

Functional implication of Wnt/beta-catenin signaling in keloid

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Numerous studies have shown that the Wingless type (Wnt) signaling pathways play key roles in various cellular functions including proliferation, differentiation, survival, apoptosis and migration. The aim of this study was to clarify the role of Wnt signaling pathway in keloid pathogenesis. Primary fibroblast cultures and tissue samples from keloid (KF) and normal appearing dermis (NF) were used. The expression of Wnt family members, frizzled (FZD)4 receptor, receptor tyrosine kinase-like orphan receptor (ROR)2 and the Wnt signaling downstream targets, glycogen synthase kinase (GSK)3-beta and beta-catenin were assessed using semi-quantitative RT-PCR, western blot, or immunohistochemical methods. We found that of the Wnt family members, Wnt5a mRNA and protein levels were elevated in KF as compared to NF. A higher expression of beta-catenin protein was also found in KF. No detectable levels of FZD4 receptor and ROR2 proteins were observed in both NF and KF. Functional analysis showed that treatment of NF and KF with recombinant Wnt5a peptide resulted in an increase in protein levels of total beta-catenin and phosphorylated beta-catenin at Ser33/37/Thr41 but no significant change in phosphorylated beta-catenin at Ser45/Thr41 positions. In addition, the expression of total GSK3-beta protein was not affected but its phosphorylated/inactivated form was increased in NF and KF. Inhibition of Wnt5a by specific anti-Wnt5a antibody reversed these effects. Taken together, these findings highlight a potential role for a Wnt/beta-catenin pathway triggered by Wnt5a in keloid pathogenesis. Wnt5a/beta-catenin signaling pathway may provide a new molecular target for developing therapeutic strategies for keloid.

Biography

Mohammad Ghazizadeh has completed his MD in 1975 and residency in urologic surgery in 1980. He has received his Doctor of Medical Sciences from the University of Tokushima School of Medicine, Japan in 1984. He is an Associate Professor and Chief at the Department of Molecular Pathology, Institute of Gerontology, Nippon Medical School, Japan. He has served as the Director of the Central Institute for Electron Microscopy Research at Nippon Medical School, Tokyo, Japan. He has published more than 100 papers in reputed journals and is serving as an editorial board member of the Journal of Nippon Medical School, The Open Dermatology Journal, World Journal of Dermatology, and Journal of Submicroscopic Cytology and Cytopathology.

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