Press Release

PLoS Genetics publication on modeling of tumor heterogeneity and chemotherapy response by CPO, NMI, NMI TT Pharmaservices and collaborators

Reutlingen and Berlin, Germany, April 10, 2019 – A study on tumor heterogeneity and its impact on patients' response to cancer chemotherapeutics has been published in the peer-reviewed journal *PLoS Genetics* by academic partners and collaborators from the industry, including CPO cellular phenomics & oncology, the NMI Natural and Medical Sciences Institute at the University of Tübingen, and NMI TT Pharmaservices.

The paper entitled "Heterogeneous pathway activation and drug response modelled in colorectal-tumor-derived 3D cultures" is a collaborative work with researchers from Charité Universitätsmedizin Berlin, German Cancer Consortium (DKTK), Albert-Ludwigs-University Freiburg, Eli Lilly and Company, EPO Experimental Pharmacology & Oncology Berlin, Otto-von-Guericke-University Magdeburg, Medical University of Innsbruck, Medical University of Graz, and ASC Oncology.

The study describes how patient-derived three-dimensional cell models, so-called patient-derived 3D organoids (PD3D®), established from biopsies of colorectal cancers, were subjected to *in vitro* testing with commonly used standard of care chemotherapies, in parallel to genetic and protein profiling. Although the organoids recapitulated the genomic constitution of the donor tumors, their treatment response was variable, which remained not sufficiently explainable by genetic factors. Moreover, organoid cultures from different tumor regions of one donor showed considerable differences in drug response, as measured by CPO, thus indicating significant intra-tumoral heterogeneity, and additional profiling of total and phospho proteins, analyzed by NMI's DigiWest® technology, revealed striking differences in cellular signaling pathway activities between the models. The results of this study highlight the value of patient-derived organoid models for identification of individualized therapies, and all three lines of evidence – phenotypic, genetic and protein profiles – suggest that testing of multiple subpopulations from one tumor offers better chances for understanding therapy failure and drug resistance, and for identifying more effective individualized combination treatments.

"Our study clearly shows a precision oncology type of path forward on how to cope with the individualities in drug response between patients and even within one tumor of the same patient", commented Dr. Christian Regenbrecht, CEO of CPO cellular phenomics & oncology and senior author of the publication, "Our results emphasize that 'sequencing the tumor' is not enough, and that patient-specific and intra-tumoral differences in cellular signaling pathway activation are best modeled by multiple organoid cultures that are *in vitro* tested for their response to various treatment options and for their protein activity signatures".

The full text of this publication is accessible online: https://doi.org/10.1371/journal.pgen.1008076

Contacts

NMI
Dr. Markus Templin
templin@nmi.de
www.nmi.de

CPO cellular phenomics & oncology
Dr. Christian Regenbrecht
regenbrecht@cellphenomics.com
www.cellphenomics.com

NMI TT Pharmaservices
Dr. Christoph Sachse
sachse@nmi-tt.de
www.digiwest.de