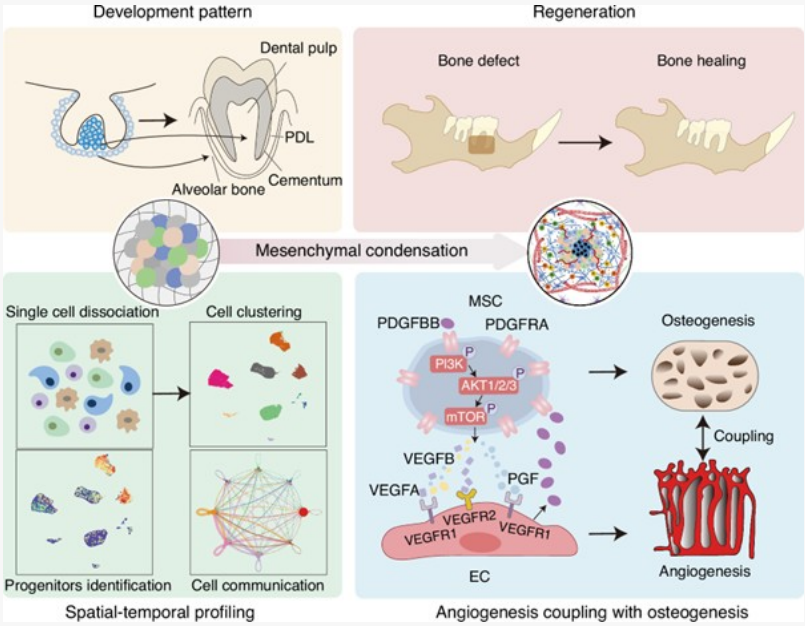
Osteogenesis – Angiogenesis Coupling via Interlineage Paracrine Signaling

Single-cell transcriptomics reveal a distinct type of progenitor cell that supports angiogenesis and odontogenesis, leading to periodontal bone regeneration.



Researchers used single-cell transcriptomics,bioinformatic and biological assays to reveal a unique interlineage crosstalk in dental regeneration.PDGFRA positive MSCs interact with ECs via VEGFA and PDGFBB which maintain the functionality of MSCs and drive angiogenesis.

CHINA, August 5, 2025 /EINPresswire.com/ -- The precise mechanism of cellular condensation and regeneration is not well-understood in organogenesis. For advances in regenerative medicine, understanding these mechanisms is crucial. In a new study, researchers used single-cell transcriptomics to understand the composition of human dental follicles and dental papillae. They found a PDGFRA+ mesenchymal stem cell with odontogenic potential that interacts with endothelial cells via paracrine signaling to stimulate angiogenesis, showing promise for future therapeutics in dental regenerative medicine.

Stem cell research, alongside the rapidly advancing field of biotechnology, has led to remarkable innovations in regenerative medicine. The principles of organization and development of organ systems, generation of complex functionalities, and intricate tissue topography have proven useful in creating unique therapeutic approaches in regenerative medicine. In particular, researchers have been drawn to a phenomenon called “cell condensation/aggregation,” where stem cells such as mesenchymal stem/stromal cells (MSCs) possess an inherent ability to form compact cell assemblies. By exploiting this mechanism, researchers have shown that inducing aggregation of cultured MSCs can boost their regenerate organ structures such as teeth through epithelial-mesenchymal inductionive potential. This regenerative approach may help address challenging oral health problems, especially periodontal bone defects that cause significant bone

damage and tissue loss.

During organogenesis, mesenchymal condensation helps create a signaling niche to recruit different interlineage progenitor cells to the specific region. For example, during tooth formation, the dental epithelium induces mesenchymal condensation in an environment that initially lacks vascularization. But the condensed mesenchyme then recruits endothelial progenitor cells (EPCs), which promote the assembly of vasculature in the tooth. However, the complex signaling mechanisms governing the interaction between MSCs and endothelial cells (ECs) that support tissue regeneration are not clearly understood.

Addressing this critical gap, a team of researchers including Dr. Fang Jin, Dr. Bingdong Sui, and Dr. Chenxi Zheng from The Fourth Military Medical University in China led a study to explore mesenchymal condensation-mediated tissue regeneration. They investigated the contribution of different stem cell types in the interlineage cell crosstalk in the context of tooth development and published their findings in the International Journal of Oral Science on 24 July 2025. Dr. Jin explains the methodological approach the team used for this study: “To tackle this complex issue, we employed single-cell RNA sequencing to explore the cellular composition and heterogeneity within the dental follicle and dental papilla developing tissues.” Using this technique, the team dissected the characteristic stem cell populations present in developing dental tissues in humans postnatally (after birth), such as dental follicle and dental papilla. Their results suggested that these two cell types have a common pool of stem cell populations.

Specifically, the stem cell populations known as dental follicle stem cells (DFSCs) and stem cells from apical papilla (SCAP) tissues exhibited similar molecular features, sharing 1,275 genes that were co-expressed in both stem cell types. To identify the genes that are specifically highly expressed in both these cell types to mark dental progenitor cells, the team performed a differential gene expression analysis and compared it with the rest of the cell populations. They found that platelet-derived growth factor receptor alpha (PDGFRA) was the only surface protein that was commonly expressed in these cell types, establishing the identity of MSCs. “As expected, PDGFRA showed expression specificity in DFSCs and SCAP and serves as a hallmark for common dental progenitor cells in DFSCs and SCAP in situ,” highlights Dr. Sui.

Further bioinformatic and biological assays demonstrated that ECs safeguard the functionality of PDGFRA+ MSCs via platelet-derived growth factor subunit BB (PDGFBB) and contribute to dental development. The PDGFRA+ MSCs in turn interact with CD31+ endomucin+ ECs via vascular endothelial growth factor A (VEGFA). This paracrine signaling mediates the formation of blood vessels during the development of periodontal development. Talking about the team’s findings in an in vivo donor-recipient bone regeneration experiment, Dr. Zheng explains, “Our in vivo experiments confirm that implanted PDGFRA+ cell aggregates persist in the recipient microenvironment, secrete factors aiding in angiogenesis, and potentially stimulate ECs to release PDGFBB for their own functional maintenance.” This communication between MSCs and ECs drives an active communication network that improves angiogenesis and osteogenesis and rapidly repairs the periodontal defects in their experiment.

Overall, the study reveals a specialized mesenchymal-endothelial crosstalk related to odontogenic condensation that could contribute to effective tissue regeneration, with potential applications in dental therapeutic strategies and even regenerative medicine in a broader context.

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Reference
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