The importance of imprinted gene expression dosage in brain function and neurodevelopmental disease
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Imprinted genes are subject to developmentally determined epigenetic regulation. Specifically, parental alleles of imprinted genes are differentially epigenetically marked, resulting in monoallelic expression from one parental copy only. Approximately half of imprinted genes are paternally expressed, whilst the remaining half are maternally expressed. Parental specific expression is a fascinating aspect of genomic imprinting, and its evolutionary significance has long been debated. Functionally, imprinted genes are important in a number of key aspects of physiology. In this talk I will focus on their role in the brain. In particular, I will address the question of whether the monoallelic status of imprinted genes makes their function sensitive to changes in expression dosage. I will provide two examples of where dosage of imprinted genes is important for brain and behaviour.

Firstly, our group is examining the role of maternally expressed Cdkn1c using a mouse model carrying a BAC-transgene resulting in 2X normal expression levels of this gene. I will present evidence showing that these animals have an altered dopamine system resulting in changes in reward and social dominance related behaviours. To conclude, my talk will focus on human studies and how over-dosage of maternal gene products from the 15q11-q13 imprinting cluster can give rise to psychotic illness in Prader-Willi syndrome, and how genetic studies from our group suggest maternal gene dosage from this interval may also be important for neuropsychiatric illness generally.