

Department of

Chemical and Environmental Engineering

2015—2016 Seminar Series

Friday, April 15, 2016

9:30-10:30am

Winston Chung Hall 205/206



**Markus Kalkum**

Professor

Beckman Research Institute at City of Hope

## Enzyme Acceleration: A Universal Platform for Ultrasensitive Diagnostic Assays

The “Assay with a Large Immunosorbent Surface Area” (ALISSA) detects atto- to femtomolar concentrations of enzymatically active analytes in complex biological samples such as human serum. ALISSA quantifies the enzyme activity of a suitable analyte in a procedure that includes its immunoaffinity capture, followed by conversion of a fluorogenic substrate. We have demonstrated the effectiveness of the ALISSA approach for a variety of enzymatically active and medically relevant diagnostic targets. These include botulinum neurotoxin serotypes A, B, and E, anthrax lethal factor, human chitotriosidase, and a novel protease secreted by the fungal pathogen *Aspergillus fumigatus* during tissue invasion. For example, ALISSA was able to detect low 25 attomolar concentrations of botulinum neurotoxin type A in 1-mL sized samples of human serum within 2-4 hours. Accordingly, the sensitivity of the assay surpassed that of mainstream methods by 4 to 5 orders of magnitude.

Kinetic measurements revealed that the immunoaffinity immobilization of enzymatically active analytes altered their biochemical properties compared to those of non-immobilized free analytes. Catalytic turnover rates were drastically accelerated and substrate/enzyme affinities were improved. We introduce a theoretical model in support of the observed enzyme acceleration effect and demonstrate its usefulness for the development of a variety of diagnostic assays.

**Biosketch:** Dr. Markus Kalkum is a Professor in the Department of Immunology, and also the Director of the Mass Spectrometry and Proteomics Core Facility, of the Beckman Research Institute at City of Hope. In his research laboratory, Dr. Kalkum is developing novel diagnostic assays for microbial diseases, researches probiotic immunomodulators, and mycosis vaccines. He is known for a very sensitive detection assay for botulinum neurotoxin. Dr. Kalkum holds a Ph.D. in Chemistry, Biology, and Pharmacology from the "Freie Universität" Berlin, Germany. Previously, he had worked at the Max-Planck Institute for Molecular Genetics in Berlin, and conducted postdoctoral research at the Rockefeller University in New York City.