SE-05-02

Development of oligopeptide DNP MRI molecular probes for *in vivo* studies

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Abstract

Peptides, composed of amino acids, are biomolecules involved in various biological processes through sequence-specific metabolisms and interactions with proteins. In addition, peptides are recognized as a class of pharmaceutical reagents. Therefore, there is a growing interest in detecting and tracking *in vivo* dynamics of peptides, including the metabolism and localization. Hyperpolarization, one of the quantum sensing technologies, can markedly enhance the detection sensitivity of nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) and enables *in vivo* real-time analysis using NMR/MRI. Hyperpolarized ^{13}C-enriched molecules, such as [1-^{13}C]pyruvate, have been utilized as reagents for hyperpolarized *in vivo* bioimaging, and human clinical trials for early diagnosis of diseases have been conducted. However, the highly sensitive NMR signal, which is created by hyperpolarization technology, decays back to that in a thermal equilibrium state according to the spin-lattice relaxation time (T_1). Due to the limitation of molecular structures that affect T_1, hyperpolarized molecular probes derived from amino acids and peptides are only amino acid monomers and dipeptides.

In this presentation, we report the development of hyperpolarized oligopeptide molecular probes on the basis of nuclear spin science and appropriate molecular design[1]. Structure-based T_1 relaxation analysis suggests that the C-terminal [1-^{13}C]Gly-d_2 residue affords sufficient T_1 for *in vivo* studies, even in oligopeptides. The developed oligopeptide molecular probes, ^{13}C-β-casomorphin-5 and ^{13}C-glutathione, were successfully utilized

to monitor the dynamic *in vivo* metabolisms of the oligopeptides.

1. Yohei Kondo, Yutaro Saito, Tomohiro Seki, Yoichi Takakusagi, Jumpei Morimoto, Hiroshi Nonaka, Koichiro Miyanishi, Wataru Mizukami, Makoto Negoro, Abdelazim Elsayed Elhelaly, Fuminori Hyodo, Masayuki Matsuo, Natarajan Raju, Rolf E. Swenson, Murali C. Krishna, Kazutoshi Yamamoto, Shinsuke Sando, *Sci. Adv., in press*.