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Discovery of a debilitating genetic syndrome

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Canadian researchers announce the discovery of MEDNIK Syndrome, a debilitating genetic syndrome. In a study published today in the online version of PLoS Genetics, and in the December edition, a research team led by Dr. Patrick Cossette, from the Université de Montréal Hospital Research Centre (CRCHUM) and Associate Professor, Université de Montréal (U de M), has demonstrated that this syndrome is caused by a newly found mutation in the AP1S1 gene.

MEDNIK syndrome was discovered in a group of families in Quebec from the Kamouraska region, sharing a common ancestor, suspected from clinical manifestations showing striking similarities to those of a similar syndrome. Caused by a mutation in the AP1S1 gene, this syndrome is characterized by mental retardation, enteropathy, deafness, and peripheral neuropathy, ichthyosis, and keratodermia (MEDNIK).

"Our observations strongly suggest that MEDNIK Syndrome is caused by impaired development of various neural networks, including the spinal chord (ataxia and neuropathy), the inner ear (sensorineural deafness) and possibly the brain (microcephaly and psychomotor retardation)," notes Dr. Cossette. "Disruption of the AP1S1 gene in humans may be associated with more widespread perturbation in the development of various organs, including the gut and the skin. These results suggest interesting avenues for both basic and clinical research to improve our understanding of the mechanisms underlying MEDNIK and related genetic neurocutaneous syndromes."

By using zebrafish as an animal model, the team of researchers from

CRCHUM, U de M, Ontario Institute for Cancer Research, McGill University, Université de Sherbrooke, and Centre hospitalier régional du Grand-Portage in Rivière-du-Loup observed that the loss of the AP1S1 gene resulted in these broad defects, including severe motor deficits due to impairment of spinal cord development.

By inducing the expression of the human AP1S1 gene instead of the zebrafish gene, the research team found that the normal human type could rescue these developmental deficits but not the AP1S1 gene bearing the disease-related mutation. This research appears to be the first report of a mutation in human AP1S1.

Source: Université de Montréal Hospital Centre