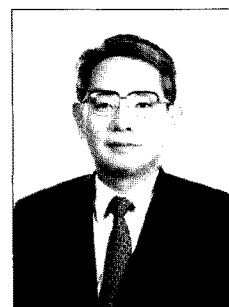




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Present position

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|--------------|--|
| 1998-present | Director of the Institute of Reproductive Medicine and Population
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- 1984-present Director of ART Program
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- 1977-1987 Ph.D., Postgraduate Medical School, SNU
- 1975-1979 Ob & Gyn, Seoul National University Hospital, Resident
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-

Differentiation of Human Embryonic Stem Cells into Insulin-Producing Cell Clusters

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Human embryonic cells (hESCs) could play an important part as a potential cell source for cell replacement therapy by the efficient differentiation into specific cell types *in vitro*. The generation of insulin-producing cell clusters (IPCCs) from hESCs has been extensively studied for the alternative treatment of diabetes, however, the differentiated cells have still various limitations in both quality and quantity. In this study, we tried a novel protocol improved with useful factors affecting the differentiation of IPCCs. First of all, a low glucose condition was introduced into the culture and differentiation of hESCs, focusing on that the long-term exposure of hESCs in high glucose concentrations, common as a nutrient in culture media, could hinder the differentiated IPCCs from producing insulin upon glucose stimulation. Activin A and betacellulin were also administered to promote the efficiency of IPCC differentiation. As a result, we confirmed that SNUhES3 adapted in 7.8 mM-glucose concentration maintained the stemness with normal karyotype, furthermore, showed a higher growth rate and the effective generation of cystic embryoid bodies. Fully differentiated IPCCs showed the expression of C-peptide, a by-product of insulin biosynthesis, and Pdx-1, an important transcription factor of islet differentiation, in appropriate locations with a high ratio. It was notable that the C-peptide content was considerably increased in IPCCs differentiated in a low glucose condition, and the insulin release in response to glucose stimulation was following the normal secreting machinery. In conclusion, these results suggest that our novel protocol would be efficient in inducing functional IPCCs.

Key Word: human embryonic cells, insulin-producing cell clusters, pancreatic β -cells, low glucose condition, diabetes mellitus, differentiation, cell replacement therapy
