



Universiteit
Leiden
The Netherlands

Integrating clinicopathological and molecular data in the breast cancer patient : towards precision medicine

Engels, C.C.

Citation

Engels, C. C. (2016, May 19). *Integrating clinicopathological and molecular data in the breast cancer patient : towards precision medicine*. Retrieved from <https://hdl.handle.net/1887/39789>

Version: Not Applicable (or Unknown)

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/39789>

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/39789> holds various files of this Leiden University dissertation

Author: Engels, Charla Chábeli

Title: Integrating clinicopathological and molecular data in the breast cancer patient : towards precision medicine

Issue Date: 2016-05-19

**INTEGRATING CLINICOPATHOLOGICAL AND MOLECULAR DATA IN THE
BREAST CANCER PATIENT**

Towards precision medicine

Charla Chábeli Engels

**INTEGRATING CLINICOPATHOLOGICAL AND MOLECULAR DATA IN THE
BREAST CANCER PATIENT**

Towards precision medicine

Proefschrift

Ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van de Rector Magnificus prof. mr. C.J.J.M. Stolkers,
volgens besluit van het College voor Promoties
te verdedigen op donderdag 19 mei 2016
klokke 13.45 uur

door

Charla Chábeli Engels
geboren te Curaçao
in 1986

Promotor Prof. dr. C.J.H. van de Velde

Co-promotor(en) Dr. G.J. Liefers
Dr. P.J.K. Kuppen

Leden promotiecommissie Prof. dr. V.T.H.B.M. Smit
Prof. dr. ir. J. J. M. van der Hoeven, Radboudumc/LUMC
Prof. dr. S.C. Linn, AvL
Dr. C. M. Seynaeve, Erasmus MC

Printing of this thesis was financially supported by:
ChipSoft B.V., Boehringer-Ingelheim B.V., and Greiner Bio-One B.V.

CONTENTS

Chapter 1.	General introduction	7
 Part I. Prognostic biomarkers in breast cancer		
Chapter 2.	The prognostic value of apoptotic and proliferative biomarkers in breast cancer	25
Chapter 3.	Tumor immune subtypes distinguish tumor subclasses with clinical implications in breast cancer patients	49
Chapter 4.	Immunological subtypes in breast cancer are prognostic for invasive ductal but not for invasive lobular breast carcinoma	79
Chapter 5.	The prognostic and predictive value of Tregs and tumor immune subtypes in postmenopausal, hormone receptor positive breast cancer patients treated with adjuvant endocrine therapy: A Dutch TEAM Study Analysis	95
Chapter 6.	The clinical prognostic value of molecular intrinsic tumor subtypes in older breast cancer patients: a FOCUS study analysis	121
 Part II. Predictive biomarkers in breast cancer and targeted treatment		
Chapter 7.	The influence of Insulin-like Growth Factor-1-Receptor expression and endocrine treatment on clinical outcome of postmenopausal hormone receptor positive breast cancer patients: A Dutch TEAM substudy analysis	139
Chapter 8.	The clinical value of HER-2 (<i>ERBB2</i>) overexpression and PIK3CA mutations in the older breast cancer population: A FOCUS Study analysis	157
 Part III. Aging in the breast cancer patient		
Chapter 9.	HIF1 α and its metabolic targets are highly expressed in breast tumors of patients of 65 years or older but not in patients younger than 65 years of age	179
Chapter 10.	HIF1 α and PKM2 are important drivers of age associated clinical functional decline and disease in the elderly breast cancer population: A FOCUS study analysis	199
 Part IV. Precision medicine in the (older) breast cancer patient		
Chapter 11.	How does genome sequencing impact surgery?	235
Chapter 12.	General discussion	261
 Appendices.		
	Nederlandse samenvatting	287
	List of publications	305
	List of co-authors	309
	Curriculum vitae	313
	Dankwoord/Acknowledgements	315

A circular arrangement of DNA sequence data and stick figures. The sequence is composed of four concentric rings of text, starting from the outermost ring and moving inward:

- Outermost ring: ACTGGATAC
- Second ring: CCTTAACTC
- Third ring: GAGCTTCAT
- Innermost ring: ATGAAATT

Interspersed between the sequence rings are numerous stick figures, all oriented in the same direction (right side up). There are approximately 150 stick figures in total.