Data Published in Nature Communications Demonstrate the Power of Fluidigm's CyTOF and Imaging Mass Cytometry Technologies to Transform Cancer Drug Discovery and Enable New Precision Medicine Approaches in Clinical Oncology

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Study Suggests Mass Cytometry Is a Valuable Tool for Predicting Individual Patient Response to Therapies

SOUTH SAN FRANCISCO, Calif., May 06, 2021 (GLOBE NEWSWIRE) -- Fluidigm Corporation (NASDAQ:FLDM), an innovative biotechnology tools provider with a vision to improve life through comprehensive health insight, today announced the publication of data that further validate the potential of its mass cytometry technologies, CyTOF® and Imaging Mass Cytometry™ (IMC™), to provide new approaches to evaluating cancer therapies ir animal models using human tumor xenografts, potentially identifying which patients are most likely to benefit from specific targeted cancer therapies.

The research was led by scientists at the Cancer Research UK (CRUK) Cambridge Institute at the University of Cambridge in collaboration with the Imaging and Molecular Annotation of Xenografts and Tumors (IMAXT) Cancer Grand Challenges Consortium, and the data have been published online in *Nature Communications*. This work was funded by Cancer Grand Challenges, AstraZeneca, a European Research Council Advanced Grant and the EU Marie Sklodowska-Curie Research program.

Researchers developed a panel of 33 antibodies designed to detect and differentiate human tumor cells from the surrounding mouse cells and to detect activation of cancer-related signaling pathways as well as markers of cell death (including programmed cell death). The breast cancer mass cytometry (BCMC) antibody panel was validated in a variety of well-characterized cell lines and then used to evaluate 53 human breast cancer xenograft samples capturing the diversity of breast cancers observed in patients, as previously shown and published in *Cell* (Bruna *et al.*, 2016).

This large biobank of human tumor xenografts was established at the CRUK Cambridge Institute by implanting human tumor tissue into a mouse and is used as a powerful preclinical platform to accelerate drug development, allowing high-content drug screens both *in vitro* and *in vivo.*

Xenograft samples were examined via suspension mass cytometry and IMC to evaluate the presence and distribution of distinct cell phenotypes in breast cancer tumors and their surrounding microenvironments. Results of these analyses identified several unique phenotypic profiles not previously detected using genomic or gene expression assessments, and also correlated these phenotypes with breast cancer molecular features.

The study also used drug screening data generated in the same xenograft platform to correlate BCMC-determined cellular phenotypes with response or resistance to specific therapies (caldaslab.cruk.cam.ac.uk/bcape/). These analyses demonstrated that mass cytometry-based phenotypic footprints captured distinct features not detected using typical genetic and genomic evaluations. Examples include the identification of two distinct types of triple-negative breast cancers, which are typically aggressive and hard to treat, and the determination that each group has distinct drug response profiles when treated with standard of care chemotherapy and targeted therapies.

Also, a specific cellular architecture (luminal cell clusters) was identified and was correlated with response to the PI3K-inhibitors, a class of drugs for which genomic analysis is a poor predictor of response.

"To date, most studies on tumor heterogeneity have focused on genetic diversity, and only a handful have evaluated phenotypic diversity at the protein level. We employed mass cytometry to identify and characterize core cellular phenotypes in a large cohort of breast cancer xenografts, part of a well-characterized preclinical platform in our lab," said Dimitra Georgopoulou, PhD, Research Associate at the CRUK Cambridge Institute and lead author of the publication. "Integrating phenotypic data with molecular and drug response data from the same xenografts, we found that phenotypic heterogeneity at the cellular level is a critical determinant of drug response. This finding has major implications in both preclinical and clinical efforts in breast cancer."

"In the current study we also combined the data from the suspension mass cytometry approach with Imaging Mass Cytometry performed on the same xenograft models," said Dario Bressan, PhD, Head of the IMAXT Laboratory at the CRUK Cambridge Institute. "In a previous work (Ali *et al.*, 2020), we also performed IMC on the primary tumor from which these xenografts were generated. This was really key to expanding our understanding of how specific cell phenotypes are spatially distributed and their clinical relevance. This approach allowed us to map the cellular phenotypes across mass cytometry platforms and from xenograft to clinical samples: something quite unique which was never successfully attempted before."

An additional key finding from the study is the demonstration that defined cell phenotypes with different responses to treatment co-exist within a single tumor. Importantly, this phenotypic variability does not appear to correlate with genetic intra-tumor variability. This finding has critical implications for both preclinical drug screening methods and translational medicine, suggesting that new combination therapies may need to be developed in order to address multiple cell types within an individual tumor.

The authors suggest that mass cytometry could potentially be used to directly profile biopsy samples from patients undergoing therapy to more accurately assess their response to treatment and determine if continued therapy is likely to provide benefit.

"Our findings open the door to new and potentially more informative models for evaluating cancer therapy and for predicting an individual patient's response to potential therapies, both of which are important for enabling precision oncology medicine," said Georgopoulou.

“This study underscores the importance of global collaboration among leaders in diverse aspects of cancer research to yield breakthroughs for the entire oncology research community,” said Chris Linthwaite, Fluidigm President and CEO.

“Fluidigm is committed to harnessing the power of our technologies to improve life, and this important study demonstrates our ability to support cutting-edge preclinical and translational medicine approaches that truly transform our understanding of cancer and identify new paths for improving care and outcome. These data highlight the true benefits of integrating IMC and mass cytometry to create dual-mode assessments and workflows that enable efficient generation of rich datasets.”

Learn more: cancergrandchallenges.org/teams/imaxt

About Fluidigm
Fluidigm (Nasdaq:FLDM) focuses on the most pressing needs in translational and clinical research, including cancer, immunology, and immunotherapy. Using proprietary CyTOF and microfluidics technologies, we develop, manufacture, and market multi-omic solutions to drive meaningful insights in health and disease, identify biomarkers to inform decisions, and accelerate the development of more effective therapies. Our customers are leading academic, government, pharmaceutical, biotechnology, plant and animal research, and clinical laboratories worldwide. Together with them, we strive to increase the quality of life for all. For more information, visit fluidigm.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, among others, statements regarding applications for and benefits of Fluidigm products in cancer research. Forward-looking statements are subject to numerous risks and uncertainties that could cause actual results to differ materially from currently anticipated results, including but not limited to risks relating to the potential adverse effects of the coronavirus pandemic on our business and operating results; company research and development and distribution plans and capabilities; interruptions or delays in the supply of components or materials for, or manufacturing of, Fluidigm products; potential product performance and quality issues; intellectual property risks; competition; and reductions in research and development spending or changes in budget priorities by customers. Information on these and additional risks and uncertainties and other information affecting Fluidigm business and operating results is contained in Fluidigm’s Annual Report on Form 10-K for the year ended December 31, 2020, and in its other filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof. Fluidigm disclaims any obligation to update these forward-looking statements except as may be required by law.

Available Information
We use our website (fluidigm.com), investor site (investors.fluidigm.com), corporate Twitter account (@fluidigm), Facebook page (facebook.com/Fluidigm), and LinkedIn page (linkedin.com/company/fluidigm-corporation) as channels of distribution of information about our products, our planned financial and other announcements, our attendance at upcoming investor and industry conferences, and other matters. Such information may be deemed material information, and we may use these channels to comply with our disclosure obligations under Regulation FD. Therefore, investors should monitor our website and our social media accounts in addition to following our press releases, SEC filings, public conference calls, and webcasts.

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