SL05 **Development of Drugs for Diagnosis and Medical Treatments on the Basis of Innate Immunity**

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During last twenty-five years, we have involved in the studies of host innate immunity. First, by using *Tenebrio molitor* as a holometabolous insect model system, we purified many proteins modulating activation of Toll-signaling pathway, leading to the production of host antimicrobial peptides. Our group firstly determined the extracellular activation mechanism of Toll-signaling cascade by *in vitro* reconstitution experiments. These studies provided us a core concept for detection of bacterial peptidoglycan for Gram-positive infection. From last six years, we changed our insect model from holometabolous insect to hemimetabolous insect, *Riptortus pedestris* (bean bug), a notorious pest in Asian area. This insect harbored a unique gut symbiont, *Burkholderia* species, in their midguts. We intensively studied how this gut symbiont regulates host insect's development, immunity and fitness. During this work, we have addressed what kinds of gut symbiont-derived molecules are involved in the regulation of host immunity and development. Also, during last 10 years, our group tried to understand how mammalian host defense proteins recognize invading pathogenic bacteria. We firstly determined that human mannose-binding lectin (MBL) recognizes a major cell glycopolymer, wall teichoic acid (WTA), of *Staphylococcus aureus* bacteria, indicating that bacterial cell wall component plays important roles for regulating host innate and acquired immunity.

Based on these experiences, from last five years, we tried to screen a novel *S. aureus* cell wall components that can induce activation of host innate and acquired immunity against methicillin-resistant *S. aureus* (MRSA) infection, supporting that these molecules will be useful molecule for development of MRSA vaccine candidates. As results, we found that pre-immunization of purified *S. aureus* particulate cell walls (PCWs) harboring 1 μm particle size showed potent protective effects against USA300 LAC MRSA infection. But, their soluble cell wall (SCW) did not show ant protection effects. Furthermore, we have determined how these PCWs can activate host innate and acquired immunity. In this talk, I will emphasize the importance of molecular understanding of host defense responses, leading to getting a chance to develop novel drug candidates for diagnosis and clinically effective vaccine candidates.