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Researchers identify severe genetic disease prevalent in Moroccan Jews

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Ben-Gurion University of the Negev (BGU) researchers have unraveled the genetic basis of a hereditary disease that causes severe brain atrophy, mental retardation and epilepsy in Jews of Moroccan ancestry, according to a study published this week online in the *Journal of Medical Genetics*.

The disease, which the researchers have called PCCA2 (Progressive Cerebello-Cerebral Atrophy Type 2), is caused by two mutations in the VPS53 gene. It results in defective circulation of vacuoles (endosomes) within patents' cells and leads to detrimental excessive storage of "junk" within the cells.

Children who contract the disease are seemingly fine at birth and develop well until about six months of age. However, deterioration begins soon after with brain atrophy, severe retardation and epilepsy by age one.

One of every 37 Moroccan Jews carries one of the two mutations and based on the high carrier rate, PCCA2 is the most common severe genetic disease in Moroccan Jews discovered to date. Fifteen percent of Israel's total population (1 million people) is of Moroccan ancestry. Nearly 100,000 Moroccan Jews also live in the United States, largely in New York City, Washington D.C., Boston, and Florida.

In Israel, carrier testing and prenatal diagnosis of PCCA2 will enable eradication of this severe disease. Routine carrier testing in Moroccan Jews will likely begin within months. PCCA2 is a recessive disease: if

both parents are carriers of a VPS53 mutation there is a 25 percent risk of the disease in each pregnancy.

The research team was led by Prof. Ohad Birk, head of the Genetics Institute at Soroka University Medical Center and the Morris Kahn Lab at the National Institute for Biotechnology in the Negev at BGU. The study was conducted by Miora Feinstein in Prof. Birk's lab as part of her doctoral thesis.The study was funded by the Israel Science Foundation and the Legacy Heritage Fund.

Prof. Ohad Birk's research has led to the discovery of more than 20 genetic diseases common in Arabs and in Sephardic Jews, providing insights into the nature of illness and unraveling molecular pathways of normal human development. In 2010, Prof. Birk's group discovered another gene for a similar disease, PCCA, which is also common in Jews of Moroccan and Iraqi descent.

Prof. Birk's translational approach has led to dozens of routine massive genetic carrier tests, prevention and practical eradication of numerous severe neurological disorders common in Arabs and in Sephardic/non-Ashkenazi Jews.

"There was an idea that Ashkenazi [of European descent] Jews have more disease than others, but when one begins looking at Sephardic Jewish diseases, they are there," Birk says. "They have just not been sorted out. Because they have not been sorted out, there was no carrier testing, no prevention programs or anything. I have shifted part of my lab into Jewish non-Ashkenazi—or Sephardic Jewish—diseases."

Ashkenazi Jewish diseases that now have carrier testing in the U.S. and Israel include Tay-Sachs disease, Canavan, Niemann-Pick, Gaucher, Familial Dysautonomia, Bloom Syndrome, Fanconi anemia, Cystic Fibrosis, and Mucolipidosis IV.

Provided by American Associates, Ben-Gurion University of the Negev