, Alsina D, Cabisco E, Tamarit J, Ros J (2013) "Metabolic remodeling in frataxin-deficient yeast is mediated by Cth2 and Adr1." <i>Biochim Biophys Acta.</i> 1833 : 3326-37.	Proteomics (2D-electrophoresis with tryptic digestion and MS/MS ion search)	https://www.ncbi.nlm.nih.gov/pubmed/24100161
Irazusta V, Cabisco E, Reverter-Branchat G, Ros J, Tamarit J. (2006) "Manganese is the link between frataxin and iron-sulfur deficiency in the yeast model of Friedreich ataxia." <i>J Biol Chem.</i> 281 :12227-32.	Proteomics (2D-electrophoresis)	https://www.ncbi.nlm.nih.gov/pubmed/16510442
Gabrielli N, Ayté J, Hidalgo E. (2012) "Cells Lacking Pfh1, a Fission Yeast Homolog of Mammalian Frataxin Protein, Display Constitutive Activation of the Iron Starvation Response" <i>J Biol Chem.</i> 287 :43042-51.	Dimethyl-labeled proteins used for MS/MS	https://www.ncbi.nlm.nih.gov/pubmed/23115244
MCK-FXNKO Mouse		
Sutak R, Xu X, Whitnall M, Kashem MA, Vyoral D, Richardson DR. (2008) "Proteomic analysis of hearts from frataxin knockout mice: marked rearrangement of energy metabolism, a response to cellular stress and altered expression of proteins involved in cell structure, motility and metabolism." <i>Proteomics.</i> 8 : 1731-41.	Proteomics (2D-electrophoresis with tryptic digestion and MS/MS ion search)	https://www.ncbi.nlm.nih.gov/pubmed/18340635
Martin AS, Abraham DM, Hershberger KA, Bhatt DP, Mao L, Cui H, Liu J, Liu X, Muehlbauer MJ, Grimsrud PA, Locasale JW, Payne RM, Hirschey MD. (2017) "Nicotinamide mononucleotide requires SIRT3 to improve cardiac function and bioenergetics in a Friedreich's ataxia cardiomyopathy model." <i>JCI Insight.</i> 2 : e93885.	nanoLC-MS/MS	https://www.ncbi.nlm.nih.gov/pubmed/28724806

FA-Patient iPSC-Derived Cells		
Shan B, Xu C, Zhang Y, Xu T, Gottesfeld JM, and Yates JB 3rd. (2014) "Quantitative proteomic analysis identifies targets and pathways of a 2-aminobenzamide HDAC inhibitor in Friedreich's ataxia patient iPSC-derived neural stem cells." <i>J Proteome Res.</i> 13 : 4558-66.	Proteomics (MuDPIT: Multi-Dimensional Protein Identification Technology)	https://www.ncbi.nlm.nih.gov/pubmed/24933366
FA Patient Lymphocytes		
Télot L, Rousseau E, Lesuisse E, Garcia C, Morlet B, Léger T, Camadro JM, and Serre V. (2018) "Quantitative proteomics in Friedreich's ataxia B-lymphocytes: A valuable approach to decipher the biochemical events responsible for pathogenesis." <i>Biochim Biophys Acta.</i> 1864 : 997-1009.	LC-MS/MS quantitative proteomics	https://www.ncbi.nlm.nih.gov/pubmed/29329987
Patient Plasma		
Swarup V, Srivastava AK, Padma MV, Rajeswari MR. (2013) "Quantitative profiling and identification of differentially expressed plasma proteins in Friedreich's ataxia." <i>J Neurosci Res.</i> 91 : 1483-91.	Proteomics (2D-electrophoresis of protein samples labeled with fluorescent cyanine (Cy) dyes; internal standard prepared by mixing equal amounts of all samples with a Cy dye). LC-MS/MS	https://www.ncbi.nlm.nih.gov/pubmed/23996585
Bulteau AL, Planamente S, Jornea L, Dur A, Lesuisse E, Camadro JM, Auchere F. (2012) "Changes in mitochondrial glutathione levels and protein thiol oxidation in Yfh1 deficient yeast cells and the lymphoblasts of patients with Friedreich's ataxia." <i>Biochim Biophys Acta.</i> 1822 : 212-25.	Proteomic analysis of glutathionylated mitochondrial proteins (MALDI MS and MS/MS)	https://www.ncbi.nlm.nih.gov/pubmed/22200491

Published Metabolomic FA Studies		
Reference	Method	Sample
KIKO FA Mouse Model		
Hayashi G, Shen Y, Pedersen TL, Newman JW, Pook M, Cortopassi G. (2014) "Frataxin deficiency increases cyclooxygenase 2 and prostaglandins in cell and animal models of Friedreich's ataxia." <i>Hum. Mol. Genet.</i> 23 :6838-47.	UPLC-tandem mass spectrometry	KIKO mouse cerebellum.

<p>MCK-FXNKO Mouse</p> <p>Martin AS, Abraham DM, Hershberger KA, Bhatt DP, Mao L, Cui H, Liu J, Liu X, Muehlbauer MJ, Grimsrud PA, Locasale JW, Payne RM, Hirschey MD. (2017) "Nicotinamide mononucleotide requires SIRT3 to improve cardiac function and bioenergetics in a Friedreich's ataxia cardiomyopathy model." <i>JCI Insight</i>. 2: e93885.</p>	<p>nanoLC-MS/MS</p>	<p>Heart of MCK-FXNKO mouse (i.e., heart and skeletal muscle FXN knockout).</p>
<p>FA Patient Platelets</p> <p>Worth AJ, Basu SS, Deutsch EC, Hwang WT, Snyder NW, Lynch DR, Blair IA. (2015) "Stable isotopes and LC-MS for monitoring metabolic disturbances in Friedreich's ataxia platelets." <i>Bioanalysis</i>. 7:1843-55.</p>	<p>Stable isotope labeling; LC-MS</p>	<p>Patient platelets.</p>



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