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## Signaling involved in blood vessel regulation during 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 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 TGF $\beta$ 1 signaling are key pathways involved in tooth development. In this research, we show that Wnt and TGF $\beta$ 1 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 semaphorin 3F displaying vascular defects. Wnt4 and TGF $\beta$ 1 have been shown to induce semaphorin 3a expression in the dental mesenchyme at early stages. Therefore, we aimed to analyze the molecular mechanisms by which Wnt and TGF $\beta$  regulate dental papilla vascularization, and whether these signals act via regulation of semaphorin expression. Experiments performed in Mesp1cre/td Tomato mice, to provide live imaging of the forming vasculature, show that, Wnt and TGF $\beta$  signaling controls semaphorin 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/td Tomato 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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