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Blame the 'Chaperone': Mutation in Gene Essential for Correct Protein-Processing Identified

A Jackson Laboratory research team led by Professor Patsy Nishina, Ph.D., has identified a mutation in a gene that's essential for correct protein-processing in cells. Defects in protein folding are associated with a variety of abnormalities and diseases.

Cells don't come prefabricated, with pieces plunked down and tacked together like modular homes offloaded from trucks. The structural proteins that give cells shape, tubulin and actin (think beams and girders), are themselves subject to essential processing before they become part of the assembly. Proteins must be folded in very specific ways to function properly, and depend on "chaperone" proteins to help them in the process. Defects in the chaperone proteins lead to disruption of the folding process, which adversely affects cellular development and growth.

The chaperones themselves, such as prefoldin, are quite complicated. Prefoldin, which stabilizes brand new proteins, has six subunits assembled into a structure that looks like a jellyfish. Nishina and colleagues identified a mutation in one of the subunits of prefoldin, Pfdn5. In mice, it causes photoreceptor degeneration in the eye, central nervous system abnormalities and male infertility. Although Pfdn5 is widely expressed in other tissues, its disruption appears to significantly affect only these cells. Defects in other subunits disrupt development in other tissues, indicating that each prefoldin subunit is important for the processing

of different proteins in different tissues.

The complex protein transport and folding process is only beginning to be fully studied in mammals. Given that disruptions in the process contribute to a variety of human disease mechanisms, the Pfdn5 mutation will be a valuable tool for further research.

Nishina published the research in the Journal of Biological Chemistry with Jackson colleagues YongSuk Lee, Richard S. Smith, Wanda Jordan, Benjamin L. King, Jungyeon Won and Juergen Naggert, as well as Jose M. Valpuesta of the Centro Nacional de Biotecnología, CSIC Campus de la Universidad Autónoma de Madrid in Spain.

The Jackson Laboratory is a nonprofit biomedical research institution based in Bar Harbor, Maine. Its mission is to discover the genetic basis for preventing, treating and curing human diseases, and to enable research and education for the global biomedical community.

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