Dentistry 2017, 7:5 (Suppl)
http://dx.doi.org/10.4172/2161-1122-C1-015

Signaling involved in migration of blood vessels in early tooth development

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The vitality of a bio engineered tooth is a major challenge in Regenerative Dentistry. The importance of migration and development of blood vessels is essential for tooth survival and optimum function. Blood vessels are a mechanism for transferring oxygen, removing waste and providing a source of nutrients for the dental apparatus. Little research has undergone to understand the signaling involved in the migration of blood vessels in early tooth development. However, it is known that Wnt and TGFβ1 signaling are key pathways involved in tooth development. In this research we show that Wnt and Tgfβ1 control vascularization of the tooth by regulating the timing of endothelial cell migration into the dental papilla. In addition to these key signaling pathways, semaphorins have been reported to be involved in vascular patterning. The semaphorin class 3 family has been reported to be essential for regulating the vascular system, with mice with mutations in Semophorin 3F displaying vascular defects. Wnt4 and TGFβ1 have been shown to induce semaphoring-3A expression in the dental mesenchyme at early stages. Therefore, we aimed to analyze the molecular mechanisms by which Wnt and TGFβ regulate dental papilla vascularization and whether these signals act via regulation of semaphorin expression. Experiments performed in Mesp1cre/tdTomato mice, to provide live imaging of the forming vasculature, show that, Wnt and TGFβ signaling controls semaphoring-3F expression and influence endothelial cell migration into the dental papilla. Future experiments will address the interaction between Wnt and VEGF in dental papilla vascularization. We will analyze the role of cell migration and cell division in this process, taking advantage of time laps live imaging in Mesp1cre/tdTomato and Mesp1cre/Fucci2a tooth explants. This study further enhances our understanding of the underlying mechanism involved in the development of blood vessels in the tooth which will aid in the future of fabricating a successful bioengineered tooth.

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