INTERNATIONAL JOURNAL OF HEALTH & ANIMAL SCIENCE & FOOD SAFETY

Keywords

Epigenetic Conversion, Pancreatic Differentiation, Glucose Concentration, Physiological Environment

CORRESPONDING AUTHOR

Alessandro Zenobi
alessandro.zenobi@unimi.it

JOURNAL HOME PAGE

riviste.unimi.it/index.php/haf

UNIVERSITÀ DEGLI STUDI DI MILANO
DIPARTIMENTO DI SCIENZE VETERINARIE PER LA SALUTE, LA PRODUZIONE ANIMALE E LA SICUREZZA ALIMENTARE

High glucose concentrations are required for endocrine pancreatic differentiation of mammalian adult fibroblasts.

A. Zenobi[a] *, F. Gandolfi[a], T. A. L. Brevini [a]

[a] *Department of Health, Animal Science and Food Safety, University of Milan, Via Celoria 10, 20133 Milan, Italy*

Abstract

Epigenetic conversion overcomes the stability of a terminally differentiated cell, allowing phenotype switch and providing an unlimited source of autologous cells of a different type. It is based on the exposure to an epigenetic modifier that increases cell plasticity, followed by a differentiation protocol. In our work we treat mammalian dermal fibroblasts with the demethylating agent 5-azacytidine. Cell differentiation is directed toward the endocrine pancreatic lineage, with a sequential combination of key growth factors. The overall duration of the process is 36 days (*Pennarossa, 2013; Brevini, 2015; Brevini, 2015*). However, this protocol, as well as all differentiation procedures described in the literature, uses high and non-physiological concentrations of glucose. Here we report experiments aimed at investigating whether the use of lower glucose concentrations, that more closely mimic the *in* vivo physiological environment, can support fibroblast conversion into β-like cells. To do so, cells were cultured as described above, but using lower and more physiological glucose levels, namely 5.5 and 8.5 mM that correspond to normoglycaemia before and after meals (*International Diabetes Federation, 2007*). Our results show that mammalian cells are not able to differentiate into insulin secreting cells in a low glucose environment. In particular, cells do not aggregate into pancreatic islet structures and display an altered gene expression pattern for several early pancreatic markers, when compared to the standard trend obtained with 17.5 mM of glucose. These results suggest that high glucose levels are essential for the achievement of the endocrine pancreatic differentiation process in mammalian cells and appear to be crucial for functional efficiency and morphological organization.

References

Brevini, T.A.L., Pennarossa, G., Acocella, F., Brizzola, S., Zenobi, A., Gandolfi, F., 2015. Skin derived insulin-secreting cells as a potential therapy for diabetes in the dog. The Veterinary Journal 211, 52-56;

Brevini, T.A.L., Pennarossa, G., Maffei, S., Zenobi, A., Gandolfi, F., 2015. Epigenetic conversion as a safe and simple method to obtain insulin-secreting cells from adult skin fibroblasts. JoVe 109, e53880;

International Diabetes Federation, 2007. Guidance for Management of Postmeal Glucose;

Pennarossa, G., Maffei S., Campagnol, M., Tarantini, L., Gandolfi, F., Brevini, T.A.L. 2013. Brief demethylation step allows the conversion of adult human skin fibroblasts into insulin-secreting cells. PNAS 110(22), 8948–8953.

ISSN: 2283-3927