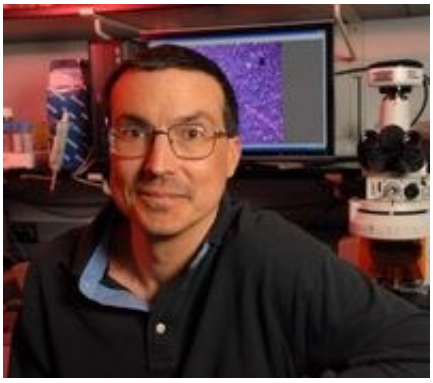
# Study predicts cancer drug responsiveness in human tumors

July 1 2013



Charles Perou, Ph.D., is senior author of the study. Dr. Perou is May Goldman Shaw Professor of Molecular Oncology Research and a member of UNC Lineberger Comprehensive Cancer Center. Credit: UNC Lineberger Comprehensive Cancer Center

It's a GEMM of a system. Genetically engineered mouse models that is. Using them allows scientists to study cancer in a way that more naturally mimics how human tumors exist within the complex environment of the body.

UNC scientists used GEMMs to develop biomarkers for challenging molecular subtypes of human breast cancer, those for which there are fewer targets and therapies. Their work helps to further establish genetically engineered mouse models as predictors of human response to therapy.

The molecular subtypes of breast cancer that the UNC group focused on – basal-like, luminal B, and claudin-low - are the most challenging types of breast cancer because these are tumors that don't typically respond to drugs such as Herceptin or aromatase inhibitors. UNC was among the first to characterize these tumor subtypes, and this new report extends the understanding of them.

The UNC team found that GEMMs were able to accurately predict human response to a standard chemotherapy drug combination commonly used in the clinic.

Charles Perou, PhD, study senior author, says, "This is a wonderful example of how well chosen mouse models can inform a human disease state. In this case we used years of research to match the models to specific human subtypes, and then treated the animals with therapies identical to what human cancer patients are receiving. We were ultimately able to develop a biomarker of treatment response from the mouse that works in humans."

Dr. Perou is the May Goldman Shaw Professor of Molecular Oncology Research and a member of UNC Lineberger Comprehensive Cancer Center.

Their findings were published in the June 19, 2013 online issue of the journal *Clinical Cancer Research*.

The team developed murine-derived gene signatures that corresponded to a distinct treatment response and then tested their predictive potential using human patient data. Their research tested single agents carboplatin, paclitaxel, erlotinib and lapatinib. Although one single agent exhibited exceptional efficacy, other single agents offered more modest results.

The team identified a pair of gene expression signatures that predicted

pathological complete response to neoadjuvant anthracycline (doxorubicin)/taxane (paclitaxel) therapy in human patients with breast cancer, even among the difficult to treat triple negative patient subset.

Traditional mouse model research was conducted using mice without immune systems into which human tumors or cell lines were grafted. In contrast, by manipulating genes in GEMMs scientists are able to observe how cancer develops as it does in humans, in the presence of an immune system, thus making the results more similar to human cancers.

Provided by University of North Carolina Health Care