

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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## Table of Contents

Declaration	i
Abstract	ii
Acknowledgements	iii
Table of Contents	iv
List of Figures	vii
List of Tables	x
<b>Chapter 1 – Introduction</b>	<b>1</b>
1.1 The <i>JAM</i> family	2
1.2 The role of cell surface proteins during myogenesis	4
1.3 Current opinions in myoblast fusion	6
1.4 Zebrafish as a model for vertebrate myogenesis	8
<b>Chapter 2 – Materials and Methods</b>	<b>11</b>
2.1 Cloning and homology	15
.1 Cloning of <i>jama2</i> by 3' RACE	15
.2 Cloning of <i>jamc2</i> by RT-PCR	16
.3 Gel electrophoresis of DNA or RNA	17
.4 Homology and molecular genetics analysis	17
2.2 Zebrafish husbandry and genotyping	18
.1 General husbandry and embryo collection	18
.2 Genotyping zebrafish adults and embryos	18
2.3 Protein and RNA expression detection	19
.1 Embryo fixation	19
.2 Wholemount RNA <i>in situ</i> hybridisation	19
.3 Immunohistochemistry	21
.4 Microscopy and image processing	22
2.4 Characterisation of loss-of-function mutants	22
.1 Morpholino injections	22
.2 Labelling cell membranes with membrane-targeted RFP	23
.3 Quantification of fast muscle fibres	23
.4 Acridine orange assay	24
2.5 Transplant experiments	24



2.6 Protein production and biochemistry	24
.1 Expression vectors	24
.2 Transfection and purification	27
.3 Quantification by ELISA	28
.4 Surface plasmon resonance	29
.5 Data analysis	29
<b>Chapter 3 – Cloning and homology of the zebrafish <i>jam</i> family</b>	<b>33</b>
3.1 Introduction	34
3.2 Identification and cloning of <i>jama2</i> and <i>jamc2</i>	38
3.3 Evolutionary relationships of zebrafish <i>jam</i> family orthologues	46
3.4 Discussion	50
<b>Chapter 4 – Expression patterns of the zebrafish <i>jam</i> family during development</b>	<b>55</b>
4.1 Introduction	56
4.2 Expression patterns of the <i>jam</i> family	57
4.3 Detailed expression patterns of <i>jamb</i> and <i>jamc</i>	65
4.4 Regulation by <i>prdm1</i> suggests a fast muscle-specific function for <i>jamc</i> , but not <i>jamb</i>	67
4.5 <i>Jamb</i> is located on myoblast and myofibre membranes	67
4.6 Discussion	70
<b>Chapter 5 – Determining the physical interactions within the zebrafish Jam family</b>	<b>73</b>
5.1 Introduction	74
5.2 Jam family ectodomain production and purification	79
5.3 Using surface plasmon resonance to quantify Jam family interactions	79
5.4 Comparing Jam family interactions	79
5.5 Discussion	87
<b>Chapter 6 – Characterization of the <i>jamb</i> and <i>jamc</i> mutant phenotypes</b>	<b>91</b>
6.1 Introduction	92

## Table of Contents

6.2	General characteristics of the <i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> alleles and mutants	95
6.3	<i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> mutants display a complete block in myoblast fusion	97
6.4	Fast muscle fibres are overabundant in <i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> mutants	102
6.5	Myoblast proliferation is repressed in <i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> embryos	102
6.6	Discussion	108
<b>Chapter 7 – Physical interaction between Jamb and Jamc is necessary for myoblast fusion</b>		<b>113</b>
7.1	Introduction	114
7.2	Characterising the function of the physical interaction between Jamb and Jamc in myoblast fusion <i>in vivo</i>	116
7.3	Jamb and Jamc do not function as homophilic receptors	118
7.4	Jamb and Jamc interact <i>in trans</i> during myoblast fusion	118
7.5	Discussion	122
<b>Chapter 8 – Discussion</b>		<b>125</b>
8.1	Novel regulation of myoblast fusion in vertebrates	126
8.2	Determining candidate signalling pathways	128
8.3	Relative roles of cell surface receptors in myoblast fusion	131
8.4	Intracellular effectors of Jamb and Jamc signalling	133
8.5	Future directions	134
8.6	Concluding remarks	136
<b>Chapter 9 – Bibliography</b>		<b>137</b>

## List of Figures

Figure 2.1	Flow diagram of cloning and genotyping methods	12
Figure 2.2	Flow diagram of protein and RNA expression methods	13
Figure 2.3	Flow diagram of protein production and biochemistry methods	14
Figure 2.4	Genetic map of Jam protein expression vectors.	26
Figure 3.1	The mammalian JAM family.	35
Figure 3.2	Conserved protein features of the mammalian JAM family.	37
Figure 3.3	<i>jama2</i> is expressed at 24 h. p. f. as determined by 3' RACE.	39
Figure 3.4	Sequence of <i>jama2</i> mRNA as determined by 3' RACE.	40
Figure 3.5	Genomic alignment of <i>jama2</i> cDNA sequence and comparison of the translated open reading frame with Jama.	41
Figure 3.6	Structure of <i>jamc2</i> mRNA as determined by RT-PCR.	43
Figure 3.7	Sequence of <i>jamc2</i> mRNA as determined by RT-PCR.	44
Figure 3.8	Comparison between Jamc and Jamc2 highlights conserved features.	45
Figure 3.9	Zebrafish <i>JAM</i> family genes are distinct from related IgSF proteins and share a common ancestor with human and mouse <i>JAM</i> family genes.	47
Figure 3.10	Multi-species comparison of <i>JAM-A</i> loci reveals limited conservation of local gene structure between zebrafish and mammals.	48
Figure 3.11	Multi-species comparison of <i>Jam-C</i> loci suggest <i>jamc</i> is the derived allele from an ancient genome duplication.	49
Figure 3.12	Multi-species comparison of <i>Jam-B</i> loci suggests <i>jamb2</i> is the derived allele of an ancient genome duplication event.	51
Figure 3.13	Comparison between <i>Jamb</i> , <i>Jamb2</i> and <i>Jam-B</i> highlights conserved features and divergent cytoplasmic domains.	52
Figure 4.1	Expression patterns of <i>jam</i> family genes in the gastrula.	58
Figure 4.2	Expression patterns of <i>jam</i> family genes during early segmentation.	59
Figure 4.3	Expression patterns of <i>jam</i> family genes during late segmentation.	60
Figure 4.4	Expression patterns of <i>jam</i> family genes during the pharyngula period.	61

## List of Figures

Figure 4.5	Expression patterns of <i>jam</i> family genes during hatching.	62
Figure 4.6	Expression pattern of <i>jamb2</i> between early segmentation and pharyngula periods.	63
Figure 4.7	Detailed observation of <i>jamb</i> and <i>jamc</i> expression in somites.	66
Figure 4.8	<i>jamc</i> , but not <i>jamb</i> or <i>kirrel</i> , is misexpressed in <i>prdm1<sup>tp39</sup></i> mutants.	68
Figure 4.9	Jamb is expressed on the cell surface of myotubes and myoblasts.	69
Figure 5.1	Known extracellular interactions of JAM family proteins.	75
Figure 5.2	The surface plasmon resonance principle.	76
Figure 5.3	Real-time monitoring of protein interactions by surface plasmon resonance.	77
Figure 5.4	Production and quantification of biotinylated Jam family ectodomains.	80
Figure 5.5	Purification of histidine-tagged Jam family ectodomains.	81
Figure 5.6	Example sensorgrams of detected interactions.	82
Figure 5.7	Network of interactions detected between Jam family proteins.	83
Figure 5.8	Example plots of dissociation phase data demonstrating first-order kinetics.	86
Figure 5.9	Comparing dissociation phase data reveals a wide range of interaction strengths within the Jam family.	88
Figure 6.1	The molecular nature of <i>jamb<sup>HU3319</sup></i> and <i>jamc<sup>sa0037</sup></i> alleles.	96
Figure 6.2	Jamb is not detected in <i>jamb<sup>HU3319</sup></i> mutant embryos.	98
Figure 6.3	A pigment defect in <i>jamb<sup>HU3319</sup>/+</i> incross progeny is recessive.	99
Figure 6.4	Fast muscle fibres are mononuclear in <i>jamb<sup>HU3319</sup></i> and <i>jamc<sup>sa0037</sup></i> mutants.	100
Figure 6.5	Fast muscle fibres are mononuclear in 5 day old <i>jamb<sup>HU3319</sup></i> and <i>jamc<sup>sa0037</sup></i> mutants	101
Figure 6.6	Morpholinos targeted to <i>jamb</i> and <i>jamc</i> phenocopy mutant alleles.	103
Figure 6.7	Slow muscle develops normally in <i>jamb<sup>HU3319</sup></i> and <i>jamc<sup>sa0037</sup></i> mutants.	104
Figure 6.8	Fast muscle fibres are fully differentiated in <i>jamb<sup>HU3319</sup></i> and <i>jamc<sup>sa0037</sup></i> mutants.	105
Figure 6.9	Quantification of supernumary fast muscle fibres in both	106

	<i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> mutant embryos.	
Figure 6.10	Apoptosis does not increase in the absence of fusion.	109
Figure 7.1	Schematic of zebrafish transplant experiments.	115
Figure 7.2	The interaction between Jamb and Jamc <i>in trans</i> is required for myoblast fusion.	117
Figure 7.3	Reductive model of <i>jamb</i> and <i>jamc</i> -mediated myoblast fusion.	120
Figure 7.4	Combined knockdown of <i>jamb</i> and <i>jamc</i> does not result in a synthetic myogenesis phenotype.	121
Figure 8.1	Proposed model of primary fast muscle development.	129
Figure 8.2	Co-expression of fluorescent reporter genes in transfected zebrafish embryos.	135

## List of Tables

Table 2.1	Oligonucleotide sequences.	31
Table 3.1	Nomenclature of the <i>JAM</i> family.	36
Table 4.1	Expression patterns of zebrafish <i>jam</i> family genes determined by wholemount RNA <i>in situ</i> hybridisation.	64
Table 4.2	Identity of coding sequence and amino acid sequence of immunoglobulin domains between <i>jam</i> family members.	72
Table 5.1	Dissociation rate constants for interactions amongst JAM family proteins.	84
Table 5.2	Calculated half-lives for interactions amongst JAM family proteins.	85
Table 6.1	Pigment defect is not linked to <i>jamb</i> <sup>HU3319</sup> allele.	99
Table 6.2	Quantification of number of fast muscle fibres per myotome in wild-type, <i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> embryos.	107
Table 6.3	Statistical significance of comparisons between fast muscle fibre number in wild-type, <i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> embryos.	107
Table 6.4	Calculated number of nuclei per myotome in wild-type, <i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> embryos.	110
Table 6.5	Statistical significance of comparisons between number of nuclei per myotome in wild-type, <i>jamb</i> <sup>HU3319</sup> and <i>jamc</i> <sup>sa0037</sup> embryos.	110
Table 7.1	Quantification of fused (multi-nucleated) and unfused (mono-nucleated) fluorescently-labelled fast muscle fibres in transplanted hosts.	119