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SCIENCE – IN THE NEWS

Down Syndrome Cell Adhesion Molecule – A Common Determinant of Brain and Heart Wiring

Down Syndrome (DS), the most common cause of mental retardation, is a genetic disorder caused by the presence of either all or part of an extra human chromosome 21 (HSA21) (1). Phenotypic traits commonly associated with DS include congenital heart disease, short stature, decreased muscle tone, and hearing loss. DS patients also show an increased risk of developing leukemia or early onset Alzheimer disease. Down Syndrome Cell Adhesion Molecule (DSCAM) is an HSA21 axon guidance molecule involved in the development of the nervous system (2).

In murine models of DS, the DSCAM homologue is expressed in adult and embryonic brain and heart where it modulates inter-cell connections (1). In mouse brain, three copies of DSCAM result in an overexpression of the protein, which contributes to a severe disorganization of dendritic spines. Normally, dendritic spines develop postnatally and provide the necessary plasticity required for cognition (1). In mouse heart, DSCAM regulates the transduction of electromechanical impulses. Abnormal expression of DSCAM results in defects in the septum and atrioventricular canal (3), which contribute to cardiomyopathy (J. Korenberg, unpublished data). Further investigation of the role mouse *DSCAM* plays during development may provide an explanation for the brain and cardiovascular abnormalities associated with DS.

The *Dscam* gene of the fruit-fly, *Drosophila melanogaster*, has the same domain structure as mammalian *DSCAM*. As in the murine model, *Drosophila* Dscam has been shown to play a role in axon guidance (4) The brains of *Dscam1* and *Dscam2* mutants show regional patterns of disorganization most likely due to defective neural wiring during development (4,5).

Collectively, these investigations provide evidence for a common factor involved in disruption of brain and heart wiring. Understanding the mechanisms and factors that link these genetic defects to their ultimate phenotype will help scientists develop targeted therapies that prevent the disorders associated with DS. This line of investigation, spanning from *Drosophila* to mouse and ultimately to humans, provides the promise of novel treatment strategies in the future. – *Julia Baumann*

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