Name	PETER VAN LOO
Position	Group Leader (2nd 6)
Year joined *(Crick or founder institute)*	2014

Career History

2008 - PhD in Medical Sciences, University of Leuven, Leuven, Belgium (main supervisor: Prof. Dr. Peter Marynen)
2008 -Postdoctoral researcher, Department of Genetics, Institute for Cancer Research, University of Oslo, Norway (Prof. Dr. Anne-Lise Børresen-Dale and Prof. Dr. Vessela Kristensen)
2008 – 2010 - Postdoctoral researcher, Human Genome Laboratory, Department of Human Genetics, VIB and University of Leuven, Belgium (Prof. Dr. Peter Marynen) and Bioinformatics group, Department of Electrotechnical Engineering, University of Leuven, Leuven, Belgium (Prof. Dr. Yves Moreau)
2010 – 2014 - Postdoctoral researcher, Cancer Genome Project, Wellcome Trust Sanger Institute, Hinxton Cambridge, UK (Dr. Peter Campbell and Prof. Dr. Michael Stratton)

Major Awards, Honours and Prizes

VIB Alumni Award, 2017
Cancer Research UK Future Leaders in Cancer Research Prize, 2015

Membership of external committees, editorial boards, review panels, SABs etc

International Cancer Genome Consortium (ICGC): co-leading working group on Evolution and Heterogeneity (70 researchers across ~20 institutions) of the Pan-Cancer Analysis of Whole Genomes (PCAWG) initiative (2014-present)
Co-organiser of DREAM challenge on tumour heterogeneity (2015-present)
Sarcoma GeCIP 100,000 Genomes Project: Genomics Lead (2018-present)
Co-organizer of Systems Genetics of Cancer conference 2015-2020
Panel member (BIO2) of Research Council of Biosciences and Environment (RCBE) of the Academy of Finland, 2016
Editorial board member NAR Cancer (2019-present)
Committee member Newton Prize 2020

Lab Name	***Cancer Genomics Laboratory***

Research programme and achievements

My lab focuses on the big question “How do tumours evolve?”. The cancer genome contains within it an archaeological record of its past. We have pioneered “molecular archaeology of cancer” methods to infer a cancer’s life history from sequencing data. Using these approaches, we have shown that multifocal prostate cancers develop as multiple independent tumours in the same individual, we have elucidated the patterns of metastatic spread in prostate cancer, providing clear evidence for polyclonal seeding of metastases, and we have traced the origin of disseminated tumour cells in bone marrow of breast cancer patients to specific tumour subclones. My group has also contributed to multiple other studies into intra-tumour heterogeneity and tumour evolution. In addition, we have been an important voice in the scientific debate on approaches to discriminate neutral evolutionary dynamics from subclonal selection. Finally, to gain insight into the strengths and weaknesses of subclonal reconstruction approaches, we developed benchmarking approaches and co-organised a cloud-based DREAM challenge to evaluate subclonal reconstruction algorithms.

Reasoning that a pan-cancer approach to study intra-tumour heterogeneity and the evolutionary history of cancer would give profound insights into tumour biology and evolution, we recently applied molecular archaeology of cancer approaches to whole-genome sequences of 2,658 tumours across 38 cancer types, as part of the ICGC Pan-Cancer Analysis of Whole Genomes (PCAWG) initiative. Our analyses allowed us to sketch out the typical evolutionary trajectories of cancer, and map them in real time relative to the point of diagnosis. We found that driver mutations often precede diagnosis by many years, and in some cases decades, providing a window of opportunity for early cancer detection. In addition, assessing subclonal evolution across the PCAWG series, we found pervasive intra-tumour heterogeneity and distinctive subclonal patterns of somatic changes across cancer types. Finally, we performed a pan-cancer survey of the landscape and timing of known punctuated mutational processes in cancer and observed that chromothripsis and chromoplexy are frequent, critically early driver events in oncogenesis.

Our present work focuses on molecular archaeology of cancer methods to gain insight into the evolutionary history of cancer, from early cancer development through metastasis. We continue to perform large-scale pan-cancer analyses on data from large-scale consortia, and we generate our own bulk and single-cell sequencing data to gain further insight into tumour evolution. In addition, we are developing new molecular archaeology of cancer methods to enable conceptually novel analyses. Our work can be structured into three key lines of research:

1. Inferring the evolutionary history and subclonal architecture of cancers from their genomes, (i) in a large-scale pan-cancer setting, focusing on the evolutionary history of cancer metastases, and (ii) combining bulk sequencing and single cell sequencing, characterising intra-tumour heterogeneity and tumour evolution in minute detail.
2. Development and large-scale application of novel approaches to study intra-tumour heterogeneity and tumour evolution from other -omics layers, such as RNA sequencing and bisulphite sequencing.
3. Analysing cancer genes and mutational processes in cancer, with a focus on identifying novel rare cancer genes, and on identifying, characterising and timing mutational processes causing copy number changes and complex structural variants in cancer evolution.

Research outputs

Gerstung, M.[#], Jolly, C.[#], Leshchiner, I.[#], Dentro, S.C.[#], Gonzalez, S.[#], Rosebrock, D., Mitchell, T.J., Rubanova, Y., Anur, P., Yu, K., Tarabichi, M., Deshwar, A., Wintersinger, J., Kleinheinz, K., Vázquez-García, I., Haase, K., Jerman, L., Sengupta, S., Macintyre, G., Malikic, S., Donmez, N., Livitz, D.G., Cmero, M., Demeulemeester, J., Schumacher, S., Fan, Y., Yao, X., Lee, J., Schlesner, M., Boutros, P.C., Bowtell, D.D., Zhu, H., Getz, G., Imielinski, M., Beroukhim, R., Sahinalp, S.C., Ji, Y., Peifer, M., Markowetz, F., Mustonen, V., Yuan, K., Wang, W., Morris, Q.D., PCAWG Evolution and Heterogeneity Working Group, Spellman, P.T.[#], Wedge, D.C.[#], Van Loo, P.[#]; PCAWG Consortium (#: equal contribution) (2020). *The evolutionary history of 2,658 cancers*. Nature 578:122-128. DOI: 10.1038/s41586-019-1907-7
This study leverages molecular archaeology of cancer approaches in a large-scale pan-cancer setting to construct timelines of tumour evolution, showing when in a tumour's evolutionary history key events typically happen. It demonstrates that tumours typically develop over multiple years to sometimes decades, highlighting opportunities for early detection.

ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium (2020). *Pan-cancer analysis of whole genomes*. Nature 578:82-93. DOI: 10.1038/s41586-020-1969-6
This is the marker paper of the Pan-Cancer Analysis of Whole Genomes consortium, describing the unique dataset and strategy for variant calling, as well as several scientific vignettes as part of its analysis. My group contributed a vignette on the landscape and timing of punctuated mutational processes, resulting in two main sections and two main figures in the paper. Our work shows that punctuated mutational processes are widespread in cancers, and that chromothripsis and chromoplexy are frequently key early driver events in tumour evolution, while kataegis is predominantly a late subclonal process.

Salcedo, A.[#], Tarabichi, M.[#], Espiritu, S.M.G.[#], Deshwar, A.G.[#], David, M., Wilson, N.M., Dentro, S., Wintersinger, J.A., Liu, L.Y., Ko, M., Sivanandan, S., Zhang, H., Zhu, K., Ou Yang, T.H., Chilton, J.M., Buchanan, A., Lalansingh, C.M., P'ng, C., Anghel, C.V., Umar, I., Lo, B., Zou, W., DREAM SMC-Het Participants, Simpson, J.T., Stuart, J.M., Anastassiou, D., Guan, Y., Ewing, A.D., Ellrott, K.[#], Wedge, D.C.[#], Morris, Q.D.[#], Van Loo, P.[#], Boutros, P.C.[#] (#: equal contribution) (2020). *A community effort to create standards for evaluating tumor subclonal reconstruction*. Nature Biotechnology 38:97-107. DOI: 10.1038/s41587-019-0364-z
This study aims to develop approaches as community standards to benchmark tumour subclonal reconstruction methods, including a scoring framework and a detailed simulator. These methods were used to set up a community-based DREAM challenge to evaluate existing subclonal reconstruction methods.

Tarabichi, M., Martincorena, I., Gerstung, M., Leroi, A.M., Markowetz, F., PCAWG Evolution and Heterogeneity Working Group, Spellman, P.T., Morris, Q.D., Lingjærde, O.C., Wedge, D.C., Van Loo, P. (2018). *Neutral tumor evolution?* Nature Genetics 50:1630-1633. Correspondence. DOI: 10.1038/s41588-018-0258-x
This correspondence highlights key shortcomings in a recent paper claiming that 30% of tumours show neutral evolutionary dynamics. It has played a key role in the scientific debate on neutral evolutionary dynamics versus subclonal selection in tumour evolution.

Demeulemeester, J.[#], Kumar, P.[#], Møller, E.K.[#], Nord, S., Wedge, D.C., Peterson, A., Mathiesen, R.R., Fjelldal, R., Zamani Esteki, M., Theunis, K., Fernandez Gallardo, E.,

Grundstad, A.J., Borgen, E., Baumbusch, L.O., Børresen-Dale, A.L., White, K.P.[#], Kristensen, V.N.[#], Van Loo, P.[#], Voet, T.[#], Naume, B.[#] (#: equal contribution) (2016). ***Tracing the origin of disseminated tumor cells in breast cancer using single-cell sequencing*****. Genome Biology 17:250. DOI: 10.1186/s13059-016-1109-7**

This paper shows that disseminated tumour cells in breast cancer disseminate late, either from the fully formed primary tumour, subclones in the primary tumour, or subclones in a lymph node metastasis that in turn originated from a subclone in the primary tumour. It also demonstrates the existence of a cell population with aberrations that does not originate from the tumour, which has previously been misinterpreted as a population of early disseminating tumour cells.