

Biographical Sketch Prof. Dr. med. Dr. rer. nat. Guy Ungerechts

Personal Statement

I am a medical oncologist and molecular biologist trained in the field of oncolytic viruses / immunotherapy at Mayo Clinic, Rochester, USA and at the Ottawa Hospital Research Institute (OHRI), Ottawa, Canada. My clinical focus is GI oncology with particular interests in translational medicine and early clinical trials of immuno(viro)therapy. I am heading the *Early Clinical Trial Team* at the National Center for Tumor Diseases (NCT) Heidelberg. Furthermore, within the German network of NCT Clinical Trial Centers (CTCs), I am co-responsible for the local Heidelberg NCT CTC. I have been deeply involved (mostly as principal investigator and coordinating physician) in the development and conduction of 14 phase I/II and III trials with different oncolytic viruses. As principal investigator, I am responsible for the very first adoptive cell transfer in the framework of a CAR T phase I clinical trial for solid tumors (BNT 211) currently conducted in Heidelberg. My research group recently demonstrated for the first time that oncolytic measles virus can be armed with immunomodulatory transgenes encoding for cytokines (e.g. IL-12), immune checkpoint blockade antibodies and bispecific T cell engager (BiTEs) for enhanced immunovirotherapy. We founded the spin-off company *CanVirex* to finance GMP compliant production of the lead candidate for clinical translation (MeV-IL-12). The *Clinical Cooperation Unit (CCU) Virotherapy* at DKFZ has allowed to strengthen and extend my research activities toward innovative oncolytic viral vectors and (combination) immunotherapies and to implement a dedicated program for their forward and reverse translation. Recently, we got regulatory clearance to release MeV-IL12 for clinical application in the framework of an *Early Clinical Access Program*. MeV-IL-12 treatment of the very first patient was initiated on February 8, 2024. With no doubt, this has been the most exciting day in my whole professional life. My ultimate goal is to generate and enable campus-developed immunotherapeutics including oncolytic viruses and cellular therapeutics for cancer immunotherapy.

Key Words

Cancer immunotherapy, oncolytic viruses, adoptive cell transfer (CAR T, TCR, TIL), clinical translation, early clinical trials, ECTU, NCT CTC, translational research, IL-12, BiTEs, checkpoint inhibition, combination therapies

Education/Degrees

Adjunct Professor at University of Ottawa, ON, Canada	since 2017
Assistant Professor ("apl.") at Ruprecht-Karls-University Heidelberg	since 2015
Board Certification in Internal Medicine and Hematology and Oncology	2013
<i>Venia legendi</i> in Molecular Oncology, Ruprecht-Karls-University Heidelberg	2012
MD Medicine, Eberhard-Karls-University Tübingen (<i>summa cum laude</i>)	2005
PhD Virology, Eberhard-Karls-University Tübingen (<i>summa cum laude</i>)	2003
M.Sc. Molecular Biology, Johannes Gutenberg-University Mainz	1999

Major previous and current Appointments

Co-speaker for NCT Heidelberg in the Network of NCT Clinical Trial Centers (CTCs)	since 2023
Head, Early Clinical Trial Team, NCT/UKHD/DKFZ Heidelberg, Germany	since 2023
Head, Clinical Cooperation Unit 'Virotherapy' D490, DKFZ Heidelberg, Germany	since 2019
Deputy Director, Dept. of Medical Oncology, NCT/UKHD Heidelberg, Germany	since 2017
PI/Research Group leader at the Ottawa Hospital Research Institute, Canada	2015-2020
Attending Physician, Dept. of Medical Oncology, The Ottawa Hospital, Ottawa, ON, Canada	2015-2017
Head, Max-Eder Junior Research Group Program, German Cancer Aid at NCT Heidelberg	2009-2015
Attending Physician, Dept. of Medical Oncology, NCT/UKHD Heidelberg,	2013-2015
Residency, Heidelberg University Hospital, Heidelberg, Germany	2008-2013
Postdoctoral researcher, Mayo Clinic (Roberto Cattaneo Lab), Rochester, MN, USA	2005-2007
PhD Student and Postdoctoral researcher, University of Tuebingen, Germany	1999-2005

Selected Activities in the Scientific Community

- Member of Scientific Advisory Board at Riddell Centre for Cancer Immunotherapy/Calgary
- European Medicines Agency (EMA) Scientific Advisory Group Oncology (invited expert)
- Reviewer for the Canadian Cancer Society (CCS)
- Member of the Canadian BioCanRx Research Management Committee
- Reviewer for the Canadian Institutes of Health Research (CIHR)
- Nomination for the ZKBS (Central Committee on Biological Safety)
- Frequent reviewer for the German Cancer Aid (DKH) and the German Research Foundation (DFG)

Selected Honors and Awards

- Terry Fox New Investigator Award, 2016
- Ontario Institute for Cancer Research (OICR) Investigator Award, 2015
- Carl-Liebermeister Award, Eberhard-Karls University Tuebingen, 2003

Five selected peer-reviewed Key Publications in the Career

1. Appleton E, Chiocca A, **Ungerechts G**, Melcher A, Vile R. Oncolytic Viruses: Beacons of Hope for Immuno-oncology or A Case of The Emperor's New Clothes? **Lancet** 406(09):1295-1312 (2025).

Invited review article about immunovirotherapy for cancer

2. Walle T, Bajaj S, Kraske JA, Rösner T, Cussigh CS, Kälber KA, Müller LJ, Boyoung Strobel S, Burghaus J, Kallenberger S, Stein-Thöringer C, Jenzer M, Schubert A, Kahle S, Williams A, Hoyler B, Zielske L, Skatula R, Sawall S, Leber MF, Kunes RZ, Krisam J, Fremd C, Schneeweiss A, Krauss J, Apostolidis L, Berger AK, Haag GM, Zschäbitz S, Halama N, Springfield C, Kirsten R, Hassel JC, Jäger D, NCT ANTICIPATE Investigators, **Ungerechts G**. Cytokine release syndrome-like serum responses after COVID-19 vaccination are frequent and clinically inapparent under cancer immunotherapy. **Nature Cancer** 3(9):1039-1051 (2022).

In this prospective cohort study, we revealed that cytokines are commonly induced after COVID-19 vaccination of immune checkpoint inhibitor (ICI)-treated cancer patients. However, there is no association between cytokine induction by vaccination and cytokine release syndrome-related symptoms or other adverse events. Overall, this reverse translational study supports COVID-19 vaccination in patients with cancer under ICI therapy.

3. Hajda J, Leuchs B, Angelova AL, Frehtman V, Rommelaere J, Mertens M, Pilz M, Kieser M, Krebs O, Dahm M, Huber B, Engeland CE, Mavratzas A, Hohmann N, Schreiber J, Jäger D, Halama N, Sedlacek O, Gaida MM, Daniel V, Springfield C, **Ungerechts G**. Phase 2 Trial of Oncolytic H-1 Parvovirus Therapy Shows Safety and Signs of Immune System Activation in Patients With Metastatic Pancreatic Ductal Adenocarcinoma. **Clin Cancer Res** 27(20):5546-5556 (2021).

This paper reports results of the ParvOryx02 virotherapy phase II trial that I have been coordinating. Clinical responses were associated with immunological signatures.

4. Speck T, Heidbuechel JPW, Veinalde R, Jaeger D, von Kalle C, Ball CR, **Ungerechts G**, Engeland CE. Targeted BiTE Expression by an Oncolytic Vector Augments Therapeutic Efficacy Against Solid Tumors. **Clin Cancer Res** 24(9):2128-2137 (2018).

In this study, my team developed oncolytic measles viruses encoding bispecific T cell engagers (BiTEs) and demonstrated their therapeutic potency.

5. Engeland CE, Grossardt C, Veinalde R, Bossow S, Lutz D, Kaufmann JK, Shevchenko I, Umansky V, Nettelbeck DM, Weichert W, Jäger D, von Kalle C, **Ungerechts G**. CTLA-4 and PD-L1 checkpoint blockade enhances oncolytic measles virus therapy. **Mol Ther** 22(11):1949-59 (2014).

This highly cited paper is one of the first reports on oncolytic viruses genetically encoding checkpoint inhibitor antibodies and their therapeutic activity.