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Online Symposium September 30th, 2020

"Interactions of Nanomaterials with Complex Biological Systems"

University of Regensburg – Cornell University

3 p.m. **Susan Daniel**

RF Smith School of Chemical and Biomolecular Engineering

"Application of biophysical Principles for Understanding molecular Scale Interactions critical to Virus Entry and Infection of its Host"

3:45 p.m. **Margaret W. Frey**

Dept. of Fiber Science & Apparel Design

"Two Methods of Surface Functionalization of Electrospun Nanofibers for specific Biomolecule Capture"

4:30 p.m. **Claudia Fischbach-Teschl**

Meinig School of Biomedical Engineering

"Physical Sciences Approaches to analyze Tumor-associated ECM Dynamics"

Online Symposium September 30th

"Interactions of Nanomaterials with Complex Biological Systems"

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PROF. DR. SUSAN DANIEL

"Application of biophysical Principles for Understanding Molecular Scale Interactions critical to Virus Entry and Infection of its Host"

3 p.m.

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has focused attention on the need to develop effective therapies against the causative agent, SARS-CoV-2, and also against other pathogenic coronaviruses (CoV) that have emerged in the past or might appear in future. Focusing on steps in the CoV replication cycle, in particular the entry steps involving membrane fusion that are vulnerable to inhibition by broad-spectrum or specific antiviral agents, is an astute choice because of the conserved nature of the fusion machinery and mechanism across the CoV family.

For coronavirus, entry into a host cell is mediated by a single glycoprotein protruding from its membrane envelope, called spike (S). Within S, the region that directly interacts with the membrane is called the fusion peptide, FP. It is the physico-chemical interactions of the FP with the host membrane that anchors it, thus enabling the necessary deformations of the membrane that lead to delivery of the viral genome into the cell when a fusion pore opens.

Biophysicists contribute to this fundamental work by leveraging understanding of thermodynamics, kinetics, and intermolecular interactions to describe FP interactions with the host membrane at the most fundamental molecular level to facilitate the development of strategies to limit those interactions to stop the spread of infection.

In this talk, I will describe our work on understanding the impact of calcium ions on CoV infection. Using cell infectivity, biophysical assays, and spectroscopic methods, we found that calcium ions serve to stabilize the fusion peptide structure during conformational change that then allows its insertion into the host membrane, resulting in increased lipid ordering in the membrane. This lipid ordering precedes membrane fusion and has been shown to correlate with increased fusion activity, as higher extents of fusion are observed as calcium concentration increases, aligned with higher levels of infection in the presence of calcium.

Finally, depletion of calcium ions leads to structure and activity changes that correlate well with *in vitro* experiments using calcium-chelating drugs. Under these conditions, cell infection dropped, pointing to the possibility of such drugs as therapeutic interventions.

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PROF. DR. MARGARET W. FREY

"Two Methods of Surface Functionalization of Electrospun Nanofibers for specific Biomolecule Capture"

3:45 p.m.

Abstract

Two strategies for functionalizing electrospun nanofibers for specific capture of biological molecules will be discussed. First, silver-doped carbon nanofibers (SDCNF) are used as the base material for the selective capture of Escherichia coli in microfluidic systems. Polyacrylonytrile nanofibers containing silver nitrate were electrospun and carbonized to form carbon fibers with silver particles at the surface.

Antibodies are immobilized on the surface via a three-step process. The negatively charged silver particles present on the surface of the nanofibers provide suitable sites for positively charged biotinylated poly-(L)-lysine-graft-poly-ethylene-glycol (PLL-g-PEG biotin) conjugate attachment. Streptavidin and a biotinylated anti-E. coli antibody were then added to create anti-E. coli surface functionalized (AESF) nanofibers. Functionalized fibers were able to immobilize up to 130 times the amount of E. coli on the fiber surface compared to neat silver doped fibers.

To demonstrate selectivity and functionalization with both gram negative and gram-positive antibodies, anti-Staphylococcus aureus surface functionalized (ASSF) nanofibers were also prepared. Experiments with AESF performed with Staphylococcus aureus (S. aureus) and ASSF with E. coli show negligible binding to the fiber surface showing the selectivity of the functionalized membranes. Second, biotin-cellulose nanofiber membranes are successfully fabricated via "click" chemistry. Cellulose acetate (CA) is electrospun, deacetylated and substituted with an alkyne group in either a one or two step process. Azide-biotin conjugate is then "clicked" onto the alkyne-cellulosesurface via Copper-catalyzed Alkyne-Azide Cycloaddition (CuAAC).

FTIR,Scanning ElectronMicroscopy (SEM), Energy Dispersive X-ray spectroscopy (EDX), and X-ray Photoelectron Spectroscopy (XPS) are used to confirm addition of biotin without damage to the fiber structure. The biotin-cellulose nanofiber membranes are used in example assays (HABA colorimetric assay and fluorescently taggedstreptavidin assay) where streptavidin specifically binds to the pendant biotin without requiring blocking agent. Both methods yield durable attachment of the specific capture functionality at the fiber surface.

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PROF. DR. CLAUDIA FISCHBACH-TESCHL

"Physical Sciences Approaches to analyze Tumor-associated ECM Dynamics"

4:30 p.m.

Abstract

Microenvironmental conditions contribute to the pathogenesis of cancer and include altered cellular composition, extracellular matrix (ECM) deposition, and mechanical cues. However, our understanding of the specific mechanisms by which these microenvironmental perturbations impact the development, progression, and therapy response of cancer is relatively limited.

More intricate models are needed to better understand the complex biochemical and biophysical interactions that drive tumor initiation, growth, metastasis, metabolic adaptation, and immune evasion. The fields of biomaterials and tissue engineering provide increasingly sophisticated tools and strategies to recapitulate and monitor relevant properties of tumor-microenvironment interactions.

These approaches not only bear tremendous potential to advance our current understanding of cancer, but are also increasingly explored for more clinically relevant drug testing. Indeed, combining patient-specific cells with engineered culture systems promises to enhance the predictive power of precision medicine pipelines.

This talk will highlight specific examples of how the microenvironment regulates the highly dynamic nature of cancer and will outline opportunities and challenges of the field of tumor engineering.