

CHAPTER 3: THE REGION HOMOLOGOUS TO THE X-CHROMOSOME INACTIVATION CENTRE HAS BEEN DISRUPTED IN MARSUPIAL AND MONOTREME MAMMALS

The following chapter consists of a research publication from early 2007 in which I examined the evolution of the X-inactivation centre.

Hore TA, Koina E, Wakefield MJ, Graves JAM (2007) The region homologous to the X-chromosome inactivation centre has been disrupted in marsupial and monotreme mammals. *Chromosome Res* **15**: 147-161.

The search for a marsupial X-inactivation centre (and crucially an *XIST* orthologue) had been ongoing in the Graves laboratory for more than a decade, chiefly by Matthew Wakefield. However, direct searches by Southern blotting, BAC library screening, PCR, RT-PCR and bioinformatic searches had been uniformly unsuccessful. With my supervisor Jenny Graves, I devised a strategy for searching for flanking markers.

I provided much of the experimental design for the work reported in this publication and performed all experiments except for the historical library screenings depicted in Table 3.1, which provided no positive results (contributed by Edda Koina and Matthew Wakefield) and the bioinformatic analysis that lead to Figure S4 (Matthew Wakefield). I wrote the first draft of this manuscript, which was critiqued by my supervisors Jenny Graves and Edda Koina. I generated all figures except Figure S4. As corresponding author, I was responsible for liaison with editorial staff, for all revisions and proofs.

This paper has had a major impact on the mammalian X inactivation field because it showed that the region homologous to the X-inactivation centre is situated in two distant regions of the marsupial X chromosome and platypus chromosome 6. In addition, this paper showed that, although parts of the *XIST* gene are highly conserved in all four superordinal clades of eutherian mammals, no *XIST* orthologue is present in marsupials. While this publication was in preparation, another manuscript providing independent

support for the proposal that marsupials lack *XIST* was published (Duret *et al.*, 2006), many aspects of which the next chapter extends and corrects.

Pages 57-78 cannot be shown as they derive from the copyrighted publication:

Hore TA, Koina E, Wakefield MJ, Graves JAM (2007) The region homologous to the X-chromosome inactivation centre has been disrupted in marsupial and monotreme mammals. *Chromosome Res* **15**: 147-161. doi:10.1007/s10577-007-1119-0

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