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**A search for quantitative trait loci involved in
physiological processes related to milk production
in dairy cattle**

A thesis presented in partial fulfilment of the requirements

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Abstract

Metabolic challenges have previously been used to identify physiological markers to assist with the selection of both sexes dairy cattle at an early age to increase rate of genetic gain. Physiological markers have not been implemented in selection programmes due to low accuracy. An experiment was undertaken to investigate the use of metabolic quantitative trait loci (QTL) for improving the rate of genetic gain in dairy cattle. Three metabolic challenges (adrenaline, glucose, and thyrotropin-releasing hormone) were conducted on 882 18-month-old Friesian-Jersey F₂ crossbred heifers. An initial whole genome scan was conducted by genotyping 1679 animals within the trial pedigree for 283 microsatellite markers, obtained primarily from published marker maps. QTL analyses were performed on the Friesian-Jersey crossbred trial data using metabolic and milk production phenotypes. 581 QTL were significant at the 1% level and 275 of them were QTL of metabolic phenotypes. An objective of this study was to identify chromosomal regions in which endocrine and milk production QTL were co-located, in the hope that these regions would contain genes with a significant impact on the control of milk production. The region selected for a candidate gene study was 47-51 cM of BTA14 due to the close proximity of metabolic and milk production QTL co-located in this region. Comparative mapping was used to generate a list of 105 genes in the region of interest. The genes considered the most suitable candidates for the QTL in the region were tripartite motif-containing 55, ubiquitin-conjugating enzyme E2W (putative), nuclear receptor coactivator 2, serum/glucocorticoid regulated kinase family, member 3, opioid receptor, kappa 1, proenkephalin, corticotropin releasing hormone. A major finding of this study was that there were very few chromosomal regions in which metabolic and milk production QTL were co-located. This is likely to be due to the highly complex and integrated molecular networks controlled by many genes that influence milk production traits. The data generated in this thesis will be suitable for more advanced examinations of the genetic control of milk production using the new generations of single nucleotide polymorphism chips.

Dedicated to my mother Ellen Hutchinson,

who always nurtured my love of learning.

For you my love and gratitude knows no bounds.

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Table of Contents

Abstract	iii
Acknowledgements	vii
List of Figures	xv
List of Tables	xvii
List of Abbreviations	xix
CHAPTER 1	1
CHAPTER 2	5
2.1 <i>Introduction</i>	6
2.2 <i>Breeding schemes</i>	6
2.3 <i>Quantitative Trait Loci and Marker Assisted Selection</i>	9
2.4 <i>The Major Metabolic Pathways in the Lactating Dairy Cow</i>	11
2.5 <i>Carbohydrate Metabolism in the Ruminant</i>	14
2.6 <i>Carbohydrate metabolism in the lactating ruminant</i>	15
Glucose uptake and utilisation	15
Circulating insulin concentrations	17
Changes in insulin responsiveness and glucose use in peripheral tissues	18
The role of growth hormone in insulin resistance	21
The role of glucagon	21
Glucose uptake by mammary gland	23
Differences between high and low genetic merit dairy cattle	23
Summary	24
2.7 <i>Lipid Metabolism</i>	25
Catecholamines	29
Leptin	30
Summary	30
2.8 <i>Protein Metabolism</i>	31
Summary	34
2.9 <i>Liver</i>	34
2.10 <i>Metabolic Pathways Summary</i>	35
2.11 <i>Challenges</i>	35
Fasting and feeding	37
Insulin	38
Growth hormone	39
Adrenaline	43
Summary	44
2.12 <i>Purpose and Scope</i>	47
CHAPTER 3	49
3.1 <i>Animal Ethics</i>	50

3.2	<i>Location</i>	50
3.3	<i>Generation of experimental animals</i>	50
3.4	<i>Heifer rearing and management</i>	52
	Halter training	53
	Feed	53
3.5	<i>Experimental animals and groups</i>	53
3.6	<i>Challenge procedure</i>	57
	Time sequence	57
	Live weight measurements	60
	Catheterisation	60
	Challenges	61
3.7	<i>Hormone Assays</i>	64
	Growth Hormone	64
	Insulin-like growth factor I	64
	Prolactin	65
	Thyroid Stimulating Hormone	65
	Insulin	65
3.8	<i>Metabolite Assays</i>	66
	Non-esterified Fatty Acids	66
	Glucose	66
	Glycerol	66
3.9	<i>Other data collection</i>	67
	Milk Yields	67
	Genotyping	67
3.10	<i>Data Processing</i>	68
3.11	<i>Data adjustment</i>	72
	Unbalanced maternal grandsire distribution	72
	Data analysis	73
CHAPTER 4		75
4.1	<i>Introduction</i>	76
4.2	<i>Mean response curves</i>	76
4.3	<i>Adrenaline challenge</i>	76
	Results	78
	Discussion	81
4.4	<i>Glucose challenge</i>	82
	Results	84
	Discussion	92
4.5	<i>Thyrotropin-releasing hormone challenge</i>	96
	Results	97
	Discussion	104
4.6	<i>Finalised phenotypes</i>	105
	Adrenaline challenge phenotypes	105
	Glucose challenge phenotypes	106
	TRH challenge phenotypes	107
	Summary	107
CHAPTER 5		109
5.1	<i>Introduction</i>	110
5.2	<i>Phenotype generation</i>	110
5.3	<i>QTL analysis using WEBQTLANA</i>	111

Example output from WEBQTLANA-----	113
5.4 <i>Endocrine and milk production QTL</i> -----	117
5.5 <i>Candidate genes</i> -----	120
5.6 <i>Summary</i> -----	122
CHAPTER 6 -----	125
6.1 <i>Introduction</i> -----	126
6.2 <i>Phenotypes in the region</i> -----	129
6.3 <i>Candidate genes</i> -----	133
6.4 <i>Protein metabolism candidate genes</i> -----	133
Ribosomal protein L7 and ribosomal protein S20-----	134
Ribosome biogenesis regulator homolog (<i>S. cerevisiae</i>)-----	138
Mitochondrial ribosomal protein L15-----	140
Ubiquitin-conjugating enzyme E2W (putative)-----	141
COP9 constitutive photomorphogenic homolog subunit 5 (<i>Arabidopsis</i>)-----	144
Tripartite motif-containing 55-----	146
Musculin (activated B-cell factor-1)-----	148
Summary-----	149
6.5 <i>Control points in metabolic pathways</i> -----	150
Nuclear receptor coactivator 2-----	151
Serum/glucocorticoid regulated kinase family, member 3-----	155
Regulator of G-protein signalling 20-----	157
RAB2, member RAS oncogene family-----	160
ADP-ribosylation factor guanine nucleotide-exchange factor 1(brefeldin A-inhibited)-----	164
ATPase, H ⁺ transporting, lysosomal 50/57kDa, V1 subunit H-----	166
Summary-----	170
6.6 <i>Food intake control candidate genes</i> -----	170
Opioid receptor, kappa 1 (OPRK1)-----	171
Proenkephalin (PENK)-----	174
Corticotropin releasing hormone (CRH)-----	179
Neuropeptides B/W receptor 1 (NPBWR1)-----	182
Summary-----	184
6.7 <i>Summary</i> -----	185
CHAPTER 7 -----	187
7.1 <i>The challenges</i> -----	188
7.2 <i>Mapping QTL</i> -----	191
7.3 <i>Usefulness of metabolic challenges</i> -----	192
7.4 <i>QTL and genomic selection</i> -----	196
7.5 <i>Conclusion</i> -----	199
CHAPTER 8 -----	201
CHAPTER 9 -----	245
<i>Appendix A: Catheterisation Procedures</i> -----	246
Consumables-----	246
Insertion procedure-----	248
<i>Appendix B: Infusate preparation</i> -----	251
Adrenaline-----	251
Glucose-----	253
TRH-----	255

<i>Appendix C: Iodination procedures</i> -----	258
Iodination of bovine GH using Iodogen -----	258
Iodination of bovine TSH using Chloramine T -----	260
<i>Appendix D: Significance tables</i> -----	263
<i>Appendix E: Metabolic Phenotypes</i> -----	265
Adrenaline challenge -----	265
Glucose challenge-----	267
TRH challenge -----	269
<i>Appendix F: QTL locations</i> -----	272
<i>Appendix G: List of genes in region of interest on BTA 14</i> -----	290
<i>Appendix H: Information on genes discarded from candidate gene study</i> -----	294
LYPLA1 - lysophospholipase 1 -----	294
Potassium voltage-gated channel, Shab-related subfamily, member 2 -----	294
CPA6 – carboxypeptidase A6 -----	295
SULF1 – sulfatase 1 -----	296
TGS1 – trimethylguanosine synthase homolog (<i>S. cerevisiae</i>) -----	296
MYBL1 – v-myb myeloblastosis viral oncogene homolog (avian)-like 1 -----	297
<i>Appendix I: Phenotypic correlations</i> -----	300

List of Figures

Figure 2.1 Example of the structure of a dairy cattle breeding scheme in New Zealand	8
Figure 2.2 Schematic representation of some of the metabolic changes that occur in the periparturient dairy cow	13
Figure 2.3 Some metabolic pathways of adipocytes and their adaptations to lactation	27
Figure 3.1 Experimental design for Friesian-Jersey crossbred trial	51
Figure 3.2 Diagrammatic representation of the segregation that occurs in an F ₂ experimental design	52
Figure 3.3 Live weight of heifers at the time they underwent challenges	55
Figure 3.4 Age of heifers at the time they received the challenges	56
Figure 3.5 Time between heifers receiving challenges and when they calved	56
Figure 3.6 Percentage of heifers in each challenge group that did not have a calving date	57
Figure 3.7 Mean insulin release for each challenge group before and after a glucose infusion at time zero	70
Figure 3.8 Mean NEFA release for each challenge group before and after a glucose infusion at time zero	70
Figure 3.9 Mean insulin release for two subgroups in group 4 before and after a glucose infusion at time zero	71
Figure 4.1 Mean plasma glycerol concentrations before and after an intravenous adrenaline injection at time zero.	79
Figure 4.2 Mean plasma glycerol concentrations, by challenge year and by sire, before and after an intravenous adrenaline injection at time zero.	79
Figure 4.3 Mean plasma NEFA concentrations before and after an intravenous adrenaline injection at time zero.	80
Figure 4.4 Mean plasma glucose concentrations before and after an intravenous adrenaline injection at time zero	81
Figure 4.5 Mean glucose concentrations in the plasma of heifers, before and after an intravenous glucose infusion at time zero	84
Figure 4.6 Mean insulin concentrations in the plasma of heifers, before and after an intravenous glucose infusion at time zero	85
Figure 4.7 Linear regression between glucose clearance and insulin peak	86
Figure 4.8 Mean insulin concentrations in the plasma by challenge year and by sire before and after an intravenous glucose infusion at time zero	87
Figure 4.9 Mean glucose concentrations in the plasma by challenge year and by sire, before and after an intravenous glucose infusion at time zero.....	87
Figure 4.10 Mean NEFA concentrations in the plasma of heifers, before and after an intravenous glucose infusion at time zero	88
Figure 4.11 Mean plasma insulin concentrations and peak concentrations of glucose in plasma in response to an intravenous glucose challenge	89
Figure 4.12 Regression between a subset of original and re-analysed plasma insulin samples taken 10 minutes post glucose infusion	90

Figure 4.13 Mean GH concentrations in the plasma of heifers, before and after an intravenous TRH injection at time zero	98
Figure 4.14 Mean plasma GH concentrations of all heifers, grouped by challenge year and by sire, before and after an intravenous TRH injection at time zero	98
Figure 4.15 Mean prolactin concentrations in the plasma of heifers, before and after an intravenous TRH injection at time zero	99
Figure 4.16 Linear regression between group means of the prolactin concentration in plasma samples taken 5 minutes after an intravenous TRH injection and the day length in minutes on the day each group was challenged	100
Figure 4.17 Mean TSH concentrations in the plasma of heifers, before and after an intravenous TRH injection at time zero	101
Figure 4.18 Plasma TSH concentrations of individual heifers before and after an intravenous TRH injection at time zero	101
Figure 4.19 Mean plasma TSH concentrations of all heifers, grouped by challenge year and by sire, before and after an intravenous TRH injection at time zero	102
Figure 4.20 Mean plasma NEFA concentrations of heifers, before and after an intravenous TRH injection (0.3 µg TRH/kg lwt) at time zero	103
Figure 4.21 Mean plasma IGF-I concentrations of all heifers, grouped by challenge year and by sire, before and after an intravenous TRH injection at time zero	103
Figure 4.22 Mean plasma NEFA, GH, TSH, and prolactin concentrations in response to an intravenous TRH injection at time zero, grouped by challenge group	104
Figure 5.1 Example of the output generated by QTLANA from a 'multimasher' scan	112
Figure 6.1 Schematic representation of some of the metabolic changes that occur in the periparturient dairy cow	130
Figure 6.2 Diagram showing the major routes of secretion across the mammary epithelial cell	163
Figure 6.3 A diagrammatic representation of the bovine V-ATPase	167
Figure 7.1 The diagram constructed in the literature review of this thesis and an illustration of a target gene network and a protein to protein interaction network	194
Figure 7.2 Enlarged images of the corresponding boxes on the network diagram presented in Figure 7.1	195

List of Tables

Table 3.1 Number of animals per group and cohort, their age and live weight at the time they were challenged.....	54
Table 3.2 Example schedule for one week during the challenge period	59
Table 3.3 Description of the types of errors identified in the data	69
Table 4.1 The significance of the effect of fixed and environmental parameters on insulin concentrations in dairy heifers, before and times after a intravenous infusion of glucose.....	91
Table 4.2 The significance of the effect of fixed parameters on insulin concentrations in dairy heifers, before and after an intravenous infusion of glucose	91
Table 5.1 Examples of regions of interest found using the metabolic and milk production QTL.....	117
Table 6.1 The predicted locations, level of significance, maximum F-value and 95% confidence intervals for the QTL locations in the region of interest on <i>BTA14</i>	126
Table 6.2 Genes that were investigated for relevance to QTL of interest between 47 and 51 cM on <i>BTA14</i>	128
Table 9.1 Significance levels of fixed effects on responses to a thyrotropin-releasing hormone challenge.	263
Table 9.2 Significance levels of fixed effects on responses to an adrenaline challenge.....	264
Table 9.3 Methods used to calculate metabolic phenotypes from adrenaline challenge response data....	265
Table 9.4 Methods used to calculate metabolic phenotypes from glucose challenge response data	267
Table 9.5 Methods used to calculate metabolic phenotypes from TRH challenge response data	269
Table 9.6 The best predicted location for the metabolic and milk production QTL together with the level of significance, maximum F-value, and 95% confidence intervals of the QTL location.....	272
Table 9.7 Explanation of the abbreviations used for milk production phenotypes and QTL	289
Table 9.8 List of genes candidate genes generated for the region 47-51 cM on BTA 14	290
Table 9.9 Pearson Correlation Coefficients between glucose challenge response and milk production phenotypes followed by the probability that R is different from zero and the number of observations.	300
Table 9.10 Pearson Correlation Coefficients between glucose challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	301
Table 9.11 Pearson Correlation Coefficients between glucose challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	302
Table 9.12 Pearson Correlation Coefficients between glucose challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	303
Table 9.13 Pearson Correlation Coefficients between adrenaline challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	304
Table 9.14 Pearson Correlation Coefficients between adrenaline challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	305

Table 9.15 Pearson Correlation Coefficients between adrenaline challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	306
Table 9.16 Pearson Correlation Coefficients between adrenaline challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	307
Table 9.17 Pearson Correlation Coefficients between TRH challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	308
Table 9.18 Pearson Correlation Coefficients between TRH challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	309
Table 9.19 Pearson Correlation Coefficients between TRH challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	310
Table 9.20 Pearson Correlation Coefficients between TRH challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	311
Table 9.21 Pearson Correlation Coefficients between TRH challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	312
Table 9.22 Pearson Correlation Coefficients between TRH challenge response and milk production phenotypes, followed by the probability that R is different from zero and the number of observations.	313

List of Abbreviations

ALS	Acid labile subunit
ARF	ADP-ribosylation factor
ARC	Arcuate nucleus
ATP	Adenosine triphosphate
AUC	Area under the (response) curve
BCS	Body condition score
BTA	<i>Bos taurus</i> autosome
BI	Breeding index
cAMP	Cyclic adenosine-3',5'-monophosphate
CNS	Central nervous system
COP	Coat protein complex
DMI	Dry matter intake
DNA	Deoxyribonucleic acid
EB	Energy balance
ER	Endoplasmic reticulum
ERGIC	Endoplasmic reticulum-Golgi intermediate complex
FAS	Fatty acid synthetase
FFA	Free fatty acids
FJXB	Friesian-Jersey crossbred
GAP	GTPase-activating protein
GAPDH	Glyceraldehyde 3-phosphate dehydrogenase
GDP	Guanosine diphosphate
GEF	Guanine nucleotide-exchange factor
GH	Growth hormone
GHR	Growth hormone receptor
GHRH	Growth hormone releasing hormone
GLUT	Solute carrier family 2 (facilitated glucose transporter)
GM	Genetic merit
GPCR	7-membrane-spanning G-protein coupled receptor
GTP	Guanosine-5'-triphosphate
HBI	High breeding index
HGM	High genetic merit
HPA	Hypothalamo-pituitary-adrenal
ICV	Intracerebroventricular
IGF-I	Insulin-like growth factor I

IGFBP	Insulin-like growth factor binding protein
LBI	Low breeding index
LIC	Livestock Improvement Corporation
LPL	Lipoprotein lipase
MAS	Marker assisted selection
ME	Metabolisable energy
MEC	Mammary epithelial cell
NR	Nuclear receptor
PC	Pyruvate carboxylase
POMC	Pro-opiomelanocortin
PVN	Paraventricular nucleus
mRNA	Messenger ribonucleic acid
NEFA	Non-esterified fatty acids
NPY	Neuropeptide Y
NZ	New Zealand
QTL	Quantitative trait loci/locus
rRNA	Ribosomal ribonucleic acid
TIDA	Tuberoinfundibular dopamine
TRH	Thyrotropin-releasing hormone
TSH	Thyroid stimulating hormone
UPP	Ubiquitin-proteasome pathway
VFAs	Volatile fatty acids
VMH	Ventromedial nuclei
3-MH	3-methyl histidine