BIOGRAPHICAL SKETCH

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NAME: Drost, Jarno

POSITION TITLE: Principal Investigator

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	END DATE	FIELD OF STUDY
Free University, Amsterdam	MS	08/2005	Biomedical Sciences
The Netherlands Cancer Institute, Amsterdam	Graduate Student	03/2012	Molecular Biology, Biotechnology, Cancer Biology
The Netherlands Cancer Institute, Amsterdam	Postdoctoral Fellow	08/2012	Molecular Biology, Biotechnology, Cancer Biology
Hubrecht Institute, Utrecht	Postdoctoral Fellow	10/2016	Cancer & Stem Cell Biology, Molecular Biology, Biotechnology

A. Personal Statement

After getting his M.Sc. degree (*with honors*), Jarno started my Ph.D. in the lab of Prof. Agami at the Netherlands Cancer Institute (Amsterdam, the Netherlands). He studied the genetic alterations that are required for the transformation of human primary cells into cancer cells (Drost & Mantovani et al., Nature Cell Biology 2010), as well as the role of non-coding RNAs and post-transcriptional gene regulation in cancer (amongst others Melo & Drost et al., Molecular Cell 2012; Elkon, Drost & van Haaften et al., Genome Biology 2012).

To pursue his interest in cancer and stem cell biology, he undertook postdoctoral training in the lab of Prof. Clevers at the Hubrecht Institute (Utrecht, the Netherlands). Here, he exploited intestinal stem cells, which can be expanded in a culture dish as “organoids”, to study multistep tumorigenesis. He was the first in the world to combine organoid and CRISPR/Cas9 technology for cancer research and established colorectal cancer (CRC) progression models (Drost et al., Nature 2015). He used these models to, amongst others, dissect the genetic alterations that are required for tumor cell migration and metastasis (Fumagalli & Drost et al., PNAS 2017) and to study mutational signatures in cancer (Drost & Van Boxtel, Science 2017). Moreover, he established organoid cultures from primary and cancerous prostate tissue (Karthaus et al., Cell 2014; Drost et al., Nature Protocols 2016). His postdoctoral work was awarded a prestigious NWO Veni career grant and the Dr. Patrick Hanlo Award for best postdoctoral researcher of the Hubrecht Institute.

In November 2016, he started his independent research group at the Princess Máxima Center for Pediatric Oncology. His group aims to unravel the molecular and cellular mechanisms underpinning childhood solid tumors with the purpose of identifying new therapeutic opportunities. His group develops and exploits novel preclinical model systems. As such, they were the first in the world to apply organoid technology to pediatric tumors (Schutgens et al., Nature Biotechnology 2019; Calandrini et al., Nature Communications 2020; Meister et al., EMBO Molecular Medicine 2022). In 6 years, they have established organoids from >200 patient-derived tumor tissues (>25 MRT and AT/RT), for which preclinical models were so far scarce. Using pediatric cancer organoid models, patient material, and cutting-edge genomics and single-cell transcriptomics technologies, they revealed the cellular identity of different childhood solid tumors (Custers et al., Nature Communications 2021; Young et al., Nature Communications 2021). The approaches described in these papers are broadly applicable to childhood cancers. Jarno has received several awards such as the Young Investigator Award from the Dutch Cancer Society, the prestigious ERC Starting and NWO-Vidi grants, the Dutch cancer institute “Oncode” membership, and the AACR St. Baldrick’s career development award for emerging leaders in the field of pediatric oncology.

B. Positions and Honors

Positions and Employment

2019 - Principal Investigator, Oncode Institute, Utrecht
2016 - Principal Investigator, Princess Maxima Center for Pediatric Oncology, Utrecht

Other Experience and Professional Memberships

2022 - Member of the Advisory board of The Wilms Cancer Foundation
2021 - Member, (Innovative Therapies for Children with Cancer in Europe) Solid Tumor Committee
2019 - Member, SIOPE brain tumor (BT) ATRT working group
2019 - Advisory Board, Review Commons
2018 - 2021 Member, ITCC Biology group

Honors

Fellowships, awarded grants and prizes

2012 Graduation with honors M.Sc. degree, Free University, Amsterdam (the Netherlands)
2014 NWO Veni Grant - National grant for talented post-doctoral researchers, the Netherlands Organisation for Scientific Research
2016 Young Investigator Grant/Bas Mulder Award - Prestigious award for talented young researchers, Dutch Cancer Society (KWF)
2017 Dr. Patrick Hanlo Award - Award for best post-doctoral researcher of the Hubrecht Institute, Hubrecht Institute
2017 Foundation Children Cancerfree (KiKa) Research Grant, KiKa
2018 Foundation Children Cancerfree (KiKa) Research Grant, KiKa
2019 Elected to become a member of Oncode Institute, Oncode Institute
2019 Foundation Children Cancerfree (KiKa) Pilot Grant, KiKa
2019 European Research Council (ERC) Starting Grant, ERC
2020 American Association for Cancer Reserach (AACR) St. Baldrick's career development award.
2021 NWO Vidi Grant – National grant for experienced researchers, the Netherlands Organisation for Scientific Research

Relevant invited and plenary talks

2015 Invited Speaker: Symposium Berlin Institute for Medical Systems Biology, Max Delbrück Center for Molecular Medicine, Berlin (Germany)
2015 Selected Speaker: EMBO|EMBL Symposium "Frontiers in Stem Cells and Cancer", Heidelberg (Germany)
2016 Invited Speaker: Young scientist meeting "Host-Microbial Interactions and Mucosal Immunity", Bern (Switzerland)
2016 Invited Speaker: "Cancer and Cancer Stem Cells" , Karolinska Institutet, Stockholm (Sweden)
2017 Invited Speaker: National Cancer Research Institute (NCRI) Cancer Conference, Liverpool (UK)
2018 Invited Speaker: IRI Life Sciences Colloquium series "Organoids - Life in 3D", Humboldt University, Berlin (Germany)
2018 Selected Speaker: International Rhabdoid Tumor Meeting, Lake Louise (Canada)
2018 Invited Speaker: ITCC-P4 International Workshop "Improving pediatric oncology drug development through preclinical research", ITCC-P4, Amsterdam (the Netherlands)
2018 Invited Speaker: International seminar at PhD program in Molecular Biomedicine, University of Trieste, Trieste (Italy)
2018 Invited Speaker: 2nd Precision Cancer Medicine (PreCanMed) project meeting and workshop, Udine (Italy)
2018 Invited Speaker: SIOP-RTSG (Renal Tumor Study Group) Committee meeting, Copenhagen (Denmark)

2019 Invited Speaker: Comprehensive Cancer Center Developmental Biology and Solid Tumor Program, St. Jude Children's Research Hospital, Memphis (USA)
2019 Invited Speaker: American Association for Cancer Research (AACR) Advances in Pediatric Cancer Research, Montreal (Canada)
2019 Invited speaker: SIOP international conference St. Baldrick's foundation symposium "Development and Use of Pediatric Cancer Models", Lyon (France)
2019 Invited speaker: German Cancer Consortium (DKTK) mini-retreat "Molecularly Targeted Therapy", Frankfurt (Germany).
2019 Invited speaker: Oncode - CGC annual conference "Fundamental Cancer Biology", Amsterdam (the Netherlands).
2020 Invited Speaker: International seminar at Institut Curie, Paris (France).
2020 Invited Speaker (virtual): International seminar at University of Ghent, Ghent (Belgium).
2021 Invited Speaker (virtual): Wellcome Genome Campus Advanced Courses and Scientific Conferences "Organoids: Advances and Applications", Hinxton (UK).
2021 Invited Speaker (virtual): French Society of Immunotherapy, Paris (France).
2021 Invited Speaker (virtual): SIOP-RTSG Annual meeting.
2022 Invited Speaker (virtual): International seminar at the Cancer Research Center of Lyon, Lyon (France).
2023 Invited Speaker: Neurobiology and Brain Tumor Cancer Center Program seminar series at St. Jude Children's Research Hospital, Memphis (US)

C. Contribution to Science

1. Untangling tumor suppressor networks

My Ph.D. research focussed on identifying novel coding and non-coding genetic elements that contribute to tumorigenesis. Using genome-wide loss of function screens, I identified bromodomain-containing 7 (BRD7) as a new tumor suppressor gene and demonstrated that it serves as a P53 transcriptional co-factor which expression is deregulated in cancer. I also discovered that P53 exerts part of its tumor-suppressive functions by regulating transcription through binding to enhancer elements. These are all seminal findings, highly relevant for cancer research.

a. Melo CA*, Drost J*, Wijchers PJ, van de Werken H, de Wit E, Oude Vrielink JA, Elkon R, Melo SA, Léveillé N, Kalluri R, de Laat W, Agami R. eRNAs are required for p53-dependent enhancer activity and gene transcription. Mol Cell. 2013 Feb 7;49(3):524-35. PubMed PMID: 23273978.
b. Elkon R*, Drost J*, van Haaften G*, Jenal M, Schrier M, Oude Vrielink JA, Agami R. E2F mediates enhanced alternative polyadenylation in proliferation. Genome Biol. 2012 Jul 2;13(7):R59. PubMed Central PMCID: PMC3491381.
c. Drost J*, Mantovani F*, Tocco F, Elkon R, Comel A, Holstege H, Kerkhoven R, Jonkers J, Voorhoeve PM, Agami R, Del Sal G. BRD7 is a candidate tumour suppressor gene required for p53 function. Nat Cell Biol. 2010 Apr;12(4):380-9. PubMed PMID: 20228809.
d. Drost J, Agami R. Transformation locked in a loop. Cell. 2009 Nov 13;139(4):654-6. PubMed PMID: 19914159.

2. Study multistep tumorigenesis using organoid and gene editing technologies

As a postdoctoral fellow, my research mainly focused on the use of three-dimensional stem cell cultures (so-called "organoids") for prostate and colorectal cancer research. I was the world's first scientist to combine CRISPR-gene editing with organoid technology for cancer research. I generated unique tumor progression models by introducing combinations of mutations in colon organoids and used these to study the processes underlying tumor initiation and progression. These findings are of wide-spread interest and the general approach has now been adopted across many other medical research fields.

a. Drost J, Clevers H. Organoids in cancer research. Nat Rev Cancer. 2018 Jul;18(7):407-418. PubMed PMID: 29692415.

b. Drost J*, van Boxtel R*, Blokzijl F, Mizutani T, Sasaki N, Sasselli V, de Ligt J, Behjati S, Grolleman JE, van Wezel T, Nik-Zainal S, Kuiper RP, Cuppen E, Clevers H. Use of CRISPR-modified human stem cell organoids to study the origin of mutational signatures in cancer. Science. 2017 Oct 13;358(6360):234-238. PubMed Central PMCID: PMC6038908.

c. Fumagalli A*, Drost J*, Suijkerbuijk SJ, van Boxtel R, de Ligt J, Offerhaus GJ, Begthel H, Beerling E, Tan EH, Sansom OJ, Cuppen E, Clevers H, van Rheenen J. Genetic dissection of colorectal cancer progression by orthotopic transplantation of engineered cancer organoids. Proc Natl Acad Sci U S A. 2017 Mar 21;114(12):E2357-E2364. PubMed Central PMCID: PMC5373343.

d. Drost J, van Jaarsveld RH, Ponsioen B, Zimberlin C, van Boxtel R, Buijs A, Sachs N, Overmeer RM, Offerhaus GJ, Begthel H, Korving J, van de Wetering M, Schwank G, Logtenberg M, Cuppen E, Snippert HJ, Medema JP, Kops GJ, Clevers H. Sequential cancer mutations in cultured human intestinal stem cells. Nature. 2015 May 7;521(7550):43-7. PubMed PMID: 25924068.

3. Molecular dissection of childhood solid tumors

In November 2016, I was appointed group leader at the Princess Máxima Center for Pediatric Oncology. My group aims to unravel the molecular and cellular mechanisms underpinning childhood solid tumors to identify new therapeutic opportunities. By combining our unique organoid models, cutting-edge genomics and single-cell transcriptomics technologies, my lab revealed the cellular identity of different renal tumors and malignant rhabdoid tumors. Moreover, we established several research lines to study clonal dynamics during tumor progression and therapy resistance using orthotopic xenograft models and intravital imaging approaches.

a. Custers L, Khabirova E, Coorens THH, Oliver TRW, Calandrini C, Young MD, Vieira Braga FA, Ellis P, Mamanova L, Segers H, Maat A, Kool M, Hoving EW, van den Heuvel-Eibrink MM, Nicholson J, Straathof K, Hook L, de Krijger RR, Trayers C, Allinson K, Behjati S#, Drost J#. Somatic mutations and single-cell transcriptomes reveal the root of malignant rhabdoid tumours. Nat Commun. 2021 Mar 3;12(1):1407.

b. Meister, M.T., Groot Koerkamp, M.J.A., de Souza, T., Breunis, W.B., Frazer-Mendelewska, E., Brok, M., DeMartino, J., Manders, F., Calandrini, C., Kerstens, H.H.D., Janse, A., Dolman, M.E.M., Eising, S., Langenberg, K.P.S., van Tuil, M., Knops, R.R.G., van Scheltinga, S.T., Hiemcke-Jiwa, L.S., Flucke, U., Merks, J.H.M., van Noesel, M.M., Tops, B.B.J., Hehir-Kwa, J.Y., Kemmeren, P., Molenaar, J.J., van de Wetering, M., van Boxtel, R., Drost, J.#, Holstege, F.C.P#. Mesenchymal tumor organoid models recapitulate rhabdomyosarcoma subtypes. EMBO Mol Med. 2022 Aug 2; e16001.

c. Young, M.D.*, Mitchell, T.J.*, Custers, L.*, Margaritis, T., Morales-Rodriguez, F., Kwakwa, K., Khabirova, E., Kildisiute, G., Oliver, T.R.W., de Krijger, R.R., van den Heuvel-Eibrink, M.M., Comitani, F., Piapi, A., Bugallo-Blanco, E., Thevanesan, C., Burke, C., Prigmore, E., Ambridge, K., Roberts, K., Vieira Braga, F.A., Coorens, T.H.H., Del Valle, I., Wilbrey-Clark, A., Mamanova, L., Stewart, G.D., Gnanapragasam, V.J., Rampling, D., Sebire, N., Coleman, N., Hook, L., Warren, A., Haniffa, M., Kool, M., Pfister, S.M., Achermann, J.C., He, X., Barker, R.A., Shlien, A., Bayraktar, O.A, Teichmann, S., Holstege, F.C., Meyer, K.B., Drost, J.#, Straathof, K.#, Behjati, S.#. Single cell derived mRNA signals across human kidney tumors. Nat Commun. 2021 Jun 23; 12(1):3896.

d. Calandrini C, Schutgens F, Oka R, Margaritis T, Candelli T, Mathijsen L, Ammerlaan C, van Ineveld RL, Derakhshan S, de Haan S, Dolman E, Lijnzaad P, Custers L, Begthel H, Kerstens HHD, Visser LL, Rookmaaker M, Verhaar M, Tytgat GAM, Kemmeren P, de Krijger RR, Al-Saadi R, Pritchard-Jones K, Kool M, Rios AC, van den Heuvel-Eibrink MM, Molenaar JJ, van Boxtel R, Holstege FCP, Clevers H, Drost J#. An organoid biobank for childhood kidney cancers that captures disease and tissue heterogeneity. Nat Commun. 2020 Mar 11;11(1):1310. PubMed Central PMCID: PMC7066173.

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