

Expression of polydom in dermal neurofibroma and surrounding dermis in von Recklinghausen's disease

Neurofibromas in von Recklinghausen's disease (vRD) can develop in the dermis. Therefore, we hypothesized that a dermal niche exists that promotes the development of these neurofibromas in subjects with vRD. Kamitani et al examined the function of polydom, known as a ligand for integrin, mediating cell adhesion, and expressed in mouse nerve tissue, in promotion of neurofibroma. Polydom mRNA levels were significantly higher in neurofibroma tissue than in control tissue. qRT-PCR analysis of RNA purified from primary cultured dermal neurofibroma cells demonstrated significantly higher polydom mRNA expression in cells derived from the surrounding dermis of neurofibromas. RNA sequencing was used to compare gene expression between cultured cells derived from dermal neurofibroma-surrounding tissue with or without polydom knockdown. Subsequent gene ontology assays revealed that ITGB8, a factor that releases TGF- β from pro-TGF- β , was downregulated following polydom knockdown, suggesting upregulation of polydom-mediated TGF- β production. Furthermore, we observed a strong association between polydom expression and the increase in PDGFB expression in primary cultured cells from the surrounding dermis of neurofibromas exposed to TGF- β 1.

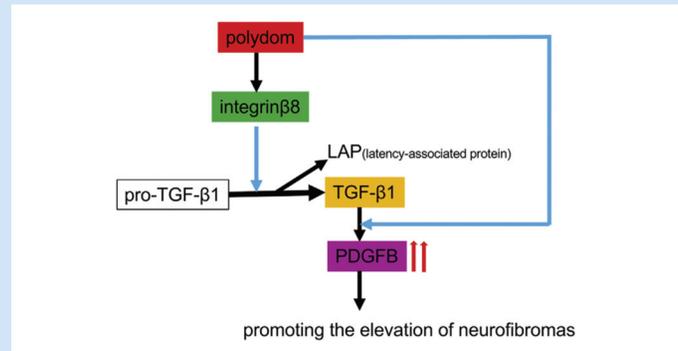


Fig. 4. Hypothesis. Increased polydom expression in the dermis leads to increased integrin β 8, resulting in higher TGF- β 1 levels, which leads to increased PDGFB. Polydom also facilitates the production of PDGFB mediated by TGF- β 1, and promotes neurofibroma development

3,6-Anhydro-L-galactose increases hyaluronic acid production via the EGFR and AMPK α signaling pathway in HaCaT keratinocytes.

Hyaluronic acid (HA) is an important factor in skin hydration maintenance. In mammalian keratinocytes, hyaluronan synthase 2 (HAS2) is a critical enzyme in HA production. Therefore, the promotion of HAS2 expression in keratinocytes may be a strategy for maintaining skin moisture. Lee JE et al determined the skin hydration effect and regulatory mechanisms of 3,6-anhydro-L-galactose (L-AHG), a main component of red macroalgal carbohydrates in human keratinocytes. L-AHG upregulates HA production and may enhance HAS2 expression by activating EGFR-mediated ERK, PI3K/Akt, and STAT3 signaling pathways. L-AHG activated the AMPK α signaling pathway which in turn could regulate HAS2 expression in HaCaT cells. The effects of L-AHG on HA production were observed in the 3D reconstructed human skin model. These results suggest that L-AHG may enhance skin moisture retention by increasing HA synthesis in human epidermal keratinocytes.

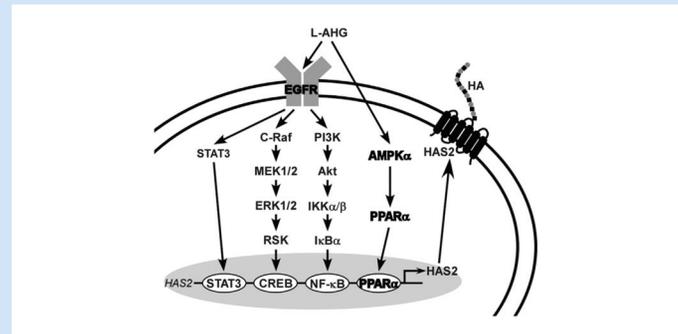


Fig. 6. Schematic diagram explaining skin moisturizing mechanisms of L-AHG. L-AHG enhances HA synthesis in HaCaT cells by inducing HAS2 expression, which in turn is upregulated by EGFR-mediated activation of the ERK, Akt, and STAT3 pathways and by EGFR-independent activation of the AMPK α signal pathway

Y-27632 preserves epidermal integrity in a human skin organ-culture (hSOC) system by regulating AKT and ERK signaling pathways

The human skin organ culture (hSOC) developed a century ago has been widely used to study various aspects of human skin development, differentiation, function, disease as well as skin appendages biology, however, maintaining the integrity of epidermal structure in long-term culture, has remained a challenge. Zhang X et al establish a culture system using supplemented William's E medium in the presence of a ROCK inhibitor Y-27632 to maintain epidermal architecture in the long-term hSOC and to investigate the underlying mechanisms. Y-27632 not only enhanced both basal cell proliferation and expression of suprabasal cell differentiation markers, but also maintained the balance of keratinocyte proliferation and differentiation through activation of AKT pathways on one hand and inhibition of ERK pathways on the other hand. The AKT inhibitor MK-2206 blocked the epidermal preservation effect of Y-27632, while the MEK/ERK inhibitor U0126 enhanced the preservation of epidermal structure in the hSOC. Y-27632 can maintain skin epidermal integrity through regulation of AKT and ERK activity in the hSOC.

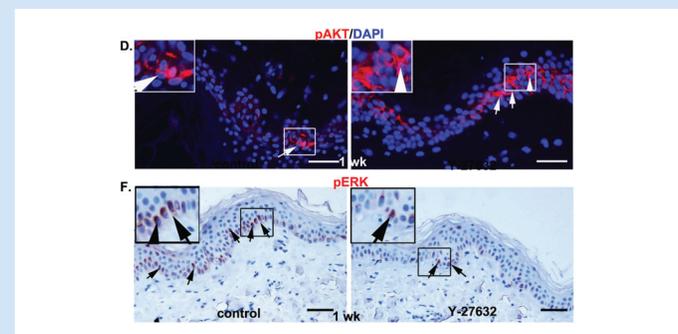


Fig. 5. Y-27632 increases AKT activation and inhibits ERK activity of keratinocytes cultured *in vitro* suspension assay. **D–G:** IF analysis of pAKT in **D**, IHC analysis of pERK in **F** in skins at 1 week of hSOC. The arrows indicate either pAKT or pERK positive cells. The insert in upper-left corner of each image is a zoom of the square area as indicated