The Zebrafish Homologues of JAM-B and JAM-C are Essential for Myoblast Fusion

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Dedicated to

my mother and father, Lizbeth and David;

my siblings, Alexis, James, Robert, William and Rosie;

and

my love, Nirvana.

Declaration

This dissertation is the result of my own work and includes nothing which is the outcome of work done in collaboration except where specifically indicated in the text. This dissertation does not exceed the word limit set by the Biology Degree Committee.

Abstract

The cell surface proteins JAM-B and JAM-C are a receptor:ligand pair that is important for leukocyte extravasation, tight junction formation and cell polarity. Both proteins are expressed during embryogenesis, but their developmental function has not yet been described. Through studying the biochemistry and embryonic expression patterns of the zebrafish homologues, named *jamb* and *jamc* respectively, I have hypothesised that the interaction between them has a role in vertebrate myoblast fusion. Consistent with this, zebrafish embryos mutant for *jamb* or *jamc* develop mononuclear fast muscle fibres. This suggests that these proteins are a novel receptor:ligand pair that function in myoblast fusion in vertebrates. The severity of the phenotype suggests that *jamb* and *jamc* are critical for the initiation of fusion.

In contrast to the *Drosophila* paradigm, loss of myoblast fusion in the *jamb* or *jamc* mutant results in an increase in fast muscle fibres with no apparent accumulation of unfused myoblasts. This suggests that every myoblast is able to form a mature muscle fibre. Also, *jamc* is misexpressed in *prdm1* mutant embryos, which lack the transcriptional repressor that is known to control the differentiation of slow and fast muscle. Expression of *jamc* is dynamic throughout primary differentiation. Taken together, these results suggest that myoblast fusion is regulated by relative expression of both Jamb and its binding partner Jamc, and that zebrafish myoblasts are not specified into sub-populations of founder cells and fusion-competent myoblasts.

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