In-Person Departmental Colloquium

Department of Materials Science and Chemical Engineering

Wednesday
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1:00 – 2:00 p.m.

Professor Miriam Rafailovich

Department of Materials Science and Chemical Engineering
Stony Brook University
Stony Brook, New York

Molecular basis for surface initiated non-thrombogenic clot formation following viral infection

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Prof. Miriam Rafailovich (E-mail: miriam.rafailovich@stonybrook.edu)

Department of Materials Science and Chemical Engineerng
Stony Brook University, Stony Brook, New York

Abstract

In order to design effective anti-viral medications it is important to understand the molecular basis for the damage induced by viral infection. One of the most serious consequences of Covid-19 infection is the formation of non-thrombogenic clots following viral infection. Clot formation normally occurs following the release of thrombin, an enzyme which cleaves segments of the natural blood protein, fibrinogen, unfolding the molecule and allowing it for form a fibrin gel. We have previously shown that materials surfaces, which are hydrophobic, can have a similar effect when in contact with blood. In this case, strong adsorption of the fibrinogen molecules can change their conformation, and initiate cross linking. In order to investigate the source of non-thrombogenic clot initiation on living tissue surfaces, human epithelial and MDCK cells were infected with H1N1 influenza, OC43 corona virus, or human adenovirus. After infection the epithelial cells were exposed to fibrinogen, which was observed to undergo fibrillogenesis in the absence of thrombin, on the tissue surface. Conditioned media was collected from the epithelial cell cultures and used to treat human lung microvascular cells. Again large fibers were observed after one or more hours of exposure on the epithelium tissue surfaces. Contact angle goniometry of the conditioned media indicated that these observations were analogous to the non-thrombogenic clots we previously reported on hydrophobic surfaces, associated with distorting the structure of fibrinogen and release of the a-C-domains without enzymatic cleavage. Exposure of the cultures following infection to florescent lipid stain confirmed the presence of large amounts of lipid droplets, associated with standard inflammatory response of the epithelium, which were then transferred to the endothelium, rendering both tissue surfaces hydrophobic and providing the ideal conditions for thrombi initiation. The molecular level detail can be used to both predict predisposition to thrombosis as well as design of peptides to prevent it. As example, we illustrate the effect of P12, a fibronectin derived peptide, which binds to the a-C-domain, preventing fibrillogenesis, and which has been shown clinically to prevent microthrombii formation responsible for wound progression following burn injury.

Biosketch

Miriam Rafailovich received her PhD from Stony Brook University in Applied Nuclear Physics. She then did her post doctoral work at Brookhaven National Laboratory and the Weizmann Institute. Miriam was associate professor of Physics and Astronomy at CUNY, Queens College and is currently a distinguished professor at Stony Brook University in the Department of Materials Science and Chemical Engineering. Her research interests span a broad spectrum which includes, polymer nanocomposites for additive manufacturing, biopolymers, biosensors, tissue engineering scaffolds, nanotoxicology, flame retardant composites, and polymers for green energy applications.