If you have any medical updates for Dr Kimonis please contact her or members of her team. If you are having surgery please consider donating some tissue such as muscle, bone etc.

The manuscript entitled Genotype-Phenotype studies of VCP-associated Inclusion Body Myopathy with Paget Disease of Bone and/or Frontotemporal Dementia has been submitted to Clinical Genetics journal and is pending publication. She will also be participating in the American Society of Human Genetics conference in San Francisco to present her research work.

The Kimonis lab has maintained a database of all the patients recruited for its studies and Dr. Kimonis has continued contact with them. She has collected autopsy samples and developed standards of care for genetic counseling for presymptomatic patients.

Our pilot comprehensive clinical studies at UC Irvine have included detailed analysis in individuals with VCP mutations and controls including first degree unaffected relatives. These studies comprise of extensive tests over two days including history, physical exam, blood work, EMG, DEXA scan, bone scan, MRI, and muscle biopsy. Dr. Khare is also currently working on analyzing data on the individuals who participated in the UC Irvine IBMPFD Natural History study. Ultimately, we are hoping that our research will achieve novel therapeutic targets to benefit our patients with VCP disease.


Clinical Data Updates

Dr. Manaswitha Khare, a physician with Kimonis laboratory since 2011, is working on the clinical studies of VCP-associated disease. There are 25 mutations in the VCP gene that have been identified to date. She is currently working on delineating the association between different genetic subtypes and various clinical features. Approximately 10-15% of individuals have amyotrophic lateral sclerosis (ALS) and some individuals/families have been identified with Parkinson’s disease.

High Fat Diet Rescues the Homozygous Mouse

We have crossed our VCP mice to produce mice with two mutations. These mice typically die by 21 days. We have rescued the mice by feeding a diet high in soya oil. The diet has high amount of linoleic acid (omega 6 oil) and oleic acid (omega 9 oil). We are in the process of refining this observation for the purpose of developing a treatment for patients with VCP disease.

The Kimonis Laboratory has generated a Neomycin cassette-free novel VCP155H/+ knock-in mouse as a true model of the disease, which expresses the mutant VCP allele at an endogenous level without interference from the Neomycin cassette. The VCP155H/+ mouse model, demonstrates muscle weakness, typical histopathology, and progressive accumulation of TDP-43, ubiquitin, and LC3 in muscle, resembling the onset in humans in the 30s-40s. The VCP155H/+ mice show milder, but typical muscle and brain pathology and mild increase in the TDP-43, ubiquitin, and LC3 pathology. Additionally, the spinal cords of these animals demonstrate neuronal atrophy and astrocyte proliferation, and electrophysiological studies reveal a neurogenic pattern seen in ALS. This VCP155H/+ knock-in mouse can be exploited for the development of novel strategies and treatments without potential interference from the Neomycin cassette.

Dr. Nalbandian is currently working on exercise physiology regimens in animal models to further understand the effects of exercise in VCP-associated disorders. She recently attended the Neuromuscular Colloquium in Newport Beach, CA and will be attending the American Society of Human Genetics Conference in San Francisco, CA in November to present her research. These are very exciting times in the Kimonis Laboratory as we are making groundbreaking discoveries and gaining novel insights into the mechanisms of these diseases in order to develop therapeutic agents for our patients. We are truly grateful for all our patients and their selfless support and dedication of our research studies.


**MTAP Disease (Canada family)**

Dr. Llewellyn has started working on an autosomal-dominant disease called Diaphyseal medullary stenosis with malignant fibrous histiocytoma (DMS-MFH). Patients with this syndrome suffer from bone fracturability with poor healing, myopathy, bone cancer, premature graying and soft skin. We now know that mutations within the MTAP gene are the cause of this disease. Scientists think that this is through dysregulation of the newly discovered MTAP splice variants. She focuses on characterizing the myopathy and understanding how dysregulation of the MTAP splice variants could cause this disease. She has recently found that some of the proteins affected in IBMPFD seem to be affected within this disease as well. With similar phenotypes it is likely that the same pathways affected by IBMPFD are affected by DMS-MFH. Hopefully, we can increase awareness and interest to help find a viable treatment or cure for DMS-MFH. 


**VCP Exercise Study**

We are planning a study that will investigate the influence of exercise on muscle strength in VCP Disease. It is an exercise regimen conducted three times a week over the course of 12 weeks. The routine will consist solely of an exercise called knee extensors. This exercise can be performed at your local gym or your home with ankle weights. At each training session you will do three sets of ten knee extensors. Each week the amount of weight used will be increased. You will be asked to keep a log following each training program and rate your level of fatigue. At the start and end of the 12 weeks of training we will ask you to visit UC Irvine so we can conduct an analysis using a battery of tests consisting of strength measurements, MRI, and muscle biopsy.

**Study Participation:** It would be very helpful if more families participated in our studies. If you know of others who may be interested, please contact: Study Coordinator Marie Wencel: (949) 824-0521.

**Organ Donation:**

We are actively seeking organ donations to further our research and find a cure for IBMPFD. Please contact Dr. Kimonis at (949) 824-0571 if you wish to donate your body.

Please contact us if you can donate samples of muscle, bone, or other tissue at the time of planned or emergency surgery.

Please visit our website at: http://mammag.hs.uci.edu/InclusionBodyMyopathyAssociatedWithPagetSDiseaseOfBoneAndFrontotemporalDementia or Google ‘Kimonis laboratory’

**Funding:** We have limited funding from the NIH and MDA. To be able to develop cures for genetic disorders, your help is essential. Please consider organizing fundraisers and donating to our research program at: www.uadv.uci.edu/IBMPFDMyopathyPagetAndDementiaResearch

Please notify Dr. Kimonis when you have made a donation.

**Donate Today!!**

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More information on IBMPFD, as well as support group information, can be found at http://www.ibmpfd.com.