P53-PDGF Signaling Regulates Vasculatures To Control The Heterogeneity Of MSCs

Tingwei Guo, Fei Pei, Mingyi Zhang, Takahiko Yamada, Jifan Feng, Junjun Jing, Thach-Vu Ho, Yang Chai Center for Craniofacial Molecular Biology, Herman Ostrow School of Dentistry, USC School of Dentistry

BACKGROUND

Center for

Biology

Craniofacial Molecular

Microenvironmental cues provided by stem cell niches are important for regulating the fate of mesenchymal stem cells (MSCs), and the detailed mechanisms of the crosstalk between them are of significant interest. Blood and lymphatic vasculature have well-known roles in transporting oxygen and nutrients, as well as removing waste and CO2. However, the vasculature's role as a niche component in regulating MSCs remains largely unclear.

PURPOSE

To investigate the role of vasculature in regulating stem cell homeostasis in adult tissue.

MATERIAL AND METHOD

The transgenic mouse model used in this study is Gli1-CreER^{T2};Trp53^{fl/fl}. Cellular and molecular experiments used in this study included immunohistochemistry, in situ hybridization. CoIP. RNA-seq. scRNA-seq and ChIPaPCR.

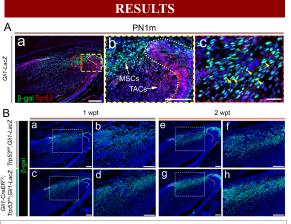


Fig 1. Loss of Trp53 in GLI1+ lineage cells results in impaired tissue homeostasis of adult mouse incisor.

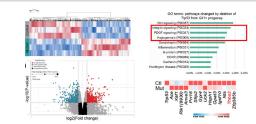


Fig 2. Deletion of Trp53 in the GLI1+ cells alters gene expression profile and pathways related to vasculatures are mostly affected.

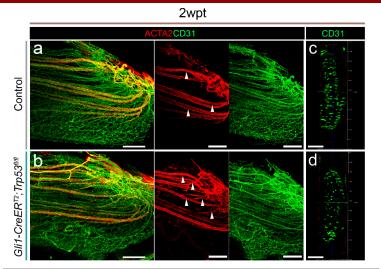


Fig 3. Trp53 alters vasculature in adult mouse incisor.

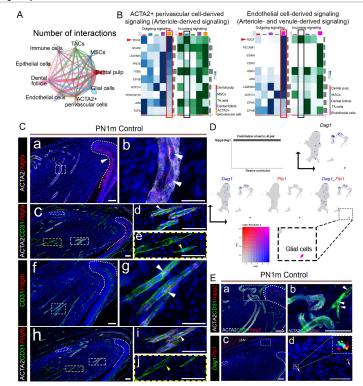
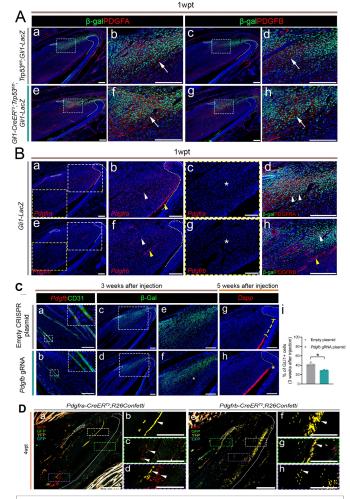


Fig 4. Different vessels may regulate different subpopulations of MSCs and PDGF signaling derived from arteries regulate MSCs in adult mouse incisor.



the Herman Ostrow

of USC

Fig 5. PDGFRA+ and PDGFRB+ cells differentially contribute to defined cell lineages in the adult mouse incisor.

CONCLUSION

This study shows how different vessels can provide unique microenvironmental cues to regulate subpopulations of MSCs and maintain their heterogeneity, and establishes mechanistic insight into the crosstalk between vasculature and mesenchymal stem cells.

ACKNOWLEDGEMENTS

We appreciate the funding support from the National Institute of Dental and Craniofacial Research, National Institutes of Health (R01 DE012711, R01 DE025221, and U01 DE028729 to Yang Chai).