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Understanding the regulation of Ror2-dependent pathway in hair follicle stem cells Veltri Anthony

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Multipotent adult stem cells (SCs) can self-renew and generate tissue-specific progenies to replenish an entire tissue during homeostasis and upon injury. To sustain this function throughout organism's life span, it is required to have a precise regulation between microenvironmental cues and intracellular signaling that balances SC quiescence and activation. Thus, investigating the underlying signaling pathways controlling this balance is fundamental to understand the regulation of SCs and tissue regeneration. Several signaling pathways have been indicated to regulate SC proliferation, differentiation and maintenance. Among those pathways, Wnt signaling is one of the major regulators across different adult SCs. However, while canonical Wnt/β-catenin pathway is broadly studied, the function of non-canonical Wnt pathways in adult SCs remains unclear. To unravel their unaddressed roles in SCs, we use murine hair follicles, which undergo cyclic bouts of growth, degeneration and rest, as a model to investigate the regulation of non-canonical Wnt signaling mediated by the tyrosine kinase-like orphan receptor 2 (Ror2) in hair follicle stem cells (HFSCs). We first examined Ror2 signaling activities in activated and quiescent HFSCs, and found elevation of Ror2 expression levels and its downstream JNK activity in activated HFSCs. To delineate Ror2-dependent regulation in HFSCs, we then generated a HFSC-specific conditional knockout (cKO) mouse line for Ror2, and characterized its functional significance in the regulation of HFSC behaviors. In doing so, we found deletion of Ror2 in activated HFSCs caused a delay of HFSC activation and hair cycle entry. By analysing purified Ror2 cKO HFSCs, we uncovered that cultured Ror2 cKO HFSCs displayed reduced self-renewal capacity and eventually underwent differentiation. More interestingly, using a double mutant strategy, we identified the collaborative effect of Ror2 and β-catenin in hair follicle fate determination. As a summary, our results together unravel previously unidentified function of Ror2-mediated signaling in regulation of HFSCs.

Biography

Veltri Anthony graduated in Biochemistry and Cellular and Molecular Biology. He has grown an interest in Cancer and Stem Cell Biology. In order to explore those research fields, he first joined the *In Vivo* Pharmacology Oncology Department at Thrombogenics. In order to expand his knowledge and skills in Stem Cells Research, he is pursuing a PhD in Stem Cells Biology at de Duve Institute. Under Dr. Wen-Hui Lien's supervision, he is investigating the potential role of a non-canonical Wnt signalling pathway in the regulation of hair follicle stem cells.

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