# The DNA Methylation Landscape of Developmental Language Disorder

***Anitha Ayyappan Pillai, PhD[1];*** **Nisha Melempatt, MASLP[1]; Mary Iype MD, DM[1,2]; Sanjeev V. Thomas MD, DM[1,2]**

[1]Institute for Communicative and Cognitive Neurosciences (ICCONS), Shoranur 679 523, Kerala, India;
[2]ICCONS, Trivandrum 695 033, Kerala, India

**Background:** Developmental language disorder (DLD), a common language disorder, is a neurodevelopmental condition. Prevalent in about 7% of school-age children, DLD is defined as the failure to develop normal speech and language skills in the absence of environmental/medical/genetic impairment. DNA methylation has a pivotal role during neurodevelopment, regulating transcriptional plasticity in the developing brain. Alterations in DNA methylation could provide cues to the pathogenesis of neurodevelopmental disorders. In this study, we examined any differential DNA methylation of genes in individuals with DLD compared with healthy controls.

**Methods:** Twelve individuals with DLD and 12 age- and gender-matched healthy controls were recruited for the study. Genome-wide DNA methylation was examined using Infinium Methylation EPIC BeadChip. Any differential methylation between the DLD and control samples was examined.

**Findings:** The differentially methylated genes were found to be enriched in biological processes such as, WNT signaling (*APCDD1*, *AMOTL1*, *LRP5, TMEM64*, *BANK1*, *VEPH1*, *WNT2B*, *TRABD2B*, *MARK2*), G protein coupled receptor (GPCR) signaling (*GNB5*, *GNG5*, *GNG7*, *NGEF, VAV2*, *VAV3*) and Notch signaling (*FCER2*, *JAG1*, *MIB1*, *NOTCH4*, *POFUT1*, *DTX1*).

**Interpretation:** WNT signaling is fundamental for several neurodevelopmental and post-neurodevelopmental processes, such as central nervous system regionalization, neural progenitor differentiation, axon guidance, synaptogenesis, and neural plasticity. The GPCRs are involved in several physiological functions including vision, taste, olfaction, and sympathetic and parasympathetic nervous functions. They are abundantly expressed in the brain, and known to regulate cognition, mood, appetite and pain. The Notch signaling pathway is involved in a wide range of developmental processes including hematopoiesis and neurogenesis, and has been implicated in early neurodevelopment, learning, and memory. Alterations in these signaling pathways have been reported in other neurodevelopmental disorders (e.g., autism). This is the first study that indicates the impairment of these signaling pathways in DLD.

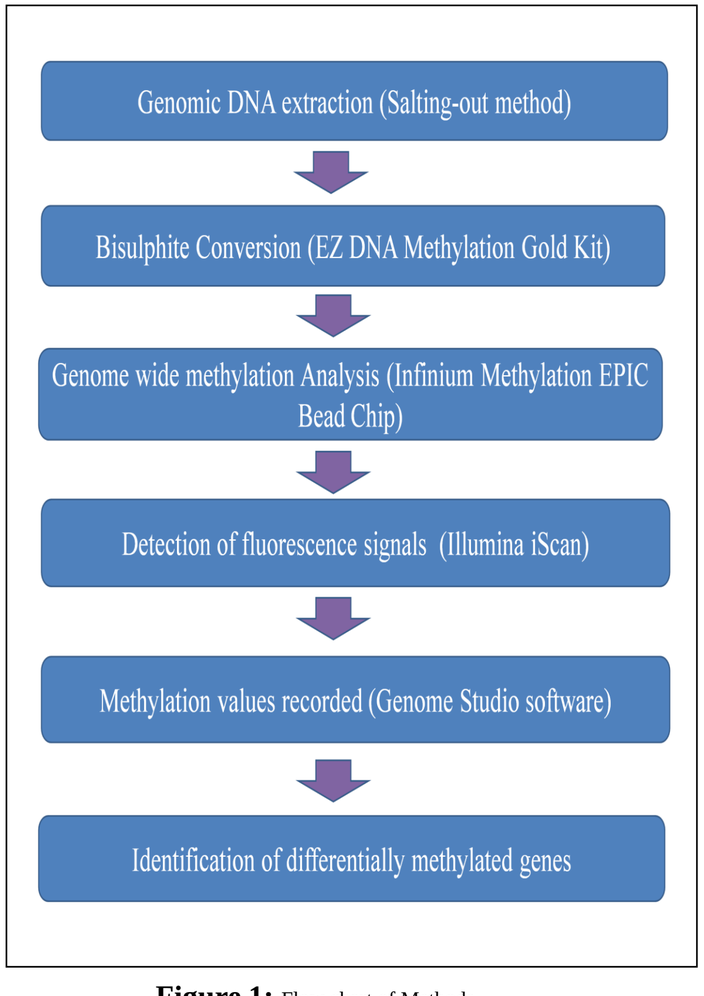


**Figure 1:** Flow chart of Methods

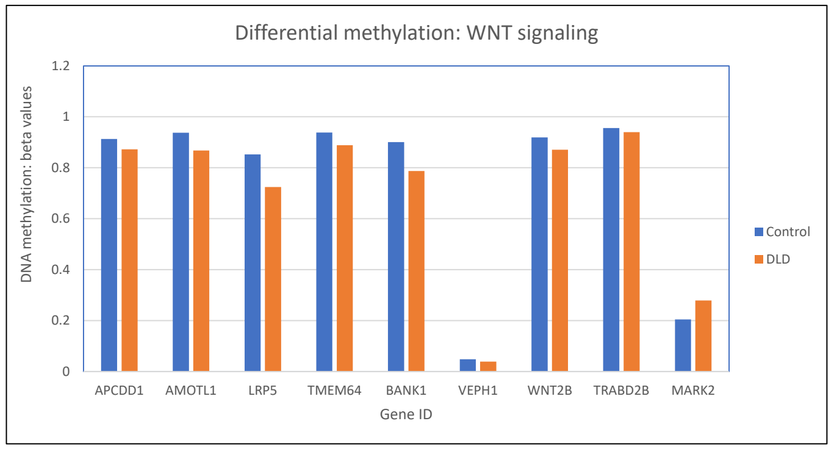


**Figure 2:** Differential methylation of genes involved in WNT signaling

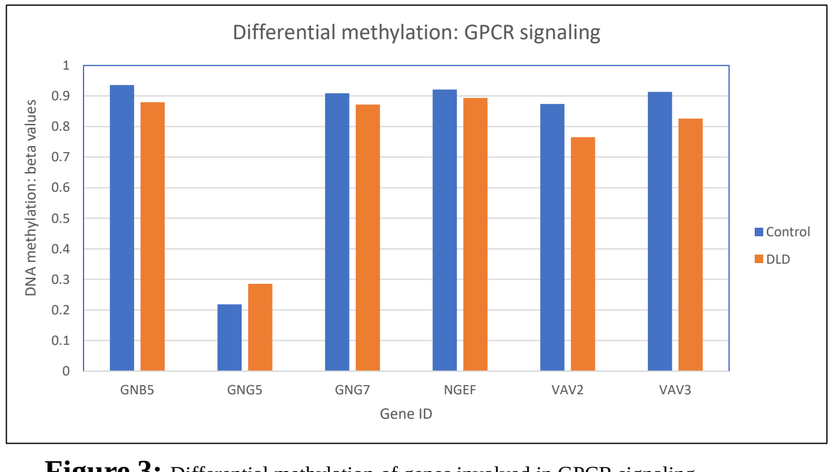


**Figure 3:** Differential methylation of genes involved in GPCR signaling

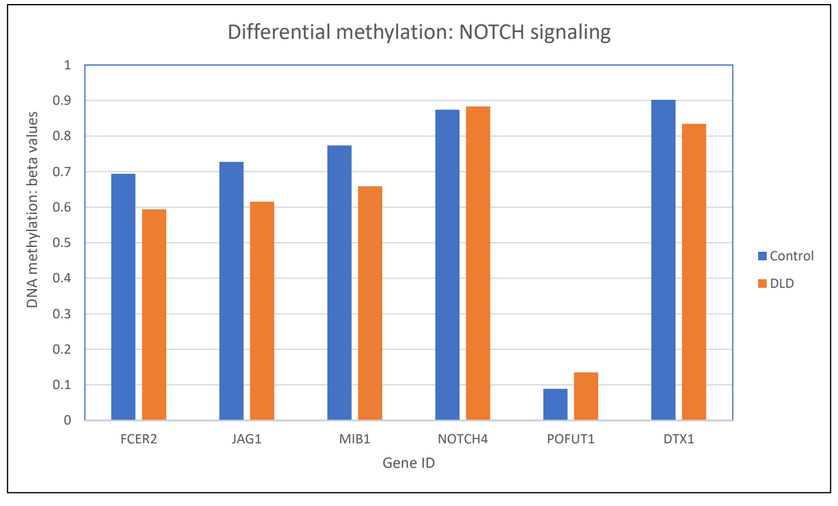


**Figure 4:** Differential methylation of genes involved in NOTCH signaling

## Biography

Dr. Anitha Ayyappan Pillai did her Ph.D. at Rajiv Gandhi Centre for Biotechnology, Trivandrum, India in the field of Population Genetics. She then worked as Assistant Professor at Hamamatsu University School of Medicine, Japan. Now, she is an Associate Professor at Institute for Communicative and Cognitive Neurosciences (ICCONS), Shoranur, India. Her research area is Neurogenetics. She has received research grants from national and international funding agencies. She has authored >45 scientific papers in leading international journals and has co-authored book chapters.

anitha.a72@gmail.com