日本薬学会九州支部特別講演会

演題 ：Structural Biology of the c-Myc/Max/Mad/Miz-1 Network and the development of therapeutic b-HLH-LZs for the treatment of Cancer

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日時：平成 28 年 8 月 19 日（金）
17:30～18:30

会場：長崎国際大学・薬学部・会議室（1F)

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Structural Biology of the c-Myc/Max/Mad/Miz-1 Network and the development of therapeutic b-HLH-LZs for the treatment of Cancer

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The product of the oncogene *c-myc* (c-Myc) is a b-HLH-LZ (basic-region-Helix-Loop-helix-Leucine Zipper) transcription factor (TF) that is stabilized by common driver oncogenes (e.g. *kras* and *efgr*). In complex with Max (another b-HLH-LZ TF) persistent and tumorigenic c-Myc causes the sustained transcription of gene networks that allow tumor cells to proliferate more rapidly than normal cells while escaping apoptosis. While c-Myc has long been considered undruggable, recent studies have demonstrated that the systemic inhibition of c-Myc is a promising target to treat a plethora of cancers. We have recently discovered that b-HLH-LZ domains can spontaneously penetrate cells and translocate to the nucleus. This has opened a new therapeutic approach. Based on the structural knowledge of the b-HLH-LZ of Max, c-Myc and Mad1 (an antagonist of c-Myc) we have developed b-HLH-LZs that can inhibit c-Myc in cancer cells and lead to the preferential apoptosis of tumor cells *vs.* normal cells. During my lecture I will review our structural work by NMR that led to the design of our b-HLH-LZs, our recent progress in the characterization of their mode of action *in cellulo* and their therapeutic potential *in vivo*.