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Hair re-growth and wound-induced hair neogenesis by targeting CXXC5, a negative feedback regulator of the Wnt/beta-catenin signaling

The Wnt/β-catenin pathway has been implicated in hair follicle development and hair regeneration in adult life. Considering the significance of the Wnt/β-catenin pathway in hair regeneration, this pathway could be an ideal target for treating hair loss, including Androgenetic Alopecia (AGA). We recently determined that CXXC5 is a negative feedback regulator of the Wnt/β-catenin pathway that is involved in hair re-growth and Wound-Induced Hair Follicle Neogenesis (WIHN) via an interaction with Dishevelled (Dvl). We found an inverse correlation between β-catenin and CXXC5 expression in the balding human scalps of patients with AGA; β-Catenin expression was down-regulated and CXXC5 expression was up-regulated in the bald scalps, indicates the clinical implication of CXXC5 in the AGA pathogenesis. We also demonstrated that CXXC5 attenuated alkaline phosphatase activity and proliferation in human Hair Follicle Dermal Papilla Cells (HFDPCs) via Wnt3a-dependent induction and subsequent interaction withDvl-1. CXXC5-/- mice exhibited accelerated hair re-growth and treatment of the Wnt/β-catenin pathway activator further induced hair re-growth in the CXXC5-/- mice. In addition, induction of epithelial stem cell marker keratin 17 by in vivo blockade of CXXC5 function with Wnt/β-catenin pathway activation in mice wounds potentiated WIHN, a possible treatment of AGA caused by loss of hair follicle stem cell. A PTD-DBM peptide that specifically disrupted CXXC5 binding to Dvl enhanced promoted hair-regrowth and neogenesis and co-treatment with a combination of PTD-DBM and Wnt3a revealed further increment of the effects. The promotion effect much more hair regrowth than minoxidil, a currently FDA-approved treatment for hair loss. We also observed significant enhancement of WIHN together with induction of β-catenin and Fgf9, a growth factor involved in WIHN, after co-treating mice wounds with PTD-DBM and valproic acid, a GSK3β inhibitor. Overall, combination treatment with a Wnt/β-catenin pathway activator and the peptide that blocks the CXXC5-Dvl interaction may be a potential therapeutic strategy to promote hair regeneration and treat hair loss without side effects.

Biography

Kang-Yell Choi has been performed research related with cell signaling especially the Wnt/beta-catenin signaling related with the hair regeneration and wound healing, etc. Recently, he characterized CXXC5, a protein harboring the CXXC type zinc finger, as a negative feedback regulator or Wnt/□-catenin signaling functioning via binding Dishevelled. He investigated several different roles of CXXC5 such as wound healing and hair regeneration by performing both in vitro and in vivo studies by generating the CXXC5-/- mice. He is also an expertise in the development of small molecules inhibiting protein-protein interaction (cf. CXXC5-Dvl PPI), and performing research to apply those for therapeutic purposes including anti-cancer, wound healing and hair regeneration, etc.

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