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**MEETING ABSTRACT**

**A2.2**

**Mechanisms controlling the diversity of dopaminergic axon projections**

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Mesodiencephalic dopamine neurons (mDA) play crucial roles in the control of a variety of brain functions, including voluntary movement and behavioural processes such as mood, reward and attention. Two main subgroups of mDA neurons, the substantia nigra pars compacta (SNpc) and the ventral tegmental area (VTA), form the well-known nigrostriatal and mesolimbic pathways innervating the dorsal and ventral striatal regions respectively. Until now, the mechanisms involved in the segregation of these two important axonal pathways remained unknown. Here we show that two transcription factors, Lmx1a and Lmx1b, are required for the appropriate topographical axon innervation of dopamine neurons from the VTA and the SNpc.

In absence of Lmx1a/b, axon projections of SNpc neurons are misguided toward the ventral striatal region (VTA target site). Gene expression profiling experiments comparing Lmx1a/b double conditional mutants to control mice identified PlexinC1 as Lmx1a/b target gene. PlexinC1 expression is normally restricted to VTA neurons while in Lmx1a/b mutants, PlexinC1 expression is expanded to mDA neurons of the SNpc. In vitro examination of dopaminergic growth cones exposed to Sema7a, a PlexinC1 ligand, indicates that Sema7a acts as a chemorepellent for VTA neurons. The dorsal striatal region shows strong expression of Sema7a, and knockout of Sema7a results in an inappropriate innervation of VTA neurons in the dorsal striatal region. Forced expression of PlexinC1 in mDA neurons of transgenic mice results in the same axon guidance defect observed in Lmx1a/b mutant animals. Our results revealed that Lmx1a and Lmx1b act as a repressor of PlexinC1 in SNpc neurons and that Sema7a/PlexinC1 are responsible of the segregation of nigrostriatal and mesolimbic dopaminergic pathways.

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