



Universiteit
Leiden
The Netherlands

PI3K signaling and adherens junctions in invasive lobular breast cancer

Klarenbeek, S.

Citation

Klarenbeek, S. (2021, April 15). *PI3K signaling and adherens junctions in invasive lobular breast cancer*. Retrieved from <https://hdl.handle.net/1887/3154437>

Version: Publisher's Version

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

Downloaded from: <https://hdl.handle.net/1887/3154437>

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

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/3154437> holds various files of this Leiden University dissertation.

Author: Klarenbeek, S.

Title: PI3K signaling and adherens junctions in invasive lobular breast cancer

Issue date: 2021-04-15

CURRICULUM VITAE

Sjoerd Klarenbeek was born in Oss on July 14th in 1977. From 1989 he attended the Murmelliusgymnasium in Alkmaar, where he graduated in 1995. He then studied veterinary medicine at Utrecht University, where extracurricular activities included participation in research and teaching. In 2003 he received his Doctor of Veterinary Medicine degree, with a differentiation in companion animal medicine. After working as a veterinarian in several animal clinics, in 2004 Sjoerd started his training to become a specialist in veterinary pathology at the faculty of veterinary medicine of Utrecht University, and after his training he worked there as a veterinary pathologist for a year. In 2009 he passed the European board examination to become a Diplomate of the European College of Veterinary Pathologists. Sjoerd then started his PhD studies at the Netherlands Cancer Institute (NKI) in Amsterdam in the group of Jos Jonkers, which he increasingly combined with working as an experimental animal pathologist. Nowadays, Sjoerd is an experimental animal pathologist in the NKI.

A

LIST OF PUBLICATIONS

- Multiple low dose therapy as an effective strategy to treat EGFR inhibitor-resistant NSCLC tumours.** Fernandes Neto JM, Nadal E, Bosdriesz E, Ooft SN, Farre L, McLean C, Klarenbeek S, Jurgens A, Hagen H, Wang L, Felip E, Martinez-Marti A, Vidal A, Voest A, Wessels LFA, van Tellingen O, Villanueva A, Bernards R. *Nature Communications*. 2020 Jun 22;11(1):3157.
- Truncated ASPP2 drives initiation and progression of invasive lobular carcinoma via distinct mechanisms.** Schipper K, Drenth AP, van der Burg E, Cornelissen SP, Klarenbeek S, Nethe M, Jonkers J. *Cancer Research*. 2020 Apr 1;80(7):1486.
- Response of metastatic mouse invasive lobular carcinoma to mTOR inhibition is partly mediated by the adaptive immune system.** Klarenbeek S, Doornetal CW, Kas SM, Bonzanni N, Bhin J, Braumuller TM, van der Heijden I, Opdam M, Schouten PC, Kersten K, de Bruijn R, Zingg D, Yemelyanenko J, Wessels LFA, de Visser KE, Jonkers J. *Oncoimmunology*. 2020 Feb 12;9(1):1724049.
- Exogenous ER α expression in the mammary epithelium decreases over time and does not contribute to p53-deficient mammary tumor formation in mice.** Cornelissen LM, Henneman L, Drenth AP, Schut E, de Bruijn R, Klarenbeek S, Zwart W, Jonkers J. *J Mammary Gland Biol Neoplasia*. 2019 Dec;24(4):305-321.
- Conserved crosstalk between histone deacetylation and H3K79 methylation generates DOT1L-dose dependency in HDAC1-deficient thymic lymphoma.** Vlaming H, McLean CM, Korthout T, Alemdehy MF, Hendriks S, Lancini C, Palit S, Klarenbeek S, Kwesi-Maliepaard EM, Molenaar TM, Hoekman L, Schmidlin TT, Altelaar AM, van Wensem T, Dannenberg JH, Jacobs H, van Leeuwen F. *EMBO J*. 2019 Jul 15;38(14):e101564.
- Xenofilter: computational deconvolution of mouse and human reads in tumor xenograft sequence data.** Kluin RJC, Kemper K, Kuilman T, de Ruiter JR, Iyer V, Forment JV, Cornelissen-Steijger P, de Rink I, Ter Brugge P, Song JY, Klarenbeek S, McDermott U, Jonkers J, Velds A, Adams DJ, Peepers DS, Krijgsman O. *BMC Bioinformatics*. 2018 Oct 4;19(1):366.
- Transcriptomics and Transposon Mutagenesis Identify Multiple Mechanisms of Resistance to the FGFR Inhibitor AZD4547.** Kas SM, de Ruiter JR, Schipper K, Schut E, Bombardelli L, Wientjens E, Drenth AP, de Korte-Grimmerink R, Mahakana S, Phillips C, Smith PD, Klarenbeek S, van de Wetering K, Berns A, Wessels LFA, Jonkers J. *Cancer Res*. 2018 Oct 1;78(19):5668-5679.
- BRCA1-associated mammary tumorigenesis is dependent on estrogen rather than progesterone signaling.** van de Ven M, Liu X, van der Burg E, Klarenbeek S, Alexi X, Zwart W, Dijcks F, Bouwman P, Jonkers J. *J Pathol*. 2018 Sep;246(1):41-53.

- Insertional mutagenesis identifies drivers of a novel oncogenic pathway in invasive lobular breast carcinoma.** Kas SM, de Ruiter JR, Schipper K, Annunziato S, Schut E, Klarenbeek S, Drenth AP, van der Burg E, Klijn C, Ten Hoeve JJ, Adams DJ, Koudijs MJ, Wesseling J, Nethe M, Wessels LFA, Jonkers J. *Nat Genet.* 2017 Aug;49(8):1219-1230.
- Prophylactic window therapy with the clinical poly(ADP-ribose) polymerase inhibitor olaparib delays BRCA1-deficient mammary tumour formation in mice.** van de Ven M, van der Burg E, van der Gulden H, Klarenbeek S, Bouwman P, Jonkers J. *J Pathol.* 2017 Mar;241(4):511-521.
- GATA1-Deficient Dendritic Cells Display Impaired CCL21-Dependent Migration toward Lymph Nodes Due to Reduced Levels of Polysialic Acid.** Scheenstra MR, De Cuyper IM, Branco-Madeira F, de Bleser P, Kool M, Meinders M, Hoogenboezem M, Mul E, Wolkers MC, Salerno F, Nota B, Saeys Y, Klarenbeek S, van IJcken WF, Hammad H, Philipsen S, van den Berg TK, Kuijpers TW, Lambrecht BN, Gutiérrez L. *J Immunol.* 2016 Dec 1;197(11):4312-4324.
- p120-Catenin Is Critical for the Development of Invasive Lobular Carcinoma in Mice.** Tenhagen M, Klarenbeek S, Braumuller TM, Hofmann I, van der Groep P, Ter Hoeve N, van der Wall E, Jonkers J, Derkx PW. *J Mammary Gland Biol Neoplasia.* 2016 Dec;21(3-4):81-88.
- PTEN Loss in E-Cadherin-Deficient Mouse Mammary Epithelial Cells Rescues Apoptosis and Results in Development of Classical Invasive Lobular Carcinoma.** Boelens MC, Nethe M, Klarenbeek S, de Ruiter JR, Schut E, Bonzanni N, Zeeman AL, Wientjens E, van der Burg E, Wessels L, van Amerongen R, Jonkers J. *Cell Rep.* 2016 Aug 23;16(8):2087-2101.
- BRCA1185delAG tumors may acquire therapy resistance through expression of RING-less BRCA1.** Drost R, Dhillon KK, van der Gulden H, van der Heijden I, Brandsma I, Cruz C, Chondronasiou D, Castroviejo- Bermejo M, Boon U, Schut E, van der Burg E, Wientjens E, Pieterse M, Klijn C, Klarenbeek S, Loayza-Puch F, Elkon R, van Deemter L, Rottenberg S, van de Ven M, Dekkers DH, Demmers JA, van Gent DC, Agami R, Balmaña J, Serra V, Taniguchi T, Bouwman P, Jonkers J. *J Clin Invest.* 2016 Aug 1;126(8):2903-18.
- Modeling invasive lobular breast carcinoma by CRISPR/Cas9-mediated somatic genome editing of the mammary gland.** Annunziato S, Kas SM, Nethe M, Yücel H, Del Bravo J, Pritchard C, Bin Ali R, van Gerwen B, Siteur B, Drenth AP, Schut E, van de Ven M, Boelens MC, Klarenbeek S, Huijbers IJ, van Miltenburg MH, Jonkers J. *Genes Dev.* 2016 Jun 15;30(12):1470-80.
- Mammary gland-specific ablation of focal adhesion kinase reduces the incidence of p53-mediated mammary tumour formation.** van Miltenburg MH, van Nimwegen MJ, Tijdens I, Lalai R, Kuiper R, Klarenbeek S, Schouten PC, de Vries A, Jonkers J, van de Water B. *Br J Cancer.* 2014 May 27;110(11):2747-55.

- Loss of p120-catenin induces metastatic progression of breast cancer by inducing anoikis resistance and augmenting growth factor receptor signaling.** Schackmann RC, Klarenbeek S, Vlug EJ, Steloo S, van Amersfoort M, Tenhagen M, Braumuller TM, Vermeulen JF, van der Groep P, Peeters T, van der Wall E, van Diest PJ, Jonkers J, Derkzen PW. *Cancer Res.* 2013 Aug 1;73(15):4937-49.
- Genetically engineered mouse models of PI3K signaling in breast cancer.** Klarenbeek S, van Miltenburg MH, Jonkers J. *Mol Oncol.* 2013 Apr;7(2):146-64.
- A preclinical mouse model of invasive lobular breast cancer metastasis.** Doornenbal CW, Klarenbeek S, Braumuller TM, Klijn CN, Ciampicotti M, Hau CS, Hollmann MW, Jonkers J, de Visser KE. *Cancer Res.* 2013 Jan 1;73(1):353-63.
- BRCA1 RING function is essential for tumor suppression but dispensable for therapy resistance.** Drost R, Bouwman P, Rottenberg S, Boon U, Schut E, Klarenbeek S, Klijn C, van der Heijden I, van der Gulden H, Wientjens E, Pieterse M, Catteau A, Green P, Solomon E, Morris JR, Jonkers J. *Cancer Cell.* 2011 Dec 13;20(6):797-809.
- Cross-species comparison of aCGH data from mouse and human BRCA1- and BRCA2-mutated breast cancers.** Holstege H, van Beers E, Velds A, Liu X, Joosse SA, Klarenbeek S, Schut E, Kerkhoven R, Klijn CN, Wessels LF, Nederlof PM, Jonkers J. *BMC Cancer.* 2010 Aug 24;10:455.
- Expression of receptors for luteinizing hormone, gastric-inhibitory polypeptide, and vasopressin in normal adrenal glands and cortisol-secreting adrenocortical tumors in dogs.** Galac S, Kars VJ, Klarenbeek S, Teerds KJ, Mol JA, Kooistra HS. *Domest Anim Endocrinol.* 2010 Jul;39(1):63-75.
- Somatic structural rearrangements in genetically engineered mouse mammary tumors.** Varela I, Klijn C, Stephens PJ, Mudie LJ, Stebbings L, Galappaththige D, van der Gulden H, Schut E, Klarenbeek S, Campbell PJ, Wessels LF, Stratton MR, Jonkers J, Futreal PA, Adams DJ. *Genome Biol.* 2010;11(10):R100.
- Effect of growth-promoting 17beta-estradiol, 19-nortestosterone and dexamethasone on circulating levels of nine potential biomarker candidates in veal calves.** Cacciatore G, Eisenberg SW, Situ C, Mooney MH, Delahaut P, Klarenbeek S, Huet AC, Bergwerff AA, Elliott CT. *Anal Chim Acta.* 2009 Apr 1;637(1-2):351-9.
- Influence of 17beta-oestradiol, nortestosterone and dexamethasone on the adaptive immune response in veal calves.** Eisenberg SW, Cacciatore G, Klarenbeek S, Bergwerff AA, Koets AP. *Res Vet Sci.* 2008 Apr;84(2):199-205.
- Canine X-linked muscular dystrophy in a family of Grand Basset Griffon Vendéen dogs.** Klarenbeek S, Gerritzen-Bruning MJ, Rozemuller AJM, van der Lugt JJ. *J Comp Pathol.* 2007 Nov;137(4):249-252.
- A dog with alveolar echinococcosis: the larval stage of the fox tapeworm.** van Riel A, Sjollema B, Klarenbeek S, van der Giessen J. *Tijdschr Diergeneeskdt.* 2007 Nov 1;132(21):828-31.
- Reducing chloride conductance prevents hyperkalaemia-induced loss of twitch force in rat slow-twitch muscle.** van Emst MG, Klarenbeek S, Schot A, Plomp JJ, Doornenbal A, Everts ME. *J Physiol.* 2004 Nov 15;561(Pt 1):169-81.

ACKNOWLEDGEMENTS

This thesis represents the work of many. I am deeply grateful to all who contributed and supported me during the years invested in this work. You made it possible for me to grow and learn.

Jos, I thank you for your guidance and trust, for creating a great working environment with a fantastic group of people, for more opportunities than I could have wished for, for your patience, and for sharing your knowledge, your vision and your optimism with me.

Karin, you have shown me and many others how important immunology is for oncology. For me you were an excellent and supportive mentor and you and your group contributed so much to our work.

Patrick, I am grateful for the opportunity to build on the foundations that you layed as a pioneer and expert in the field of genetically engineered mouse models of ILC. You and the colleagues in your group have generously shared your efforts with us.

Tanya and Eva, you have done a tremendous amount of work and taught me so much in the wet lab and in the animal facility. Thank you so much.

Chris, you have truly been a great colleague to work with. Our experiments benefited so much from your well-structured preparation and working mentality.

Bjørn en Tania, I will never forget how you helped me with the mouse work, always interested and happy to help with treatments and imaging. Thank you.

Every colleague, roommate and co-author, and everyone at the research facilities: there are many of you, I thank you all for your contributions, your help, questions, suggestions, company, friendship, and sharing your work and insights with me.

All my friends: it has been very important for me to have a social life and spend time with you, whether it's playing tennis, making music, going on trips, or just spending time together. You make life better.

Joyce, Karel and Anne, and all of my family: you gave me all the love, support, freedom and trust I needed. I am so lucky.

Wendy, thank you for being by my side through it all, understanding and loving and supporting me. I am very thankful that you are in my life.

