STUDYING THE GENETIC BASES OF VOCAL LEARNING IN BATS

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Animal studies provide a unique opportunity to study direct causative links between genes and speech relevant behaviours, not possible in humans. Vocal learning is the ability to alter vocal outputs in response to auditory input, and is crucial for human speech (Janik & Slater, 2000). Bats are the only animals amongst the known vocal learning mammals (also including whales, dolphins, seals and elephants) that can be currently used for genetic manipulation studies, due to their small size, ease of handling and generation time (Janik & Slater, 1997; Knörnschild, 2014; Vernes, 2017).

The vast majority of studies on the neurogenetic encoding of vocal learning in the brain has been conducted in songbirds. Although this work has given us valuable insight into the genetic underpinnings of vocal learning in birds (Heston & White, 2015; Jarvis et al., 2000; Mendoza et al., 2015), their genetic and anatomical distance from humans argues for the need for similar work to be performed in mammals in order to be able to understand shared mechanisms underlying vocal learning.

FOXP2 has garnered much attention since it was identified as the first monogenetic cause of a severe speech and language disorder in humans (Lai, Fisher, Hurst, Vargha-Khadem, & Monaco, 2001). Affected individuals show structural and functional brain alterations, underlying its importance for normal brain development involved in speech and language pathways (Liegeois et al., 2003; Watkins et al., 2002). In elegant studies in songbirds, the importance of FoxP2 in vocal learning behaviour was shown by knockdown of the gene in area

X of juvenile birds, which led to disruption of song learning (Haesler et al., 2007). Taken together these data from humans and birds suggest FoxP2 as a top candidate gene to play a role in neurogenetic pathways underlying vocal learning.

Given its role in speech and language in humans and vocal learning in songbirds, we aim to determine if FoxP2 has an evolutionarily conserved role in vocal learning behaviour in bats. We have designed and tested an shRNA construct that targets the FoxP2 mRNA sequence of the pale spear-nosed bat (*Phyllostomus discolor)* and produces a functional loss of FoxP2 in cells. We are studying the effects of introducing this shRNA construct into the striatum of adult bats to determine the consequences of FoxP2 loss. In particular, histological and RNA-sequencing techniques will be used to determine the neuro-molecular consequences of FoxP2 knockdown. In the future, establishing this new knockdown model will enable demonstration of direct causative links between FoxP2 and vocal learning behaviour in a mammalian system using recently established paradigms (Lattenkamp, Vernes, & Wiegrebe, 2018). These data will demonstrate the role of FoxP2 in vocal learning mammals, bridge the evolutionary gap between birds and humans, and give a more complete picture on the evolution of vocal learning and ultimately human speech.

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