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Structure and function of the C-terminal ID region of onco-protein CagA

Helicobacter pylori, a Gram-negative bacterium that colonizes the human gastric mucosa is recognized as a major risk factor for gastric diseases, such as peptic ulcers and gastric carcinomas. *H. pylori* delivers an effector protein CagA into gastric epithelial cells and the EPIYA and CM segments in the C-terminal intrinsically disordered (ID) region of CagA (CagA-C) promiscuously interact with cellular signaling molecules, such as SHP2 and PAR1b, to deregulate these signaling proteins. To analyze the structure and function of a large protein complex formed by CagA, SHP2, and PAR1b, we started a structural biology study of the CagA-SHP2-PAR1b complex. Since our group already determined the crystal structure of the N-terminal structured region of CagA (CagA-N), we are working on structure and function of CagA-C. Our biochemical analysis suggested that the CBS segment in the CagA-C region interacts with the NBS segment in CagA-N, forming a four-α-helix bundle structure and the CagA-C region adopts a lariat-loop like structure. Interestingly, mutations in the NBS and CBS segments caused a reduced biological activity of CagA (humminbird-inducing ability in AGS cells). For further understanding of the structure-function relationship of CagA-C, we have confirmed the existence of the lariat-loop like structure. In addition, we have obtained some structural information of the CagA-C region and its interaction with SHP2. We will discuss the structural characteristics of CagA-C and its relationship to the biological activities.

Biography

Toshiya Senda has completed his PhD from Nagaoka University of Technology, Niigata, Japan in 1995. He was a Research Associate in Nagaoka University of Technology (1995-2001) and a Senior Researcher in Institute of Advanced Industrial Science and Technology (2001-2012). Presently, he is the Director/Professor of Structural Biology Research Center of High Energy Accelerator Research Organization in Japan. He was awarded the CrSJ (Crystallographic Society of Japan) Award in 2014.

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