‘Investigating the development and evolution of cortical circuits using *in vivo* assays in marsupials’

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Abstract:
The six-layered cerebral cortex integrates sensory perception with motor action, and mediates higher-order cognitive processes such as attention, learning and language. Healthy brain function relies on the precise formation of cortical circuits, and subtle developmental defects can lead to several conditions such as autism, attention deficit and schizophrenia. Most of our knowledge on healthy and pathological cortical development comes from studies in rodents and primates, as mammals are the only vertebrates that evolved a cerebral cortex. However, important questions remain open due to the lack of experimental paradigms to study the developing cortex in vivo, inside the uterus. Here I will present a marsupial model of extra-uterine cortical development (inside the pouch), the Australian fat-tailed dunnart (*Sminthopsis crassicaudata*). We have established a dunnart breeding colony and the in-pouch electroporation technique, which allows unprecedented access to selectively transfect multiple neuronal populations. By combining high-throughput RNA sequencing, molecular development and microscopy in mice and dunnarts, we are currently investigating the development and evolution of the transcriptional control of axon guidance, as only placental mammals (but not marsupials or monotremes) evolved a corpus callosum. Moreover, the skull of pouch-young dunnarts is highly translucent (hence amenable for optogenetics), allowing two-photon imaging of calcium activity in the developing neocortex at stages equivalent to prenatal humans and rodents. These features highlight the potential impact of laboratory marsupials to study the genetic and environmental influences on cortical development, while also providing important clues on the evolution of brain developmental systems.

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