# A genetic basis for schizophrenia

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Schizophrenia is a severely debilitating psychiatric disease that is thought to have its roots in the development of the nervous system; however, major breakthroughs linking its genetics to diagnosis, prognosis and treatment are still unrealized. Jill Morris, PhD assistant professor of Pediatrics at Northwestern University's Feinberg School of Medicine and a researcher in the Human Molecular Genetics Program of Children's Memorial Research Center studies a gene that is involved in susceptibility to schizophrenia, Disc1 (Disrupted-In-Schizophrenia 1).

Two recent publications by Morris and colleagues focus on the role of Disc1 in development, particularly the migration of cells to their proper location in the brain and subsequent differentiation into their intended fate. During development, cells need to properly migrate to their final destination in order to develop into the appropriate cell-type, integrate into the corresponding network of cells and function properly. Disruption of cell migration can lead to inappropriate cell development and function, resulting in disease.

The first paper, published in the July 2009 online issue of the journal *Development*, followed the role of Disc1 in cranial neural crest (CNC) cells, which are multi-potent cells that give rise to multiple cell types including craniofacial cartilage and the peripheral nervous system during development. They also are similar to neurons in their high mobility, response to signals and cellular origin. The Morris laboratory determined that Disc1 regulates two stem cell maintenance factors that have many functions in CNC cells, including the maintenance of precursor pools, timing of migration onset and the induction of cell differentiation. The

authors showed that Disc1 disruption results in increased expression of these factors, leading to hindered cell migration and a change in cell fate. "This research indicates that Disc1 may be involved in regulating stem cells and their fate," says Morris.

The second paper, published in the June 2009 online issue of *Human Molecular Genetics*, studied the hippocampus, a brain area that is involved in learning and memory, and is also associated with the pathology of schizophrenia. Disc1 is highly expressed in the hippocampus, particularly the dentate gyrus, which is considered the gateway to the hippocampus. In this study, the authors decreased Disc1 expression using RNA interference in the developing mouse hippocampus. The loss of Disc1 resulted in hindered migration of dentate gyrus granule cells to their proper location in the brain. "Improper migration of hippocampal neurons may result in altered connectivity in the brain," says Morris.

Source: Children's Memorial Hospital