Nano@Tech Virtual Seminar
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PRECISION MEDICINE IS ADVANCED BY PRECISION MICROSYSTEMS

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Link: https://tinyurl.com/NanoTechHerr

Abstract: While the biomedical importance of detecting cellular heterogeneity is widely accepted, we lack tools for detection of the vast majority of molecular heterogeneity, as expressed in proteins. In fact, oncoproteins and their proteoforms are implicated in tumor progression, metastasis, and drug resistance across different cancer types. Yet, a severely limited set of isoforms are even detectable, with single-cell resolution. A next-generation of cancer subtype classification tools that include protein isoforms are urgently needed.

Immunoassays are the de facto standard for direct measurement of endogenous, unmodified oncoproteins, including use of immunohistochemistry (IHC) in tissue analysis. Unfortunately, immunoassays lack the specificity needed for quantitation and even detection of important proteins, including truncated cancer isoforms like those of HER2 (t-erbB2).

We introduce a suite of high-specificity, protein analysis tools – with single-cell and sub-cellular resolution – that a profile protein isoform expression. The precision microfluidic tools are designed to augment classic IHC and single-cell genomics and transcriptomics – shedding light on 'blind spots' in pathology.

We will describe microfluidic systems engineered for precise cellular and molecular manipulation and measurement, centered around a single-cell immunoblotting (native, western, complexes, and isoelectric focusing). We discuss new strategies for sample preparation and imparting molecular selectivity, including through key physicochemical properties. Integration of standards to quantify and control technical variation will be presented, as both analytical variability (lack of isoform-specific antibody probes) and biological variability (small cell subpopulations diluted in bulk analysis) can render oncoproteins undetectable. We detail the important role of thermodynamic partitioning of immunoprobe into an immunoassay scaffold, and informed design of new hydrogel metrology tools and materials to overcome transport limitations.

We see refined taxonomies that include both cellular and molecular heterogeneity as essential to underpinning needed advances in cancer diagnostic and treatment strategies.

Bio: Amy E. Herr received a BS degree in Engineering & Applied Science from the California Institute of Technology and MS and PhD degrees in Mechanical Engineering from Stanford University, where she was an NSF Graduate Research Fellow. She is currently Professor of Bioengineering at the University of California, Berkeley and a Chan Zuckerberg Biohub Investigator. Until 2020, she held an appointment as the Lester John & Lynne Dewar Lloyd Distinguished Professor. Prior to joining UC Berkeley, she was a staff member in the Biosystems Research Group at Sandia National Laboratories. Her research interests include bioinstrumentation innovation to advance quantitation in the biosciences & biomedicine, in particular the study and application of electrokinetic phenomena in single-cell and sub-cellular analyses. Her pedagogical interests are in bioengineering design and transport. Prof. Herr is an elected Fellow of the American Institute of Medical and Biological Engineering and an elected member of the National Academy of Inventors. She is the recipient of numerous awards and honors, including the NSF CAREER award, NIH New Innovator Award, Alfred P. Sloan Research Fellowship, and DARPA Young Faculty Award.

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