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Subject: glycogen synthase kinase-3

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Links

Inhibition of glycogen synthase kinase-3 enhances the expression of alkaline phosphatase and insulin-like growth factor-1 in human primary dermal papilla cell culture and maintains mouse hair bulbs in organ culture.

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Dermal papilla (DP) at the hair follicle base is important for hair growth. Recent studies demonstrated that mouse vibrissa DP cells can be cultured in the presence of fibroblast growth factor-2 (FGF-2), but lose expression of versican and their follicle-inducing activity during the culture, and that activation of the Wnt signal, which is inhibited by glycogen synthase kinase-3 (GSK-3), in the DP cells promotes hair growth activity. We therefore investigated the influence of a GSK-3 inhibitor, (2'Z,3'E)-6-bromoindirubin-3'-oxime (BIO), on the growth of human DP cells and mouse vibrissa follicles in culture. We first demonstrated that, similarly to mouse DP cells, human DP cells were able to be cultured up to 15 passages in the presence of FGF-2, and lost the expression of alkaline phosphatase (ALP). When human DP cells later than ten passages were treated with BIO, the expression of ALP as well as insulin-like growth factor-1 (IGF-1), another DP marker, was significantly elevated. Nuclear and perinuclear translocation of beta-catenin was also observed. We then cultured mouse vibrissa follicles. In the presence of BIO, the follicles could be maintained for at least 3 days without detectable regression of the hair bulbs. The morphology and ALP expression were well preserved. BIO successfully retrieved the expression of DP marker molecules, such as ALP and IGF-1 in cultured human DP cells, and maintained mouse hair bulbs. Thus, treatment with BIO may be useful to prepare DP cells with hair follicle-inducing activity.

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