Major breakthrough in understanding Prader-Willi syndrome, a parental imprinting disorder

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The Hebrew University's Prof. Nissim Benvenisty. Credit: Hebrew University

(Medical Xpress)—Scientists at the Hebrew University of Jerusalem have reported a major breakthrough in understanding the molecular

basis for Prader-Willi syndrome (PWS), perhaps the most studied among the class of diseases that involves defects in parental imprinting.

The work, described in the latest online edition of the prestigious journal *Nature Genetics*, was led by Prof. Nissim Benvenisty, the Herbert Cohn Professor of Cancer Research and director of the Stem Cell Unit at the Alexander Silberman Institute of Life Sciences at the Hebrew University; and his PhD student Yonatan Stelzer. Also assisting in the research were graduate student Ido Sagi and Dr. Ofra Yanuka and Dr. Rachel Eiges.

Parental imprinting is a mode of inheritance that results in a small subset of genes to be expressed exclusively from either the mother or father. Prader-Willi syndrome is perhaps the best characterized disease of this sort. It is a multisystem disorder characterized by learning disabilities, excessive weight gain and defective sexual development, and is known to result from aberrations in paternal genes in what is known as the Prader-Willi genomic region of chromosome 15.

"What characterizes this chromosomal region is that paternal genes are active, while the maternal genes are inactive. And while most people would have one normal working and one silenced set of these genes, people with Prader-Willi syndrome have only a defective set (the paternal one) and a silenced (maternal) set," explains Stelzer.

In order to achieve a greater understanding of this process, the Hebrew University investigators created a model for the Prader-Willi syndrome by reprogramming skin cells from PWS patients into embryonic-like cells. Utilizing this system, the investigators have shown that the genes expressed from the father are actually affecting and silencing the genes that are expressed from the mother. These findings have significance in the way that we view parental imprinting and in particular the molecular basis of Prader-Willi syndrome, the scientists say.

Future research should allow further characterization of the contribution of this novel genetic region to the origin of this disease, and perhaps pave the way for identification of possible treatment and characterization of PWS patients. Furthermore, the identification of functional, genomic cross-talk in regions containing parental imprinted genes may significantly change our overall understanding of the evolution of this phenomenon in placental mammals, say the researchers.

More information: Paper: The noncoding RNA IPW regulates the imprinted DLK1-DIO3 locus in an induced pluripotent stem cell model of Prader-Willi syndrome, dx.doi.org/10.1038/ng.2968

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