

Analysis of Metabolomics Data from Twin Families

Hermanus H.M. (Harmen) Draisma

Analysis of metabolomics data from twin families

Hermanus H.M. (Harmen) Draisma

PhD thesis with summary in Dutch

ISBN: 978-90-745-3875-6

Typeset in L^AT_EX 2_ε

Produced by F&N Boekservice

Chapters 1 and 4–6 copyright ©2011 by Harmen Draisma.

Chapter 2 copyright 2008 by Mary Ann Liebert, Inc., New Rochelle, NY.

Chapter 3 copyright 2010 by American Chemical Society.

Cover: Constellation of Gemini (twins) represented as a metabolite in metabolite space. Image from the stellar atlas *Firmamentum Sobiescianum sive Uranographia* (Johannes Hevelius, 1690) kind courtesy of the U.S. Naval Observatory and the Space Telescope Science Institute.

Analysis of Metabolomics Data from Twin Families

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof.mr. P.F. van der Heijden,
volgens besluit van het College voor Promoties
te verdedigen op dinsdag 10 mei 2011
klokke 16:15 uur

door

Hermanus H.M. (Harmen) Draisma
geboren te Voorburg
in 1981

Promotiecommissie

Promotores:

Prof.dr. J. van der Greef
Prof.dr. T. Hankemeier
Prof.dr. J.J. Meulman

Copromotor:

Dr. T.H. Reijmers

Overige leden:

Prof.dr. D.I. Boomsma (Vrije Universiteit Amsterdam)
Prof.dr. M. Danhof (Universiteit Leiden)
Prof.dr. G.J.B. van Ommen (Leids Universitair Medisch Centrum)
Prof.dr. P.E. Slagboom (Leids Universitair Medisch Centrum)
Prof.dr. A.P. IJzerman (Universiteit Leiden)

The research described in this thesis was performed at the Division of Analytical Biosciences of the Leiden/Amsterdam Center for Drug Research, Leiden University, Leiden, The Netherlands. This work was part of the BioRange programme of the Netherlands Bioinformatics Centre (NBIC), which is supported by a BSIK grant through the Netherlands Genomics Initiative (NGI).

Printing of this thesis was supported financially by the Leiden/Amsterdam Center for Drug Research, and by the Netherlands Bioinformatics Centre.

Whoever saves a life, it is considered as if he saved an entire world

Mishnah Sanhedrin 4:5; *Babylonian Talmud* Tractate Sanhedrin 37a

Contents

1	General introduction	1
1.1	Something old, something new: twin studies and metabolomics	1
1.2	Metabolomics	2
1.3	Twin and family studies	5
1.4	Two alternative methods to separate “nature” from “nurture” using family data	7
1.5	Quantitative genetic analysis for systems biology	17
1.6	The value of our approach in the (post-)GWA study era	19
1.7	Outline of this thesis	20
2	Similarities and differences in lipidomics profiles among healthy monozygotic twin pairs	23
2.1	Abstract	24
2.2	Introduction	24
2.3	Methods	27
2.4	Results	30
2.5	Discussion	37
2.6	Acknowledgments	43
3	Equating, or correction for between-block effects with applica- tion to body fluid LC–MS and NMR metabolomics data sets	45
3.1	Abstract	46
3.2	Introduction	46
3.3	Materials and methods	50
3.4	Results and discussion	54
3.5	Conclusions	57
3.6	Acknowledgments	60

3.7	Supporting information	61
4	Hierarchical clustering analysis of blood plasma lipidomics profiles from mono- and dizygotic twin families	73
4.1	Abstract	74
4.2	Introduction	74
4.3	Materials and methods	76
4.4	Results and discussion	78
4.5	Conclusions	86
4.6	Acknowledgments	87
4.7	Supporting information	87
5	Contribution of genetic and environmental factors to variation in the human blood plasma metabolome: a multivariate study in twins and siblings	97
5.1	Abstract	98
5.2	Introduction	98
5.3	Materials and methods	100
5.4	Results and discussion	103
5.5	Conclusions	112
5.6	Acknowledgments	112
6	Conclusions and perspectives	113
6.1	Between-block effect correction methods in metabolomics . . .	114
6.2	Multivariate quantitative genetic analysis	116
6.3	Medical relevance of our findings	117
	Bibliography	119
	Samenvatting	135
	Curriculum vitae	139
	List of publications	141
	Nawoord	143