

**An analysis of DRONC function and its
regulation of expression during *Drosophila*
development**

By

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Table of Contents

Abstract

Statement

Acknowledgments

Publications

Chapter 1: Introduction

1.1 Programmed cell death (PCD).....	1
1.2 Conservation of the cell death machinery	
1.2.1 <i>Caenorhabditis elegans</i>	1
1.2.2 Mammals.....	2
1.2.3 <i>Drosophila melanogaster</i>	5
1.2.3.1 A model system to study cell death.....	5
1.2.3.2 The <i>Drosophila</i> PCD machinery.....	7
1.3 <i>Drosophila</i> caspases.....	8
1.3.1 <i>DCP-1</i>	9
1.3.2 <i>DECAY</i>	10
1.3.3 <i>DAMM</i>	10
1.3.4 <i>DRICE</i>	11
1.3.5 <i>DREDD</i>	12
1.3.6 <i>STRICA</i>	13
1.3.7 <i>DRONC</i>	13
1.4 Regulation of DRONC activation.....	15
1.5 Ecdysone-mediated PCD	17

1.6 EcR/Usp binding elements and target genes.....	19
1.7 The ecdysone-induced genetic regulatory hierarchy.....	21
1.8 The ecdysone-induced transcriptional hierarchy in the salivary glands.....	21
1.9 Broad-Complex (BR-C).....	22
1.9.1 BR-C-mediated regulation of <i>dronc</i> expression.....	25
1.10 The role of E93 in PCD.....	25
1.10.1 Salivary gland histolysis and its regulation	27
1.11 Caspase substrates and salivary gland destruction.....	31
1.12 The PCD genetic hierarchy and midgut cell death.....	32
1.13 Aims.....	34

Chapter 2: *Materials and Methods*

2.1 <i>Drosophila</i> stocks and crosses	
2.1.1 Genetic Interaction crosses.....	35
2.1.2 <i>dronc</i> promoter-reporter crosses	35
2.1.3 <i>dronc</i> locus deletion complementation lines.....	36
2.2 <i>Drosophila</i> protocols	
2.2.1 Staging of animals.....	37
2.2.2 Germline transformation.....	37
2.2.3 Lethality tests.....	38
2.2.4 Cell death detection	38
2.2.5 Gamma Irradiation of Larvae.....	39
2.2.6 Caspase cleavage assays.....	39
2.2.7 Histology.....	39
2.2.8 Detection of β -galactosidase expression	40

2.2.9 Quantitative β -galactosidase assays	41
2.2.10 <i>Drosophila</i> cell culture	41
2.2.11 Preparation of nuclear extracts and EMSA.....	41
2.2.12 Immunohistochemistry.....	42
2.2.13 Transmission electron microscopy (TEM).....	43
2.2.14 Haemocyte analysis.....	43
2.3 <i>Drosophila</i> cell line manipulations	
2.3.1 Cryopreservation of <i>Drosophila</i> cell lines.....	44
2.3.2 Thawing cryopreserved <i>Drosophila</i> cells.....	44
2.3.3 <i>Drosophila</i> cell culture RNA interference (RNAi).....	44
2.3.4 Transfection and luciferase assay.....	45
2.4 Immunoblotting.....	46
2.5 RT-PCR.....	46
2.6 Standard DNA Manipulations	
2.6.1 Quantification of DNA.....	46
2.6.2 Separation of DNA fragments by electrophoresis.....	47
2.6.3 Restriction endonuclease digestion	47
2.6.4 Purification of DNA fragments	47
a) Phenol/chloroform extraction.....	47
b) ULTRA-CLEAN™.....	48
2.6.5 End-filling DNA.....	49
2.6.6 Dephosphorylation of DNA.....	49
2.6.7 Ligation of DNA fragments.....	49
2.7 PCR amplification and sequencing of DNA	
2.7.1 PCR amplification of DNA.....	49

a) Taq polymerase amplification.....	49
b) DyNAzyme™ amplification.....	50
c) High fidelity PCR.....	50
2.7.2 Mutagenesis PCR reactions.....	50
2.7.3 DNA sequencing.....	51
2.8 Harvesting of plasmid DNA from bacterial cultures	
2.8.1 Small-scale plasmid extraction.....	52
2.8.2 Large-scale plasmid extraction.....	52
2.9 RNA Analysis	
2.9.1 Quantification of total RNA preparations.....	53
2.9.2 RNA extraction.....	53
2.9.3 RNA gel electrophoresis.....	54
2.9.4 Northern blotting.....	55
a) RNA transfer	55
b) Probe radio-labelling.....	55
c) Hybridisation and signal detection.....	56
2.10 Transformation of chemically competent bacterial Cells	
2.10.1 Preparation of competent <i>E. coli</i> cells.....	56
2.10.2 Transformation of chemically competent cells.....	57
2.11 Protein Analysis	
2.11.1 Determining protein concentrations.....	57
2.11.2 Protein extraction	57
2.11.3 Recombinant protein generation	58
2.11.4 <i>in vitro</i> translation.....	58
2.11.5 SDS-PAGE and protein transfer	59

2.11.6 Western blotting.....	60
2.11.7 Stripping Western blots.....	60
2.12 Plasmid constructs	
2.12.1 Generation of <i>dronc</i> promoter-reporter <i>LacZ</i> constructs.....	60
2.12.2 Additional constructs and vector.....	61
2.13 Primer list	
2.13.1 <i>dronc</i> promoter-reporter construct primer list.....	62
2.13.2 Complementation construct mutation primers.....	62
2.13.3 Ecdysone Receptor mutation forward primer.....	63

Chapter 3: *Drosophila* Caspase DRONC is Required for Multiple Developmental Cell Death Pathways and Stress-Induced Apoptosis

3.1 Introduction.....	64
3.2 A hypomorphic <i>dronc</i> allele.....	66
3.3 <i>dronc</i> expression in <i>KGO2994</i> midguts.....	66
3.4 <i>dronc</i> expression in <i>KGO2994</i> salivary glands.....	68
3.5 Creation of a specific <i>dronc</i> mutant.....	69
3.6 Generation of complementation transgenes.....	70
3.7 <i>CG6685⁴</i> and <i>dronc^{d5}</i> animals have different larval organ morphology.....	72
3.8 <i>CG6685⁴</i> and <i>dronc^{d5}</i> animals die at different developmental stages.....	72
3.9 <i>CG6685⁴</i> and <i>dronc^{d5}</i> animals have different developmental delays and survival rates to the late third instar stage.....	74
3.10 Cell death in larval structures is affected by loss of DRONC.....	75
3.11 DRONC is not required for larval midgut destruction	75
3.11.1 <i>dronc</i> mutant midgut destruction occurs at pupariation.....	75

3.11.2 <i>dronc</i> mutant midguts are TUNEL positive.....	76
3.11.3 Caspase activation is maintained in <i>dronc^{d5}</i> midguts.....	77
3.11.4 Aspects of autophagy are absent in <i>dronc^{d5}</i> midguts.....	78
3.12 DRONC is required for salivary gland removal.....	79
3.12.1 <i>dronc</i> mutant animals have persistent salivary glands.....	79
3.12.2 <i>dronc</i> mutant salivary glands are deficient for TUNEL.....	81
3.12.3 Effector caspase activation is DRONC-dependent in salivary glands.....	81
3.12.4 <i>dronc</i> mutant salivary gland cells have ultrastructural anomalies.....	82
3.12.5 The PCD genetic regulatory pathway is active in <i>dronc^{d5}</i> salivary glands....	83
3.13 DRONC is required for RPR-, HID- and GRIM-induced cell death in the eye..	84
3.14 <i>dronc</i> is required for radiation-induced cell death.....	84
3.15 <i>dronc^{d5}</i> animals have increased blood cells.....	85
3.16 Discussion.....	86

Chapter 4: *Distinct promoter regions regulate spatial and temporal expression of the Drosophila caspase dronc*

4.1 Introduction.....	89
4.2 <i>dronc</i> promoter-driven <i>LacZ</i> expression in embryos and adult ovaries.....	91
4.3 <i>dronc</i> regulation in midguts and salivary glands during metamorphosis.....	93
4.4 Expression of the promoter- <i>LacZ</i> transgenes in larval brain lobes.....	96
4.5 Temporal regulation of the <i>dronc</i> promoter.....	97
4.6 The Role of E74A, BR-C and E93 in the regulation of <i>dronc</i> expression.....	98
4.7 Discussion.....	102

Chapter 5: Identification of regulatory elements controlling the temporal and spatial expression of <i>dronc</i>	
5.1 Introduction.....	106
5.2 Analysis between 2.8 and 1.1kb of <i>dronc</i> promoter.....	108
5.3 A region of the <i>dronc</i> promoter contains a putative midgut repressor.....	108
5.4 A region of the <i>dronc</i> promoter is required for the spatial regulation of <i>dronc</i> .	109
5.5 <i>dronc</i> promoter contains an EcR/Usp binding element (EcRBE).....	110
5.6 An EcR/Usp binding site resides in the <i>dronc</i> promoter.....	111
5.7 The EcR-B1 isoform specifically binds the <i>dronc</i> promoter.....	111
5.8 <i>droncEcRBE</i> is important for ecdysone-mediated <i>dronc</i> transcription	113
5.9 <i>dronc</i> EcRBE is important for tissue specific <i>dronc</i> expression	114
5.10 Discussion.....	115
Chapter 6: General Discussion.....	120
Bibliography.....	131

Abstract

Correct development of multicellular organisms requires the programmed removal of supernumerary, redundant, or damaged cells, a process achieved by apoptosis. Apoptosis, or Programmed Cell Death (PCD) is executed by caspases, a highly conserved family of cysteine proteases. The removal of redundant larval tissues during metamorphosis is controlled by the steroid hormone ecdysone. Ecdysone signalling is mediated by the nuclear receptor heterodimer EcR/Usp, which in turn transcriptionally activates a host of transcription factors which then go on to regulate genes essential for PCD, like caspases. The apical caspase *dronc* is upregulated in the larval midgut and salivary glands prior to their destruction and is dependent on the BR-C and E93 transcription factors. To further understand the role of *dronc* in development, a *dronc* mutant fly was generated and a transgenic promoter-reporter strategy was employed to investigate *dronc* regulation.

Larval organs from *dronc* mutants lack dying cells and, when irradiated, fail to show a radiation-induced PCD response. The midguts from *dronc* mutants undergo apoptosis and have high caspase activity. These data indicate that a *dronc*-independent caspase activation pathway is active in the midgut. Salivary glands from *dronc* mutants failed to be removed and have reduced caspase activity. Consequently it is clear that the role of DRONC differs significantly between the midgut and salivary glands.

The employment of a transgenic *dronc* promoter-*LacZ* reporter system identified promoter regions essential for the correct temporal and spatial expression of *dronc*. A region of the *dronc* promoter between 1.1kb and 2.8kb has elements essential for *LacZ* expression in salivary glands. This region was also dependent on the BR-C and E93

transcription factors for salivary gland expression. A functional ecdysone receptor binding element (EcRBE) was identified in the *dronc* proximal promoter. The EcR-B1 isoform directly binds this EcRBE and is necessary for correct *dronc* expression in the larval salivary glands.

This work revealed some novel findings regarding the role of DRONC in development and the availability of a specific *dronc* mutant now makes it possible to explore some of the recently published non-apoptotic roles of *dronc*. This work aids in understanding how nuclear hormones control transcription and shows *dronc* to be an ideal model gene to explore these molecular and genetic processes.

Statement

This thesis contains no material which has been accepted for any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge, contains no material previously published or written by any other person, except where due reference has been made. I give my consent for this thesis to be made available for loan and photocopying.

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