

EXPLORING GENOMES OF DISTANTLY RELATED MAMMALS

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There are three groups of extant mammals, two of which abound in Australia. Marsupials (kangaroos and their relatives) and monotremes (echidna and the fabulous platypus) have been evolving independently for most of mammalian history. The genomes of marsupial and monotreme mammals are particularly valuable because these alternative mammals fill a phylogenetic gap in vertebrate species lined up for exhaustive genomic study. Human and mice (~70MY) are too close to distinguish signal, whereas mammal/bird comparisons (~310MY) are too distant to allow alignment. Kangaroos (180 MY) and platypus (210 MY) are just right. Sequence has diverged sufficiently for stringent detection of homologies that can reveal coding regions and regulatory signals. Importantly, marsupials and monotremes share with humans many mammal-specific developmental pathways and regulatory systems such as sex determination, lactation and X chromosome inactivation.

The ARC Centre for Kangaroo Genomics is characterizing the genome of the model Australian kangaroo *Macropus eugenii* (the tammar wallaby), which is being sequenced by AGRF in Australia, and Baylor (funded by NIH) in the US. We are developing detailed physical and linkage maps of the genome to complement sequencing, and will prepare and array cDNAs for functional studies, especially of reproduction and development. Complete sequencing of the distantly related Brazilian short-tailed opossum *Monodelphis domestica* by the NIH allows us to compare distantly related marsupials. Sequencing of the genome of the platypus, *Ornithorhynchus anatinus* by Washington University (funded by the NIH) is complete, and our lab is anchoring contigs to the physical map. We have isolated and completely characterized many BACs and cDNAs containing kangaroo and platypus genes of interest, and demonstrate the value of comparisons to reveal conserved genome organization and function, and new insights in the evolution of the mammalian genome, particularly sex chromosomes.