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Histone de-acetylation inhibitors (HDACi) and embryo aggregation enhance development and ntES cell derivation in cloned pig embryos

This study was aimed to improve the efficiency of nuclear reprogramming by treating embryos with HDACi. We investigated the effects of two novel inhibitors, HDACi-14 and -79, at the concentrations of 0, 1, 2, or 4 μM on the development of embryos cloned by the oocyte bisection cloning technique (OBCT). Blastocyst rates of the reconstructed embryos reached 60% in the 2 μM HDACi-14-treated groups, which was higher ($p<0.05$) compared to the untreated group (36.9%). Similarly, HDACi-79 treatment at 2 and 4 μM also conferred higher ($p<0.05$) blastocyst rates than that of the untreated group (79.4, 74.2, and 50.0%, respectively). Histone acetylation profile by both HDACi-14 (2 μM) and -79 (2 μM) treatments demonstrated a drastic increase ($p<0.05$) mainly in two cell stage embryos when compared to the control group. After seeding on the feeder cells, the aggregated cloned blastocysts produced by the HDACi-79 treatment showed a significant increase of primary outgrowths compared to the control group (60.0% vs. 42.9%; $p<0.05$). Finally, the cloned embryo-derived ES cell lines from aggregated cloned embryos produced from the HDACi-79/14 treatment and the control groups were established. These novel histone de-acetylation inhibitors can improve blastocyst formation and increase the derivation efficiency of ntES cell lines from the cloned porcine embryos produced *in vitro*.

Speaker Biography

Jyh-Cherng Ju earned his PhD training from Department of Animal Science, Cornell University, New York, USA, in 1998, and then came back to Taiwan to work for National Chung-Hsing University, Taichung, Taiwan. In 2012, he moved to Graduate Institute of Biomedical Sciences, China Medical University (CMU) and the Hospital CMUH, Taichung, Taiwan. He has been working on embryo/animal cloning by somatic cell nuclear transfer, pluripotent stem cells, particularly in domestic species, and thermal impacts on embryo development and germ layer differentiation. He has also established a Core Lab for Stem Cell Research in CMUH to differentiate human, as well as animal, ES cells into three germ layer cell lineages, such as motor neurons, cardiomyocytes and hepatocytes from normal and disease individuals, for research and therapeutic purposes.

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