## GS1-6 Enhancing effect of functional peptides on intestinal absorption of therapeutic peptides/ proteins and elucidation of their action mechanisms

◯Noriyasu KAMEI[1], Mariko MORISHITA[1], Kozo TAKAYAMA[1]

[1]Hoshi Univ.

Therapeutic peptides and proteins are often parenterally administered because of insufficient oral bioavailability caused by the low permeability through the intestinal mucosa. It is needed for development of oral delivery system for bioactive drugs to bear not only resistibility to enzymatic metabolism but also enhanced permeability through the epithelial membrane. Recently, it has been reported that drugs that are poorly permeable through the cell membrane can be taken up efficiently by diverse cells through conjugating with peptides referred to as cell-penetrating peptides (CPPs) such as HIV-1 Tat peptide and oligoarginine, and application of this functional peptides as intracellular delivery vector are hopeful. Therefore, we have attempted to develop more efficient intestinal delivery carrier using CPP as tool to improve the oral bioavailability of bioactive drugs. To date, we have demonstrated that intestinal insulin absorption is markedly enhanced without causing detectable damage in cellular integrity by coadministration of insulin with various CPPs. In addition, this enhancing effect of CPPs did not require covalent linkage between drug and CPP, and was achieved by administration of their mixed solution via intermolecular interaction among them. Since it is thought that a number of pathways were associated with intracellular transduction of CPPs, we have evaluated the enhancing mechanisms of intestinal insulin absorption by functional peptides. Thus, we attempt to develop feasible oral delivery system for bioactive drugs through these studies.