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Neuronal differentiation of skin-derived precursors by intracellular delivery of synthesized peptides derived from BC-box proteins

Several somatic stem cells have potential to differentiate to neurons, and they are hopeful to be used as grafted donor cells for neuronal regenerative therapy. However, the grated cells little survive and differentiate to functional neurons in recipient neural tissue. To overcome the problem, neural induction using neuro-trophic factors or gene transfer has been employed before grafting, but neuro-trophic factors do not occur specific neural induction, while gene transfer has risk of vector. If a neural induction domain for somatic stem cells exists in proteins to induce neural differentiation, its identification can contribute to neuronal regenerative therapy through neural induction of somatic stem cells using the neural induction domain. We previously demonstrated that von Hippel-Lindau tumor suppressor (VHL) protein has a function of neural induction in Skin-Derived Precursors (SKPs) without any neuro-trophic factors. Then, we hypothesized that a neural induction domain potentially exists in the VHL protein. Here we identify a neural induction domain for somatic stem cells in the VHL protein and show neural induction of the cells by transfer of the domain peptide linked to Protein Transduction Domain (PTD). The neural induction domain in the VHL protein contains BC-box motif [(A,P,S,T)LXXX (A,C) XXX(A,I,L,V)] corresponding to binding site of elongin BC, which is evolutionally conserved from virus to mammalian. Therefore, we proposed that other BC-box proteins also contain the neural induction domain and subsequently show to identify the neural induction domains at amino-acid sequences encoded by BC-box motif within BC-box proteins responsible for neuronal differentiation of somatic stem cells. In addition, we show that the domain has the same function for other somatic stem cells except for neural stem cells. Furthermore, when the domain peptide-transferred stem cells are grafted into recipient nervous tissue in neuronal disease models, the grafted cells differentiate to neurons and neuronal repair for neuronal disease models is achieved. Thus, a neural induction domain is identified at BC-box motif in BC-box proteins. The neuronal differentiation of somatic stem cells is caused by intracellular delivery of the neural induction domain peptide linked to PTD and would contribute to neuronal regenerative therapy.

Biography

Hiroshi Kanno is the Professor of Neurosurgery at International University of Health and Welfare, School of Medicine in Japan. His research interest has been focusing on stem cells and regenerative medicine for 20 years.

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