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Prediction of "BRCAness" in breast cancer by array comparative genomic hybridization

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Citation

Joosse, S. A. (2012, March 27). *Prediction of "BRCAness" in breast cancer by array comparative genomic hybridization*. Retrieved from <https://hdl.handle.net/1887/18632>

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Issue Date: 2012-03-27

List of Abbreviations

ALDH1	aldehyde dehydrogenase 1 family, member A1	F-CSGE	fluorescent conformational sensitive gel electrophoresis
APC	adenomatous polyposis coli	FE test	Fisher's exact test
ATM	ataxia telangiectasia mutated	FFPE	Formalin-fixed, paraffin embedded
BAC	bacterial artificial chromosome		
BARD1	BRCA1 associated RING domain 1	GAPDH	glyceraldehyde-3-phosphate dehydrogenase
BCS	breast conserving surgery	GE	gene expression
BER	base excision repair	GEP	gene expression profiling
BIC	breast cancer information core	GEO	gene expression omnibus
bp	base pair	HBOC	hereditary breast and ovarian cancer
BRCA	breast cancer, early onset		
BRCT	BRCA1 C terminus (domain)	HD	helix-rich domain
CHEK2	checkpoint kinase 2	HDPB	high-dose platinum-based
CHK1	checkpoint kinase 1	H&E	hematoxylin and eosin
CGH	comparative genomic hybridization	HR	homologous recombination
CI	confidence interval	HRD	homologous recombination deficient/deficiency
CISH	chromogenic in situ hybridization	IDC	invasive ductal carcinoma
CNA	copy number alteration	IGF	insulin-like growth factor
CSC	cancer stem cell	IHC	immunohistochemistry
CTRM	c-terminal RAD51 binding motive	ILC	invasive lobular carcinoma
DCIS	ductal carcinoma in situ	IVS	intervening sequence
DGGE	denaturing gradient gel electrophoresis	kbp	kilo base pairs
DHPLC	denaturing high-performance liquid chromatography	KRT	keratin
DNA	deoxyribonucleic acid	LC	lobular carcinoma
DOL	degree of labeling	LCIS	lobular carcinoma in situ
DSB	double-strand break	LOD	logarithm of odds
DSS1	deleted in split hand/foot protein 1	LOH	loss of heterozygosity
EDTA	ethylenediaminetetraacetic acid	LOOCV	leave-one-out cross-validation
EGFR	epidermal growth factor receptor	LUMC	Leiden University Medical Center
ER	estrogen receptor	Mbp	mega base pairs
ERBB2	human epidermal growth factor receptor 2	MLPA	multiplex ligation dependent probe amplification
ESR1	estrogen receptor 1	MRI	magnetic resonance imaging
FAMA	fluorescent-assisted mismatch analysis	MYC	v-myc myelocytomatosis viral oncogene homolog

NCBI	National Center for Biotechnology Information
NGS	next generation sequencing
NHEJ	non-homologous end-joining
NKI	Netherlands Cancer Institute
NLS	nuclear localization signals
NPP	negative predictive power
OB	oligonucleotide binding
PALB2	partner and localizer of BRCA2
PAM	predicition analysis of microarrays
PARP	poly ADP ribose polymerase
PBM	prophylactic bilateral mastectomy
PBSO	prophylatic bilateral salpingo-oophorectomy
PCR	polymerase chain reaction
PPP	positive predictive power
PR	progesteron receptor
PTEN	phosphatase and tensin homolog
PTT	protein truncation test
RAD51	RAD51 homolog
RAP80	receptor-associated protein 80
RING	really interesting new gene
RNA	ribonucleic acid
RT-PCR	realtime PCR
SC	shrunken centroids
SCD	SQ-cluster domain
SCP	single-stranded conformational polymorphism
SDS	sodium dodecyl sulfate
SNP	single nucleotide polymorphism
SSB	single-strand break
SSC	saline-sodium citrate
STK11	serine/threonine kinase 11
STR	short tandem repeat
TBE	tris/borate/EDTA
TDGS	two-dimensional gene scanning
TP53	tumor protein 53
TNM	tumor/node/metestasis
ULS	universal linkage system
UV	unclassified variant
VEGF	vascular endothelial growth factor

Curriculum Vitae

Simon Joosse was born on August 6, 1983 in IJmuiden (Velsen), the Netherlands. He started studying medical biology at the faculty of Applied Sciences at Inholland University in Alkmaar in 2000. His graduation report on the subject "Gene inactivation for cell immortality" was carried out under the supervision of Dr. R.L. Beijersbergen at the department of Molecular Carcinogenesis at the Netherlands Cancer Institute, Amsterdam, in 2004. After graduation, he worked at the Netherlands Cancer Institute as a technician for two years and performed the Master Course on Experimental Oncology in 2006, organized by the Oncology school of Amsterdam. In 2007, Simon started working as a PhD student at the department of Experimental Therapy in the Netherlands Cancer Institute, under the supervision of Dr. P.M. Nederlof in the group of Dr. L.J. van 't Veer. In 2009, he moved to Hamburg, Germany, where he started working as scientist for the Department of Tumor Biology, University Medical Center Hamburg-Eppendorf, while simultaneously finishing his PhD studies performed at the Netherlands Cancer Institute. The results of this research are described in this thesis.

List of Publications

1. **Joosse SA**, Hannemann J, Spötter J, Bauche A, Andreas A, Müller V, Pantel K. *Changes in keratin expression during metastatic progression of breast cancer: impact on the detection of circulating tumor cells*. Clin Cancer Res. 2012; [Online publication ahead of print]
2. Hannemann J, Meyer-Staeckling S, Kemming D, Alpers I, **Joosse SA**, Pospisil H, Kurtz S, Görndt J, Püschel K, Riethdorf S, Pantel K, Brandt B. *Quantitative high-resolution genomic analysis of single cancer cells*. PLOS One. 2011 Nov; 6(11):e26362.
3. **Joosse SA**, Hannemann J. *Predication of BRCA status*. CML - Breast Cancer 2011 Jul; 23(2):41-50, Leading article
4. Didraga MA, van Beers EH, **Joosse SA**, Brandwijk KI, Oldenburg RA, Wessels LF, Hogervorst FB, Ligtenberg MJ, Hoogerbrugge N, Verhoef S, Devilee P, Nederlof PM. *A Non-BRCA1/2 hereditary breast cancer sub-group defined by aCGH profiling of genetically related patients*. Breast Cancer Res Treat. 2011 Nov; 130(2):425-36.
5. **Joosse SA**, Brandwijk KI, Mulder M, Wesseling J, Hannemann J, Nederlof PM. *The genomic signature of BRCA1 deficiency in sporadic basal-like breast tumors*. Genes Chromosomes Cancer. 2011 Feb; 50:71-81.
6. Bruin SC, Klijn C, Liefers GJ, Braaf LM, **Joosse SA**, van Beers EH, Verwaal VJ, Morreau H, Wessels LF, van Velthuysen ML, Tollenaar RA, van't Veer LJ. *Specific genomic aberrations in primary colorectal cancer are associated with liver metastases*. BMC Cancer. 2010 Dec; 10(1):662.
7. Holstege H, van Beers EH, Velds A, Liu X, **Joosse SA**, Klarenbeek S, Schut E, Kerkhoven R, Klijn CN, Wessels LFA, Nederlof PM, Jonkers J. *Cross-species comparison of aCGH data from mouse and human BRCA1- and BRCA2-mutated breast cancers*. BMC Cancer. 2010 Aug; 10:455.
8. **Joosse SA**, Brandwijk KI, Devilee P, Wesseling J, Hogervorst FB, Verhoef S, Nederlof PM. *Prediction of BRCA2-association in hereditary breast carcinomas using array-CGH*. Breast Cancer Res Treat. 2010 Jul; [Online publication ahead of print].
9. Horlings HM, Lai C, Nuyten DS, Halfwerk H, Kristel P, van Beers E, **Joosse SA**, Klijn C, Nederlof PM, Reinders MJ, Wessels LF, van de Vijver MJ. *Integration of DNA copy number alterations and prognostic gene expression signatures in breast cancer patients*. Clin Cancer Res. 2010 Jan; 16(2):651-63.

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10. Puppe J, Drost R, Liu X, **Joosse SA**, Evers B, Cornelissen-Steijger P, Nederlof P, Yu Q, Jonkers J, van Lohuizen M, Pietersen AM. *BRCA1-deficient mammary tumor cells are dependent on EZH2 expression and sensitive to Polycomb Repressive Complex 2-inhibitor 3-deazaneplanocin A*. Breast Cancer Res. 2009 Aug; 11(4):R63.
 11. van den Ouweland AM, Dinjens WN, Dorssers LC, van Veghel-Plandsoen MM, Brüggewirth HT, Withagen-Hermans CJ, Collée JM, **Joosse SA**, Terlouw-Kromosoeto JN, Nederlof PM. *Deletion of Exons 1a-2 of BRCA1: A Rather Frequent Pathogenic Abnormality*. Genet Test Mol Biomarkers. 2009 Jun; 13(3):399-406.
 12. Koski TA, Lehtonen HJ, Jee KJ, Ninomiya S, **Joosse SA**, Vahteristo P, Kiuru M, Karhu A, Sammalkorpi H, Vanharanta S, Lehtonen R, Edgren H, Nederlof PM, Hietala M, Aittomäki K, Herva R, Knuutila S, Aaltonen LA, Launonen V. *Array comparative genomic hybridization identifies a distinct DNA copy number profile in renal cell cancer associated with hereditary leiomyomatosis and renal cell cancer*. Genes Chromosomes Cancer. 2009 Jul; 48(7):544-51.
 13. Holstege H, **Joosse SA**, van Oostrom CT, Nederlof PM, de Vries A, Jonkers J. *High incidence of protein-truncating TP53 mutations in BRCA1-related breast cancer*. Cancer Research. 2009 Apr; 69(8):3625-33.
 14. **Joosse SA**, van Beers EH, Tielen IH, Horlings H, Peterse JL, Hoogerbrugge N, Ligtenberg MJ, Wessels LF, Axwijk P, Verhoef S, Hogervorst FB, Nederlof PM. *Prediction of BRCA1-association in hereditary non-BRCA1/2 breast carcinomas with array-CGH*. Breast Cancer Res Treat. 2009 Aug; 116(3):479-89.
 15. Horlings HM, Bergamaschi A, Nordgard SH, Kim YH, Han W, Noh DY, Salari K, **Joosse SA**, Reyat F, Lingjaerde OC, Kristensen VN, Børresen-Dale AL, Pollack J, van de Vijver MJ. *ESR1 gene amplification in breast cancer: a common phenomenon?* Nat Genet. 2008 Jul; 40(7):807-8; author reply 810-2.
 16. Tischkowitz M, Hamel N, Carvalho MA, Birrane G, Soni A, van Beers EH, **Joosse SA**, Wong N, Novak D, Quenneville LA, Grist SA, kConFab, Nederlof PM, Goldgar DE, Tavtigian SV, Monteiro AN, Ladas JA, Foulkes WD. *Pathogenicity of the BRCA1 missense variant M1775K is determined by the disruption of the BRCT phosphopeptide-binding pocket: a multi-modal approach*. Eur J Hum Genet. 2008 Jul; 16(7):820-32.
 17. **Joosse SA**, van Beers EH, Nederlof PM. *Automated array-CGH optimized for archival formalin-fixed, paraffin-embedded tumor material*. BMC Cancer. 2007 Mar; 7:43.
 18. van Beers EH, **Joosse SA**, Ligtenberg MJ, Fles R, Hogervorst FB, Verhoef S, Nederlof PM. *A multiplex PCR predictor for aCGH success of FFPE samples*. Br J Cancer. 2006 Jan; 94(2):333-7.

Acknowledgements

This work has been made possible with the help of many people, whom I would like to thank here.

First of all, Dr. Petra Nederlof, thank you for giving me the opportunity to perform a PhD project under your supervision. Although my time as a PhD student in your lab was shorter as originally planned, we were able to produce some fine papers! I have learned an enormous amount and the years in your group were most productive.

Many thanks to my promotor Prof. Dr. Peter Devilee. You were always very kind and helpful to me and made it possible that I could finish my promotion even when I moved to Germany. Your music rocks!

I am indebted to Prof. Dr. Laura van 't Veer. It has been a real pleasure working in your group and having been witness of your groundbreaking research. Thank you for supporting me, especially in my last months at the NKI.

Prof. Dr. med. Klaus Pantel is gratefully acknowledged for allowing me to finish my PhD work at the UKE in Hamburg.

Erik van Beers, Renske Fles, and Kim Brandwijk - it has been a great experience working with you in our group! Erik, you have really taught me everything about breast cancer, array CGH, how to write a manuscript (properly and verbose), what it is like being a vegetarian, saxophone, and any other aspect of life on which we had time to talk about.

Much of the work in this thesis has been made possible with the help of the histopathology department, thank you very much for the endless amount of slides you cut and stained!! Frans Hogervorst, thank you for helping me on those occasions when I didn't understand about

those different mutation annotations again. Carla van Tiggelen and Sonja Springer for the administration of hundreds of samples. Hans Peterse, you have taught me much about pathology, thank you for always making time for me, spending hours behind the microscope, and being real critical about our work.

I would also like to acknowledge the people from our department C2 (formerly H6), especially: Adrian Begg, thank you for your time and for teaching me all about DNA repair; Els Wagenaar, it has been fun throwing away culture plates without names; Hans te Poele, it is a real joy knowing you, incredible how you could do your experiments, help every one with his/her (little) problems, run around though the building, and still have time for a chat; Thea Eggenhuizen, you knew the whole organization around the building, you have been a great help; and all other members of H6/C2, it has been a wonderful time.

My gratitude goes out to Ron Kerkhoven, Mike Heimerikx, Wim Brugman, and Marja Nieuwland from the microarray laboratory; Lodewyk Wessels for helping me with the bioinformatics and introducing me to MatLab, in which most calculation in this thesis have been performed; and Roderick Beijersbergen, for showing me the ins and outs of basic research during my internship at H2.

Last, but not least I would like to give special thanks to Juliane and Jannik. Thank you for proofreading everything I wrote (Juliane) and criticizing my plots (Jannik). Maar in het bijzonder bedank ik jullie dat jullie er elke dag voor mij zijn en de vreugde in mijn leven brengen.
