LSD Newsletter

Lysosomal Storage Disease Program at UC Irvine
The Southern California Consortium for Lysosomal Disorders

UCIrvine

Recent Events:

September 12, 2020 11am

- Fabry Support & Information Group/UCIrvine Virtual Meeting

December 19, 2020 9am-12pm

- United Pompe Foundation/UCIrvine

Virtual Pompe Meeting (a recording of the meeting can be found here: https://drive.google.com/file/d/18hJZN0P0ZmcB0w68oRdf5ESgqA68lZg_/view?usp=sharing

Kimonis Laboratory


Grace Lee


Ryan Mahoney


Yasmeen Jawhar

We are pleased to send you our end-of-the-year Lysosomal Storage Disorder (LSD) newsletter. We would like to take this opportunity to welcome Grace Lee, genetic counselor, Ryan Mahoney and Yasmeen Jawhar to the team. Daisy Tapia has graduated and now works at Sutter in San Francisco.

REGISTRY UPDATES: We ask for your participation with our new methods of collecting registry data, lab results, and re-consents:

- Specialized labs are now done by Labcorp and recommended to be drawn every 6 months using the test request form that was emailed out as a secure email. Please contact Grace Lee at leekw1@hs.uci.edu if you did not receive it or the email expired, and we can send you a new one.
- REDCap surveys/ registry questionnaires are mailed/emailed out every 6 months and need to be completed ASAP. Please contact Ryan Mahoney at rpmahone@hs.uci.edu if you have not received a survey invitation.
- We are in the process of re-consenting all patients active in the registry. If you have not already, please keep an eye out for a consent form packet in the mail (hard copies, not email), and be sure to sign and send it back.

The Southern California Consortium for Lysosomal Disorders

The objective of our program is to promote community awareness, to organize outreach events and expand research to benefit patients with LSDs.

Research in LSDs

Pompe Disease

Exercise treatment in Pompe disease A resistance exercise training program in 10 patients improved muscle strength in certain muscle groups. There was an improvement in the Maximum inspiratory pressure (MIP) with respiratory resistance training. The manuscript of this completed study is in review.

Bone density (DEXA) studies in Pompe disease: Patients have an increased risk of osteopenia/osteoporosis. We are studying the impact of ERT on bone health and optimum management of osteopenia. The manuscript of this completed study is in review.

Planned study. A further respiratory exercise study done entirely remotely is planned in collaboration with Duke University.

Clinical trials at UC Irvine:
https://www.clinicaltrials.gov/ct2/results?cond=Pompe+Disease&term=irvine&cntry=&state=&city=&dist=

Antisense oligonucleotide (ASOs) treatment in Pompe mice. Lan Weiss has performed preliminary studies in Pompe mice which provide proof of principle that knocking down muscle specific glycogen synthase (GYS1) by ASOs reduces glycogen in muscle might be a potentially promising adjunct treatment for Pompe disease.

Further work is continuing on optimizing the dose of ASOs in mice and combining this treatment together with enzyme to obtain the maximum benefit.

Ongoing studies in Fabry disease. Fabry is an X-linked disease results from deficient activity of the lysosomal enzyme, α-

galactosidase A (α-gal A). Symptoms are tingling, burning, or numbness in the fingers, hands, episodic pain crises, corneal opacities, lack of sweating, and cardiac, cerebrovascular, and renal dysfunction. Data has shown that long-term treatment with ERT may slow the progression of Fabry disease.

Brain MRI studies in Fabry disease. Patients have an increased risk for transient ischemic attack and stroke. Enzyme replacement cannot cross the blood-brain barrier, so the benefits of ERT on the central nervous system is unclear.

Bone density studies in Fabry disease: We are studying the impact of ERT on bone health and optimum management of osteopenia.

Clinical trials at UC Irvine
https://www.clinicaltrials.gov/ct2/results?cond=Fabry+Disease&term=irvine&cntry=&state=&city=&dist=

Recent Publications

1.Alandy-dy J, Wencel M, Hall K, Simon J, Chen Y, Valenti E, Yang J, Bali D, Lakatos A, Goyal N, Mozaffar T, Kimonis V.
Variable clinical features and genotype-phenotype correlations in 18 patients with late-onset Pompe disease. Ann Transl Med 2019. doi: 10.21037/atm.2019.06.48 https://pubmed.ncbi.nlm.nih.gov/31392188/
18 adult Pompe patients were studied to assess clinical features of Pompe disease, including possible genotype-phenotype correlations that may be identified with larger future studies. Some features observed in patients included BiPAP requirement, tinnitus, scoliosis, cardiomyopathy, cerebral aneurysm, Graves' disease, and testicular cancer.

2. Bonesteele G, Gargus JJ, Curtin E, Rosenbloom B, Virginia Kimonis V.
Diffuse Large B-cell non-Hodgkin's Lymphoma in Gaucher Disease. Molecular Genetics and Metabolism Reports Mol Genet Metab Rep. 2020 Oct 21;25:100663.
Gaucher disease is a rare, autosomal recessive, inherited disorder characterized by decreased activity levels of the enzyme, glucocerebrosidase. Symptoms include anemia, decrease of platelets in blood, oversized liver and spleen, and skeletal complications such as bone pain, bone lesions, osteopenia, osteonecrosis, and fractures. Treatment by enzyme replacement therapy (ERT) is available. Gaucher disease has an increased risk of certain cancers in patients, especially non-Hodgkin's lymphoma. This case study describes 2 patients with Gaucher disease type 1 and diffuse large b-cell non-Hodgkin's lymphoma. We speculate that early treatment may prevent development of lymphoma. https://www.sciencedirect.com/science/article/pii/S2214426920301099

3.Tapia D. and Kimonis V. **Stroke and Chronic Kidney Disease in Fabry Disease.** Journal of Stroke and Cerebrovascular Diseases (Accepted, in press).The kidney and central nervous system involvement in Fabry disease is discussed in this paper. Kidney disease is caused by glycosphingolipid accumulation of Gb3 throughout the nephron and leads to chronic kidney disease in the third to fifth decades of life, and eventually end-stage kidney disease in the fifth decade of life. Treatment such as enzyme replacement therapy or chaperone therapy may halt or delay the progression of kidney disease.
https://www.sciencedirect.com/science/article/abs/pii/S1052305720308417?via%3Dihub

4.Dutra-Clarke M, Tapia D, Curtin E, Rünger D, Lee G, Lakatos A, Alandy-Dy Z, Freedkin L, Hall K, Ercelen N, Alandy-Dy J, Ercelen N, Hall K, Alandy-Dy J, Knight M, Pahl M, Lombardo D, Kimonis V. **Variable Clinical Features of Patients with Fabry Disease and Outcome of Enzyme Replacement Therapy.** Molecular Genetics and Metabolism Reports (In press). 24 adults and 2 male children were studied, 20 of whom were on ERT. The vast majority of patients had symptoms of "classic" FD, and the majority of males had renal involvement, with the most common presentation being proteinuria. Pulmonary involvement, lymphedema, hearing loss, and strokes were observed. Enzyme replacement (ERT) led to improvement in renal function or health-related quality of life. Physical functioning in some patients continued to decline despite ERT treatment, which may be in part due to the late initiation of ERT

Resources

www.clinicaltrials.gov
Search by Disorder
United Pompei Foundation
https://rarediseases.org/organizations/united-pompe-foundation/
Fabry Support and Information Group
www.fabry.org
The National Fabry Disease Foundation
www.TheNFDF.org
National Gaucher Foundation
www.gaucherdisease.org
United Pompe Foundation
www.unitedpompe.com

The Kimonis Laboratory
Division of Genetics and Genomic Medicine
University of California Irvine Medical Center
101 The City Drive South, ZC4482,
Orange CA 92868
Tel: (714) 456-5791, Direct (949) 824-0571
Fax: (714) 456-5330

Email: vkimonis@hs.uci.edu
Grace Lee leekw1@hs.uci.edu

Donations help us continue our work in rare diseases
https://give.uci.edu/GeneticsRareDiseases

Services offered at UC Irvine

· Consultation and evaluation
· Diagnostic testing
· Interaction with and education of referring physicians for life-long care
· Treatment and management
· Genetic counseling
· Patient education and support group meetings
· Research updates