

“Congenital NAD Deficiency Disorder: Causes and Possible Prevention”

Speaker: Dr. Justin Szot, Developmental and Stem Cell Biology Division, Victor Chang Cardiac Research Institute



Biography:

Dr. Justin Szot was awarded his PhD in biochemistry and molecular genetics investigating the genetic causes of congenital heart disease in the laboratory of Prof. Sally Dunwoodie at the Victor Chang Cardiac Research Institute. He has continued as a post-doctoral researcher in the Dunwoodie laboratory, establishing the importance of genes involved in NAD biosynthesis for normal embryonic development in humans and mice. His work has established a new human disorder termed Congenital NAD Deficiency Disorder (CNDD) defined by the inadequate gestational synthesis of NAD and consequent multi-system birth defects. His current research seeks to better characterise the CNDD phenotype

and addresses whether this disorder is entirely preventable.

Abstract:

Nicotinamide adenine dinucleotide (NAD) is an essential coenzyme involved in over 400 cellular reactions. During embryogenesis, mammals synthesise NAD de novo from dietary L-tryptophan via the kynurenine pathway. Biallelic, inactivating variants in three genes encoding enzymes of this biosynthesis pathway (KYNU, HAAO, and NADSYN1) disrupt NAD synthesis and have been identified in patients with malformations of the heart, kidney, vertebrae, and limbs; these patients have Congenital NAD Deficiency Disorder (CNDD). Little is currently understood regarding the importance of NADSYN1 in human development. This work identifies multiple new patient cases of CNDD caused by biallelic NADSYN1 variation and, in combination with assessment of mice with similar gene inactivation, identifies a characteristic metabolic signature indicative of perturbed NAD synthesis. Finally, NAD precursor supplementation strategies are assessed with respect to embryonic outcomes and the NAD metabolome, addressing whether CNDD may be entirely prevented.

All welcome!

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