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# Characterization of Wnt signaling pathways in keloid pathogenesis

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Keloid is an abnormal wound healing lesion characterized by fibroblastic cell proliferation and abundant collagen synthesis. Keloid develops after trauma, surgery, burns, acne, or injection and its etiologic factors are elusive. Most patients suffer from tenderness or pruritis as well as disfigurement, resulting in a severe negative impact on their quality of life. 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. To elucidate the role of Wnt signaling in keloid development and identify new molecular targets for therapeutic modulation, we studied 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-β and β-catenin 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 keloid fibroblasts (KF) as compared to normal fibroblasts (NF). A higher expression of β -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 β-catenin and phosphorylated β-catenin at Ser33/37/Thr 41 but no significant change in phosphorylated β-catenin at Thr 41/Ser 41 positions. In addition, the expression of total GSK3-β protein was not affected but its phosphorylated/inactivated form was increased in NF and KF. Our results demonstrated a higher expression of Wnt5a and β-catenin and inactivation of GSK3-β in KF but no detectable expressions of FZD4 and ROR2 receptors when compared to NF. These findings highlight a potential role for a Wnt/β-catenin canonical signaling pathway triggered by Wnt5a in keloid pathogenesis thereby providing a new molecular target for modulation to achieve normal wound healing in individuals susceptible to keloid formation.

## Biography

Mohammad Ghazizadeh has completed his MD at the age of 27 years from Jundi-Shapur University, School of Medicine and PhD at age 32 from the University of Tokushima School of Medicine in Japan. 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 Resaerch at Nippon Medical School, Tokyo, Japan. He has published more than 100 papers in reputed journals and served as an editorial board member of the Journal of Nippon Medical School, The Open Dermatology Journal and Journal of Submicroscopic Cytology and Cytopathology.

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