Bioinformatic genome analysis of the necrotrophic wheat-pathogenic fungus *Phaeosphaeria nodorum* and related Dothideomycete fungi.

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This thesis is presented for the degree of Doctor of Philosophy

I declare that this thesis is my own account of my own work and contains as its main content work which has not been previously submitted for any degree at any tertiary institution.
James Kyawzwar Hane

It is a truth universally acknowledged that a single Ph. D. student in possession of a whole genome sequence must be in want of a stiff drink. Of all the genomes in all the fungi in all the world, *ToxA* horizontally transfers out of mine. To lose 11 kilobases may be regarded as a misfortune; to lose 280 kilobases looks like carelessness! It was the best of times, it was the worst of times; it was the age of genomics, it was the age of bioinformatics; it was the epoch of next-generation sequencing, it was the epoch of data analysis; it was the season of transcriptomics, it was the season of proteogenomics; it was the spring of mesosynteny, it was the winter of repeat-induced point mutation; we had everything before us, we had nothing before us; we were all going directly to Curtin, but I was going the other way. All this happened, more or less.

In my younger and more vulnerable years my supervisor gave me some advice that I've been turning over in my mind ever since: "Everything's got a moral, if only you can find it". I don't believe there's an atom of meaning in it. It would be so nice if something made sense for a change. Sometimes I've believed as many as six impossible things before breakfast. Granted: I am a student of a research institution; my supervisor is watching me, he never lets me out of his sight; there's a peephole in the door, and my supervisor's expertise is the shade of biochemistry that can never see through a bioinformatics type like me.

Oh! it is absurd to have a hard and fast rule about what one should read and what one shouldn't. More than half of scientific literature depends on what one shouldn't read. The truth is rarely pure and never simple. Scientific research would be very tedious if it were either, and scientific literature a complete impossibility! I have always been of opinion that a man who desires to get a Ph. D. should know either everything or nothing. I do not approve of anything that tampers with natural ignorance. Ignorance is like a delicate exotic fruit; touch it and the bloom is gone. The whole theory of modern education is radically unsound. Fortunately in Murdoch, at any rate, education produces no effect whatsoever. If it did, it would prove a serious danger to the upper management, and probably lead to acts of violence in Bush Court.

Of all the things that drive men to research, the most common disaster, I've come to learn, is women. Here's looking at you, kid. We'll always have Perth. You must remember this - maybe not today, maybe not tomorrow, but soon and for the rest of your life.

I have never begun a thesis with more misgiving. I write this sitting in the kitchen sink. I don't write accurately - anyone can write accurately - but I write with wonderful expression. Read the directions and directly you will be directed in the right direction. When I use a word, it means just what I choose it to mean – neither more nor less. I never travel without my thesis. One should always have something sensational to read in the train. Whether I shall turn out to be the hero of my own life, or whether that station will be held by anybody else, these pages must show.

Abstract

Phaeosphaeria nodorum (anamorph: Stagonospora nodorum) is the causal agent of Stagonospora nodorum blotch (SNB, syn. glume blotch) in wheat. P. nodorum is estimated to cause up to 31% wheat yield loss worldwide. Within Australia it is the primary pathogen of wheat and is estimated to cause losses of \$108 million per annum. The genome assembly of *P. nodorum* was sequenced in 2005 and was the first species in the class Dothideomycetes, a significant fungal taxon containing several major phytopathogens, to be publically released. The *P. nodorum* genome database has since evolved from basic sequence data into a powerful resource for studying the SNB host-pathogen interaction and advancing the understanding of fungal genome structure. The genes of *P. nodorum* have been annotated to a high level of accuracy and now serve as a model dataset for comparative purposes. P. nodorum gene annotations have been refined by a combination of several techniques including manual curation, orthology with related species, expressed sequence tag (EST) alignment, and proteogenomics. Analysis of the repetitive DNA in the *P. nodorum* genome lead to the development of software for the analysis of repeat-induced point mutation (RIP), a fungal-specific genome defence mechanism, which was a major improvement upon previous methods. Comparative genomics between P. nodorum and related species has highlighted a novel pattern of genome sequence conservation between filamentous fungi called 'mesosynteny' and has lead to the development of novel 'genome finishing' strategies.

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Table of contents

Chapter 1: Introduction	
Chapter 2: Dothideomycete-Plant Interactions Illuminated by Genome Sequencing and EST Analysis of the Wheat Pathogen Stagonospora	14-38
nodorum	
Attribution statement	14
Abstract	17
Introduction	17
Results	18
Acquisition and analysis of the genome sequence	18
Analysis of repetitive elements	18
Mitochondrial genome	19
Gene content	19
Gene expression during infection	20
Discussion	21
Phylogenetic analysis	21
Repeated elements in the nuclear genome	21
The mitochondrial genome	21
Functional analysis of proteins	23
Gene expression during infection	29
Genome architecture	31
Methods	33
Fungal strains	33
Phylogenetic analysis	33
Repetitive elements	33
Gene content	33
EST library construction	34
Quantitative PCR	34
Accession number	34
References	34
Chapter 3: RIPCAL: a tool for alignment-based analysis of repeat- induced point mutations in fungal genomic sequences	39-74
Attribution statement	41
Abstract	40
Background	41
Results	42
Validation of RIP detection by the alignment-based method	42
Identification of the dominant CpN to TpN di-nucleotide mutation in RIP-affected sequences Di-nucleotide frequency and index analysis of RIP mutation in	43
Stagonospora nodorum Alignment-based analysis of RIP mutation in Stagonospora	43 43
nodorum Discussion	46
Conclusion	48
Methods	48 48
RIP-index analysis	48 48
RIP-index analysis RIP-index sequence scan	48 50
Alignment-based analysis	50 50
Validation of alignment-based RIP analysis	
vandation of angliniciti-based KIP analysis	50

	RIP analysis of S. nodorum de novo repeat families	50
	Time of operation	51
	References	51
	Appendix 3A: RIPCAL/deRIP manual	53
	Appendix 3B: Response to thesis examination comments	64
Chan	ter 4: In silico reversal of repeat-induced point mutation (RIP)	75-98
_	ifies the origins of repeat families and uncovers obscured	73 30
	cated genes	
uupii	Attribution statement	75
	Abstract	73 77
	Background	77 77
	Results	77 79
	Validating the deRIP process using known non-RIP affected	79 79
	repeats	79
	Determining the roles and origin of RIP-degraded repeats in <i>S. nodorum</i>	82
	Discussion	88
	Conclusions	90
	Methods	90
	Analysis of RIP-mutation of <i>S. nodorum</i> repetitive DNA	90
	Predicting the original repeat sequence prior to RIP-degradation	90
	Validating the deRIP technique	91
	Predicting the origin of RIP-degraded repeats	91
	References	91
	Appendix 4A: Response to thesis examination comments	93
	rr	33
~		
	ter 5: Evolution of Linked Avirulence Effectors in Leptosphaeria	99-116
macu	lans Is Affected by Genomic Environment and Exposure to	99-116
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants	
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement	99
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract	99 101
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction	99 101 101
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results	99 101 101 102
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction	99 101 101
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of	99 101 101 102
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6	99 101 101 102 102
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6	99 101 101 102 102
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations	99 101 101 102 102 105 106
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles	99 101 101 102 102 105 106
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes	99 101 101 102 102 105 106 106 107
macu	lans Is Affected by Genomic Environment and Exposure to tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles	99 101 101 102 102 105 106 106 107 107
macu	Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance	99 101 101 102 102 105 106 106 107 107
macu	Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent	99 101 101 102 102 105 106 106 107 107
macu	Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions	99 101 101 102 102 105 106 106 107 107 108 108
macu	tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions Deletion alleles of AvrLm1 and AvrLm6 had multiple origins whilst	99 101 101 102 102 105 106 106 107 107 108 108
macu	tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions Deletion alleles of AvrLm1 and AvrLm6 had multiple origins whilst RIP alleles had a single origin	99 101 101 102 102 105 106 106 107 107 108 108
macu	tance Genes in Host Plants Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions Deletion alleles of AvrLm1 and AvrLm6 had multiple origins whilst RIP alleles had a single origin Deletions, non-synonymous and RIP mutations can confer virulence	99 101 101 102 102 105 106 106 107 107 108 108 110
macu	Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions Deletion alleles of AvrLm1 and AvrLm6 had multiple origins whilst RIP alleles had a single origin Deletions, non-synonymous and RIP mutations can confer virulence Methods	99 101 101 102 102 105 106 106 107 107 108 108 110 112 112
macu	Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions Deletion alleles of AvrLm1 and AvrLm6 had multiple origins whilst RIP alleles had a single origin Deletions, non-synonymous and RIP mutations can confer virulence Methods Brassica cultivars and Leptosphaeria maculans isolates	99 101 101 102 102 105 106 106 107 107 108 108 110 112 112 112 112
macu	Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions Deletion alleles of AvrLm1 and AvrLm6 had multiple origins whilst RIP alleles had a single origin Deletions, non-synonymous and RIP mutations can confer virulence Methods Brassica cultivars and Leptosphaeria maculans isolates Virulence testing	99 101 101 102 102 105 106 106 107 107 108 108 110 112 112 112 112 112 112
macu	Attribution statement Abstract Introduction Results Virulence of Australian isolates of L. maculans and analysis of mutations at AvrLm1 and AvrLm6 Characteristics of the genomic environment of AvrLm1 and AvrLm6 Distribution and extent of RIP mutations Transcription of AvrLm1, AvrLm6, LmCys1 and LmCys2 alleles Rate of mutations of genes Evolution and phylogenetic relationships of RIP and deletion alleles Discussion Selection pressure on frequencies of AvrLm1 and AvrLm6 alleles is imposed by extensive sowing of cultivars with Rlm1 resistance Repeat-induced point mutations may be 'leaking' from adjacent inactivated transposable elements into single copy reagions Deletion alleles of AvrLm1 and AvrLm6 had multiple origins whilst RIP alleles had a single origin Deletions, non-synonymous and RIP mutations can confer virulence Methods Brassica cultivars and Leptosphaeria maculans isolates	99 101 101 102 102 105 106 106 107 107 108 108 110 112 112 112 112

Expression analysis	113
Phylogenetic analysis	113
References	114
Appendix 5A: Response to thesis examination comments	116
Chapter 6: Effector diversification within compartments of the	117-128
Leptosphaeria maculans genome affected by Repeat-Induced Point	
Mutations	
Attribution statement	117
Abstract	119
Introduction	120
Results	120
General features of the <i>L. maculans</i> genome	120
The TEs are RIP-affected	120
The compartmentalized genome of <i>L. maculans</i>	120
The ribosomal DNA is extensively affected by RIP	122
AT-blocks as niches for effectors	122
History of genome invasion by transposable elements	123
Discussion	124
Methods	126
Phylogenetic analysis	126
Sequencing and assembly	126
L. maculans genome annotation	126
Annotation and analysis of repeated elements	126
RIP and deRIP analysis	126
Analysis of AT-blocks	127
Identification of small secreted proteins (SSPs)	127
References	127
Chapter 7: Deep proteogenomics; high throughput gene validation by	129-139
multidimensional liquid chromatography and mass spectrometry of	
proteins from the fungal wheat pathogen Stagonospora nodorum	
Attribution statement	129
Abstract	131
Background	132
Methods	132
Growth and maintenance of Stagonospora nodorum	132
Protein extraction	133
Sample preparation	133
Strong cation exchange chromatography	133
Reverse phase nano LC MALDI-MS/MS	133
Data analysis	133
Characterisation of peptide-supported genes	133
De novo proteogenomics	134
Results and Discussion	134
Gene models confirmed by Mascot analysis of the existing gene model database	134
Gene models confirmed by Mascot analysis of the 6-frame translated genome sequence	136
Gene models identified by Mascot analysis of the 6 frame translated unassembled read database	137
Sifting new and modified gene models by homology criteria	137
Conclusion	138

References	139
------------	-----

Chapter 8: A novel mode of chromosomal evolution pec	uliar to 140-160
filamentous Ascomycete fungi	
Attribution statement	140
Abstract	142
Background	142
Results	145
Taxonomic distribution of mesosynteny across the fur	ngal kingdom 147
Conclusions	152
Materials & Methods	154
Whole-genome comparisons	154
Determination of significant sequence conservation	154
Analysis of syntenic regions between conserved seque	ences 154
Classification of synteny type	154
References	155
Appendix 8A: Response to thesis examination comments	158
Chapter 9: Finished Genome of the Fungal Wheat Patho Mycosphaerella graminicola Reveals Dispensome Structu	_
• • •	are,
Chromosome Plasticity and Stealth Pathogenesis Attribution statement	1.61
Abstract	161
Introduction	163
	164
Results	164
Features of the finished genome	164
Sexual activation of chromosome plasticity and repea mutation	-
Core and dispensome chromosomes are highly different	
A new type of synteny	167
A mechanism of stealth pathogenesis	167
Discussion	169
Materials and Methods	174
Biological material	174
Initial sequencing and assembly	175
Gap closure and finishing	175
Genome annotation	175
Microarray analysis	175
Principal component analyses of core and dispensable	e chromosomes 175
Mesosynteny	176
Cazy annotation and growth profiling	176
Genome structure analyses	176
References	178
Appendix 9A: Response to thesis examination comments	180
Chapter 10: Genomic and comparative analysis of the cl	lass 181-207
Dothideomycetes	101 201
Attribution statement	181
Introduction	183
Significant phytopathogenic species	183
Order Pleosporales	
	183
Order Capnodiales	185
Dothideomycetidae of uncertain phylogenetic placem	ent 185

Genome sequencing in the Dothideomycetes	185
Phaeosphaeria nodorum	185
Mycosphaerella graminicola	191
Leptosphaeria maculans	191
Comparative Genomics	192
Synteny	192
Completion of draft genome assemblies using mesosyntenic predictions	195
Mitochondrial genomes	197
Repetitive DNA	199
Repeat-induced point mutation	200
Pathogenicity	201
Mechanisms of pathogenicity	201
Lateral gene transfer	202
Generation of diversity via RIP	203
Conclusions	203
References	204
Chapter 11: Conclusion	208-217
Supplementary data	CD-ROM