Pitt Researchers Discover Gene Mutation Linked to Lymphatic Dysfunction

Finding Could Lead to First−Ever Target for Drug Therapy for Lymphedema

PITTSBURGH, May 27 A genetic mutation for inherited lymphedema associated with lymphatic function has been discovered that could help create new treatments for the condition, say researchers at the University of Pittsburgh Graduate School of Public Health. Their findings are reported in the June issue of the American Journal of Human Genetics.

Lymphedema, the swelling of body tissues caused by an accumulation of fluid in a blocked or damaged lymphatic system, affects more than 120 million people worldwide. The most common treatments are a combination of massage, compression garments or bandaging.

Lymphedema was first described hundreds of years ago, and yet it remains a very poorly understood disease, said David N. Finegold, M.D., co−principal investigator of the study and professor of human genetics, University of Pittsburgh Graduate School of Public Health. Unfortunately, there is no drug available to cure or even treat it. Most people with inherited lymphedema suffer their entire lives with treatments that address symptom relief only.

The study is based on the University of Pittsburgh Lymphedema Family Study, which began collecting data from affected families in 1995 to learn more about the risk factors and causes of inherited, or primary, lymphedema.

Previous research has helped identify six genes linked to the development of lymphedema, but until now researchers had no insight into the genetic factors responsible for lymphatic vascular abnormalities.

In their study, Dr. Finegold and colleagues sequenced three genes expressed in families with primary lymphedema. Mutations in one of these genes, GJC2, was found in primary lymphedema families and are likely to impair the ability of cells to push fluid throughout the lymphatic system by interrupting their signaling. Without proper signaling, cell contraction necessary for the movement of fluid did not occur, leading to its accumulation in soft body tissues.

These results are significant because they give us insight into the cell mechanics that may underlie this condition, said Dr. Finegold. With further research, we may be able to target this gene with drugs and improve its function.

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