NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

BIOLOGY COLLOQUIUM

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Hosted by Assistant Professor Chae Eunyoung

Enzymatic activities of TIR domains: molecular basis and immune signalling in humans, plants and bacteria

By **Bostjan Kobe**

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TIR (Toll/interleukin-1 receptor) domains are widely distributed in animals, plants and bacteria, and function through self-association and homotypic interactions with other TIR domains (1). In plants and animals, these domains are predominantly found in proteins with immune functions [TLRs (Toll-like receptors), IL-1Rs (interleukin-1 receptors) and their adaptor proteins], and plant NLRs (nucleotide-binding, leucine-rich repeat receptors). The TIR domain of the protein SARM1, involved in nerve degeneration, was the first one found to have enzymatic activity – cleavage of NAD+ (nicotinamide dinucleotide). Subsequently, several TIR domains from plant NLRs and bacteria were also found to have enzymatic activities (2). We have studied the molecular and structural bases of these enzyme reactions and the role of the corresponding enzymatic products in signalling in these evolutionarily diverse systems (axon degeneration, plant immunity, antiviral defence in bacteria and suppression of plant immunity by bacterial effectors) (3-5). These studies will form the foundation of applications spanning the tree of life, from the treatment of neurodegenerative disorders and bacterial infections in humans to the prevention of plant diseases.

(1) Nimma et al (2021) Front Immunol 12: 784484
(2) Horsefield et al (2019) Science 365, 793
(3) Figley et al (2021) Neuron 109, 1118
(4) Shi et al (2022) Mol Cell 82, 1643-1659
(5) Manik et al (2022) Science, eadc8969

About the Speaker

Bostjan Kobe is Professor of Structural Biology and Australian Laureate Fellow at the School of Chemistry and Molecular Biosciences, University of Queensland. He received his BSc in chemistry at the University of Ljubljana, Slovenia, and his PhD in biochemistry and biophysics at the University of Texas Southwestern Medical Center at Dallas, USA. His laboratory focuses on applying structural biology approaches to understanding infection and immunity. He received the 2001 Minister's Prize for Achievement in Life Sciences, the 2009 ASBMB Roche Medal, the 2018 ASBMB Beckman Coulter Discovery Award and was named Slovenian Ambassador of Science in 2020. He was elected Fellow of the Australian Academy of Science in 2018. 41 PhD (25 as primary supervisor) students have graduated under his (co)-supervision. He is Co-Editor of Acta Crystallogr Sect D Struct Biol and Academic Editor of PLoS One. He has 280 publications and >220,000 citations, h-index 71, including Nature, Science, PNAS, Nat Struct (Mol) Biol, Nat Chem Biol, Nat Microbiol, Nat Genet, Nat Commun, Cell Host Microbe, Neuron and Mol Cell