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Researchers identify mutations causing butterfly-shaped eye pigment dystrophy

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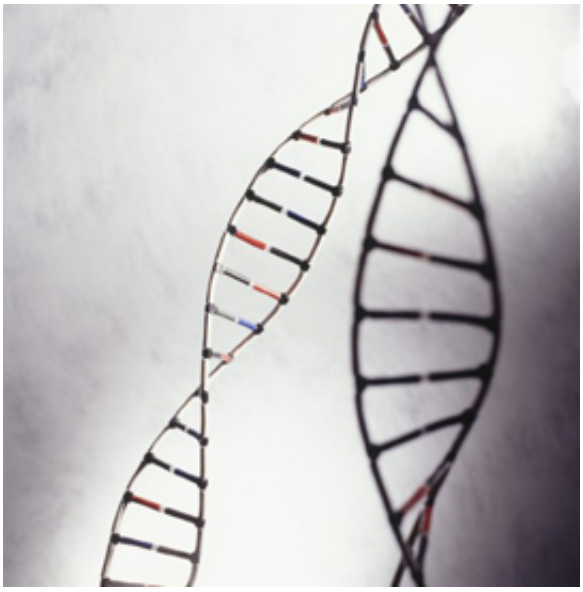

Credit: NIH

A butterfly-shaped pigment accumulation in the macula of the eye, which can lead to severe vision loss in some patients, is due to mutations in the alpha-catenin 1 gene (CTNNA1), an international research consortium including a team from The Jackson Laboratory reports in *Nature Genetics*.

The findings may have relevance to understanding macular degenerative diseases.

CTNNA1 encodes the protein CTNNA1, an alpha-catenin, which is part of the cellular machinery that glues cells to one another. Among CTNNA1's roles is building and maintaining the retinal pigment epithelium (RPE). This pigmented cell layer is critical for nourishing retinal visual cells and is sandwiched firmly between the neurosensory retina and the choroid, a capillary-rich tissue at the back of the eye.

The research team led by Anneke I. den Hollander, Ph.D., a professor at Radboud University Medical Center in Nijmegen, The Netherlands, identified CTNNA1 mutations in three families in which the butterfly-shaped pigment dystrophy of the eye is common. While relatively benign, this condition in some cases leads to severely impaired vision.

Independently, Professor Patsy Nishina's laboratory at The Jackson Laboratory discovered a mouse strain with an analogous mutation in the same gene as identified by den Hollander's team. Their collaboration revealed that the mouse model exhibits the same symptoms as the human patients, including pigmentary abnormalities, focal thickening, elevated lesions, and decreased light-activated responses in the RPE.

The researchers theorize that, although CTNNA1 is expressed in both the retina and the RPE, the disease is caused by defects in the RPE. CTNNA1 is a central component of intercellular adherens junctions, which are critical for maintaining RPE integrity.

The finding that the CTNNA1 mutations are a cause of butterfly-shaped pigment dystrophy supports the hypothesis that defects in the cadherin-based intercellular adhesion system may contribute to macular degenerative diseases.

Nishina comments, "This research nicely demonstrates the 'virtuous loop' between findings in patient data and how a good mouse model equivalent can provide detailed insight into the mechanisms of a

disease."

Other Jackson Laboratory researchers collaborating in the research were Mark P. Krebs, Wanda Hicks, Lanying Shi, Lucy Rowe, Gayle B. Collin and Jeremy R. Charette.

The Jackson Laboratory is an independent, nonprofit biomedical research institution and National Cancer Institute-designated Cancer Center. It employs 1,700 staff, and its mission is to discover precise genomic solutions for disease and empower the global biomedical community in the shared quest to improve human health.

More information: Mutations in CTNNA1 cause butterfly-shaped pigment dystrophy and perturbed retinal pigment epithelium integrity, dx.doi.org/10.1038/ng.3474

Provided by Jackson Laboratory