THE MATERIALS SCIENCE AND ENGINEERING DEPARTMENT
FALL COLLOQUIUM SERIES PRESENTS:

Goll Lecture

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Biomineralogical Signatures of Pathological Mineralization

Physiological mineralization is a delicately orchestrated process necessary for healthy tissue function, as seen in bone and tooth formation. Sometimes, however, mineral deposits form in tissues that should not have mineral. This process of pathological mineralization is associated with a wide range of diseases and tissue types, including the cardiovascular system and the tumor microenvironment of multiple types of cancer. From decades of study of physiological biomineralization mechanisms, it is generally accepted that the formation of mineralized tissues and the resulting structure-function relationships in those tissues are controlled by the interplay among the mineral, matrix, and cells. The goal of this work is to characterize the mineral-matrix-cell triad of pathological mineral deposits and develop in vitro models that recapitulates key aspects of pathological mineralization in a range of systems. We focus on two examples of pathological mineralization: microcalcifications (MCs), which are primarily biological apatite and occur in cancerous and benign breast pathologies, and calcific aortic valve disease (CAVD), in which mineralized lesions form in the leaflets of the aortic valve, inhibiting proper function. We have developed an omics-inspired approach, by which we define “biomineralogical signatures” by combining materials metrics derived from Raman microscopy and energy dispersive spectroscopy for individual mineral deposits. In our study of microcalcifications in breast tissue, we observe that: 1) calcifications cluster into physiologically relevant groups reflecting tissue type and local malignancy; 2) trace metals including zinc, iron, and aluminum, are enhanced in malignant-localized calcifications; 3) the lipid-to-protein ratio within calcifications is lower in patients with poorer prognosis, suggesting that expanding diagnostic metrics to include “mineral-entrapped” organic material may hold prognostic promise. In a related study of excised human heart valve leaflets from patients with CAVD, we find that there are multiple types of calcium phosphate (e.g., hydroxyapatite (HAp; Ca10(PO4)6(OH)2) and whitlockite (Wh; (Ca,Mg)3(PO4)2)) present during disease progression. We explore how mineral composition impacts cellular behavior through tissue engineered constructs mimicking human aortic valve leaflets. We have used Raman mapping of these tissue engineered constructs to reveal how lesion composition and morphology varies as a function of disease progression. Ongoing and future experiments will aim to expand our understanding of the role that mineral plays in driving disease progression and, ultimately, applying our understanding of pathological mineralization in different diseases towards developing strategies for new methods for prognosis and treatment.

Lara A. Estroff received her B.A. with honors from Swarthmore College (1997), with a major in Chemistry and a minor in Anthropology. Before beginning her graduate studies, she spent a year at the Weizmann Institute of Science in Rehovot, Israel as a visiting researcher in the labs of Profs Lia Addadi and Steve Weiner. During this time, she was introduced to the field of biomineralization and studied chemical approaches to archeological problems. In 2003, she received her Ph.D. in Chemistry from Yale University for work done in Prof. Andrew D. Hamilton's laboratory on the design and synthesis of bio-inspired organic superstructures to control the growth of inorganic crystals. After completing graduate school, she was an NIH-funded postdoctoral fellow in Prof. George M. Whiteside's laboratory at Harvard University (2003-2005). Since 2005, Dr. Estroff has been in Materials Science and Engineering department at Cornell University and in 2023 she was named the Herbert Fisk Johnson Professor of Industrial Chemistry. She served as the Director of Graduate Studies in the department from 2015-2019. As of August 2020, she is the current Chair of the Materials Science and Engineering department. Her group focuses on bio-inspired materials synthesis, crystal growth mechanisms, and the high-resolution characterization of pathological mineralization. She has received several awards, including an NSF Early Faculty Career Award in 2009 and a J.D. Watson Young Investigator’s award from NYSTAR in 2006.

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Small reception to follow in the Willens Wing Atrium

In person only; no Zoom

Questions? Contact allison.macknick@northwestern.edu

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