Proposition de Stage M2 S4 NEUROSCIENCES
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1. **Equipe d'Accueil de Master** (EAM) **:**
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2. **Titre du sujet : Using genetic mouse models to identify conserved roles of *Foxp2*, a gene implicated in speech and language development**

3. **Description du sujet :**

The previous identification of a mutation in the forkhead-box transcription factor Foxp2 segregating in an extended family has provided the first example of a gene causing a developmental speech and language disorder. Affected family members suffer from verbal dyspraxia and a wide array of linguistic deficits in the oral as well as the written domain. In imaging studies they display abnormalities in speech and language associated structures, in particular in cortex and striatum. Current data support the hypothesis that Foxp2-associated communication defects observed in humans are to a substantial degree based on disturbances in conserved roles of Foxp2 in neurodevelopment and function.

To identify neuronal circuits and molecular mechanisms impacted by Foxp2 deficiency we have generated Foxp2 mutant mice. These animals are studied with genetic, functional genomics, neuropharmacological and behavioral approaches. The applicant will be involved in *in-vivo* chromatin-immunoprecipitation (ChIP) and gene expression experiments to map genome wide functional Foxp2 binding sites in particular brain regions and their subsequent validation (ChIP-and q-PCR, EMSA, in-situ hybridization, immunohistochemistry). He furthermore will introduce mutations of Foxp2 in corresponding (aim1) specific brain regions at different developmental stages (e.g. via in-utero electroporation) and consecutively analyze (species-typical) behavior.

The primary objective is to identify behaviorally relevant roles of Foxp2 during development or function in specific neuronal circuits. These studies aim to further our understanding of molecular mechanisms and neuronal circuits potentially recruited for speech and language development.

See also:

Dominguez MH, Rakic P., Nature. 2009 Nov 12;462(7270):169-70.
Enard W et al., Cell. 2009 May 29;137(5):961-71.
Groszer M et al., Curr Biol. 2008 Mar 11;18(5):354-62