A vast stem-progenitor cell pool, richly vascular system and hybrid ossification drive the daily centimeter-scale elongation of bony antlers

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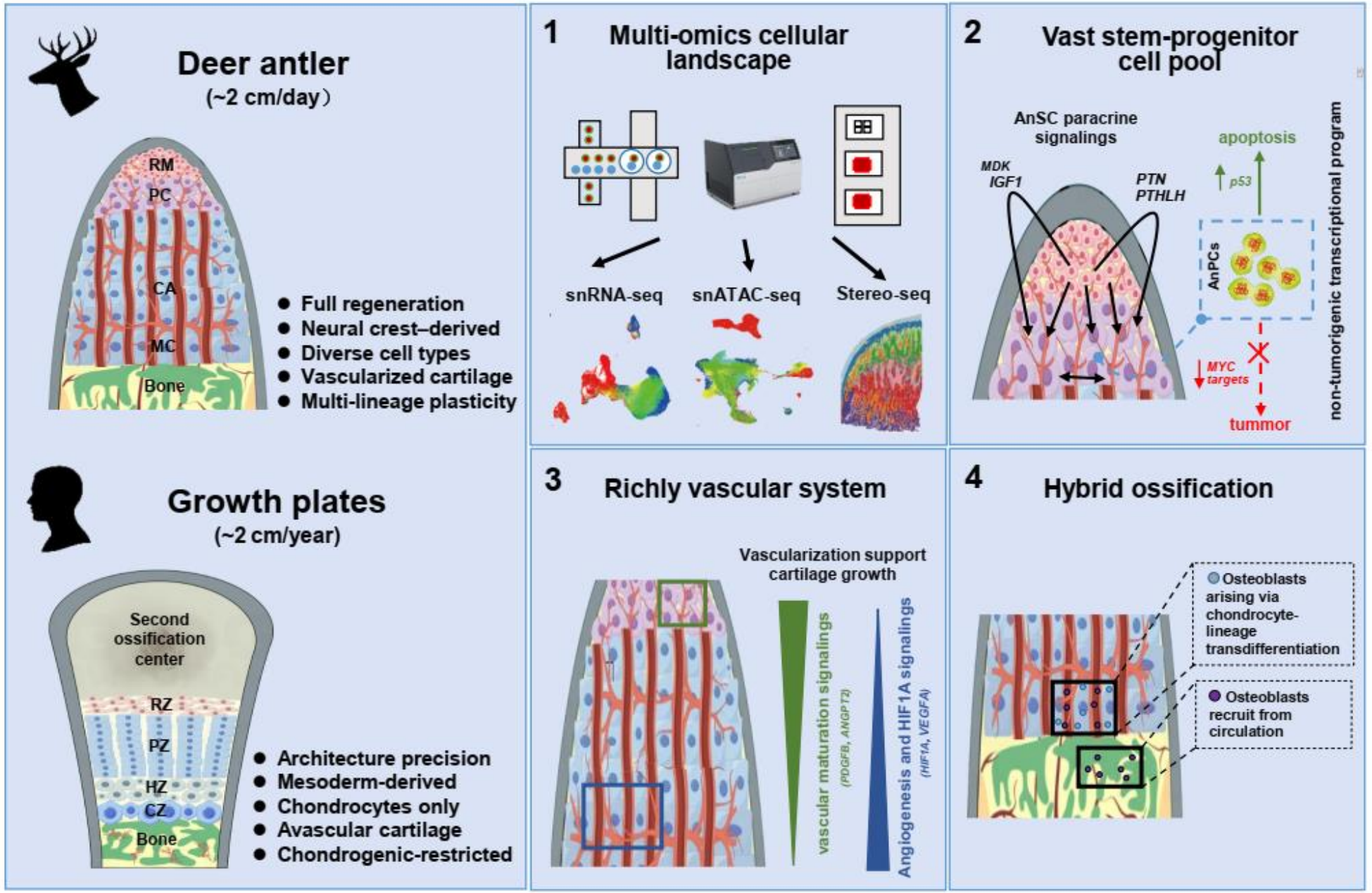
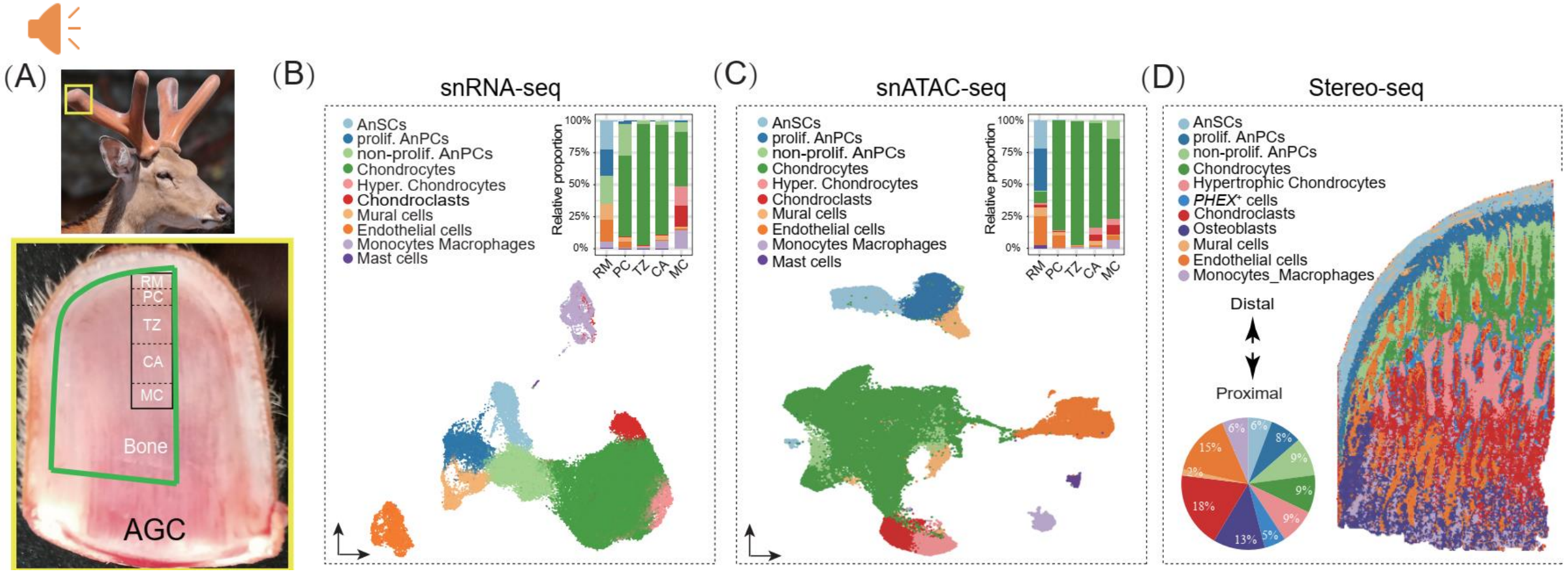
Introduction



Multi-omics atlas of the AGC cellular landscape



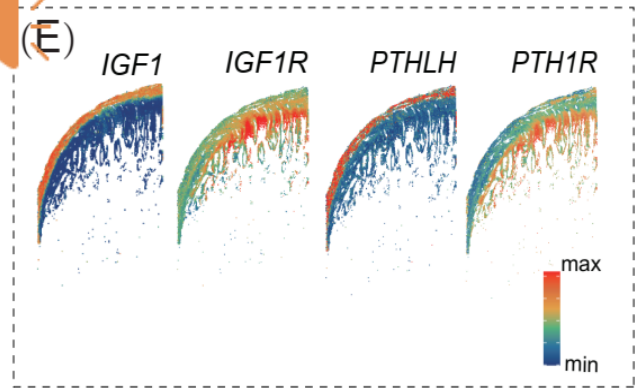
(A) Anatomical structure of the AGC and sampling sites for the three omics datasets (snRNA-seq, snATAC-seq, and Stereo-seq). The AGC consists of five layers from distal to proximal: RM, PC, TZ, CA, and MC

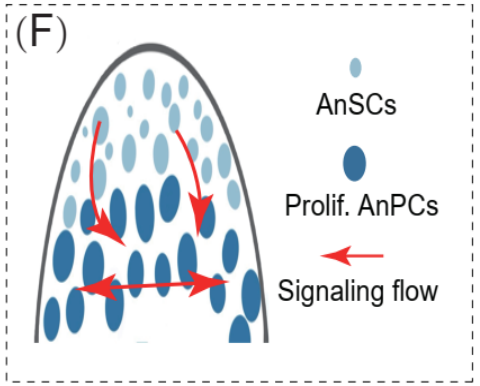
(B) UMAP of the snRNA-seq data showing ten cell types and their distribution across the five layers

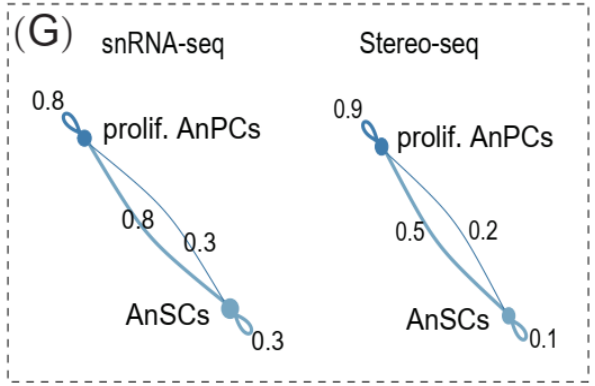
(C) snATAC-seq reveals corresponding cell types and similar distribution patterns

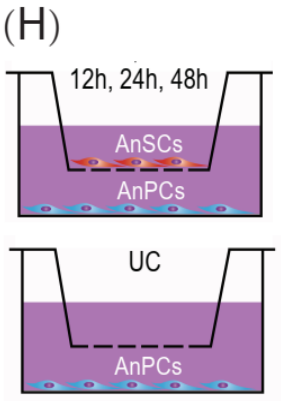
(D) Stereo-seq maps the spatial localization and proportions of 11 cell types

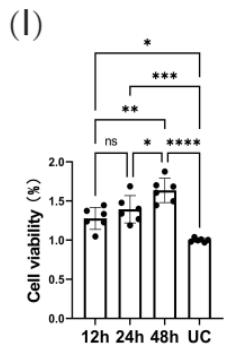
AnSC-mediated AnPC proliferation, and AnPC demonstrate transcriptomic programs distinct from osteosarcoma

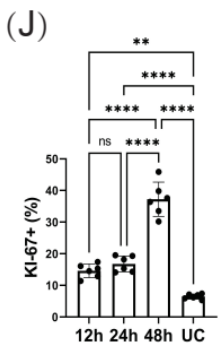


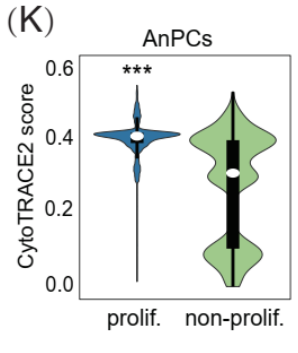


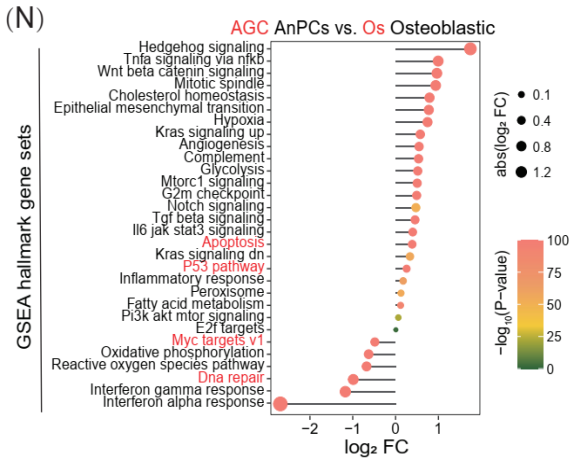


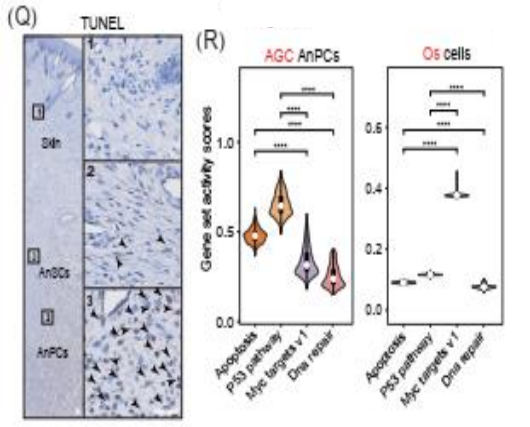


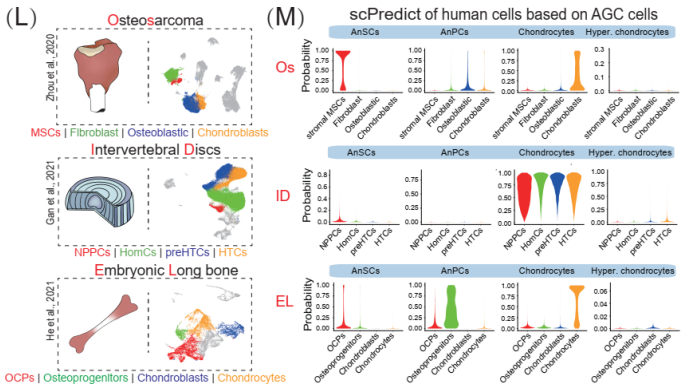


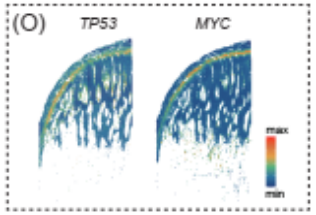


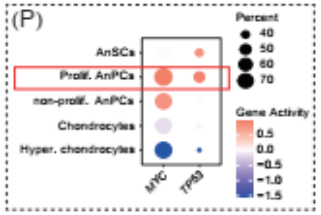


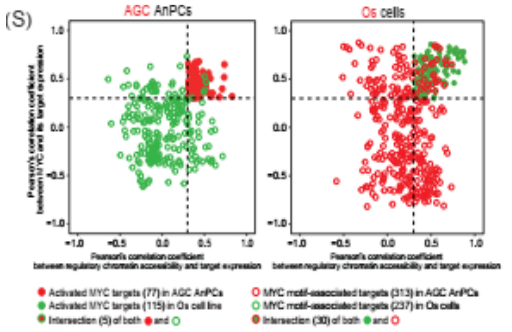






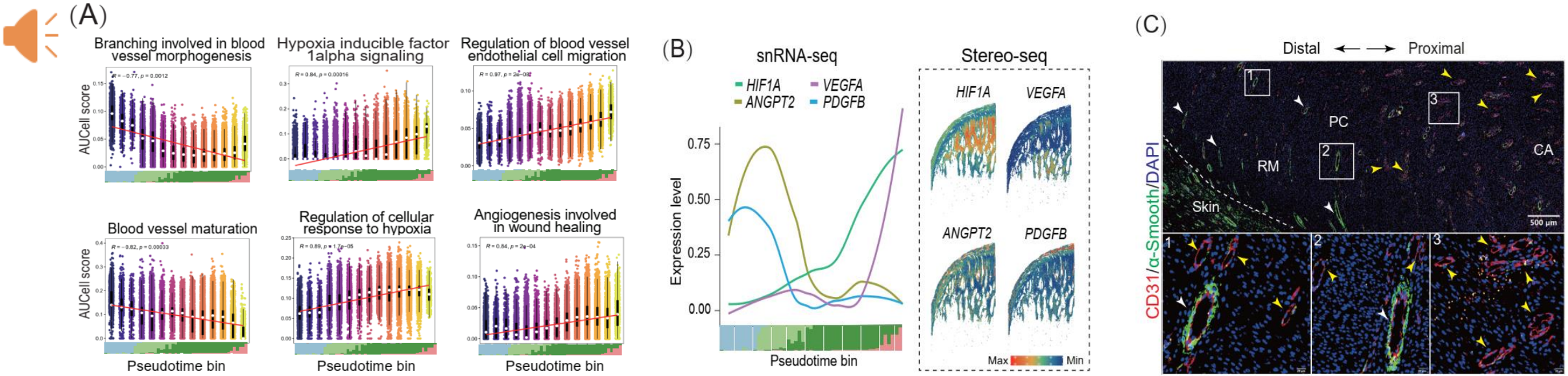


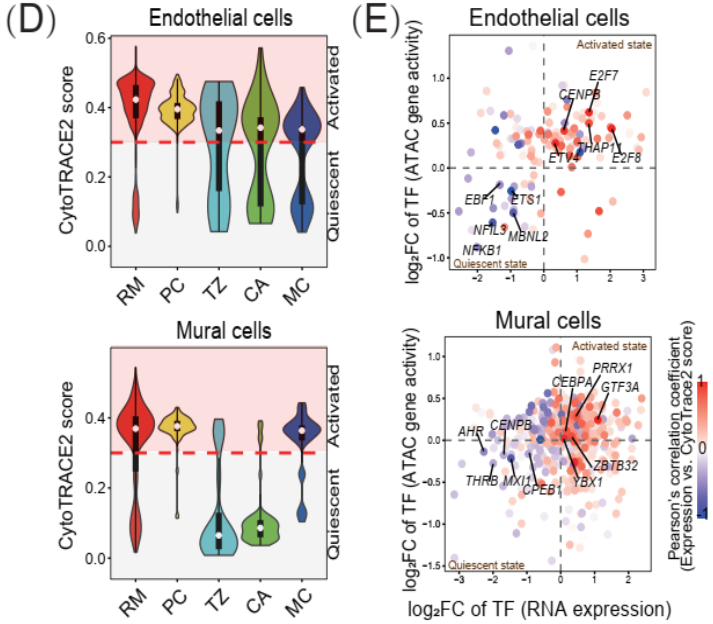




(E–G) Signaling pathways and cell–cell communication
(H–J) Functional validation: AnSCs promote AnPC proliferation
(K) Stemness and proliferative capacity.
(L–M) Comparison with bone development
(N) Pathway comparison with osteosarcoma
(O–P) TP53 and MYC expression and chromatin accessibility
(Q) Apoptosis in AnPCs
(R) accessibility score comparison
(S) Comparison of MYC target genes

AnSC-derived cells create a vascularized niche that drives vascular development





(A) AUCell dynamics of vascular development in AnSC-derived cells along pseudotime

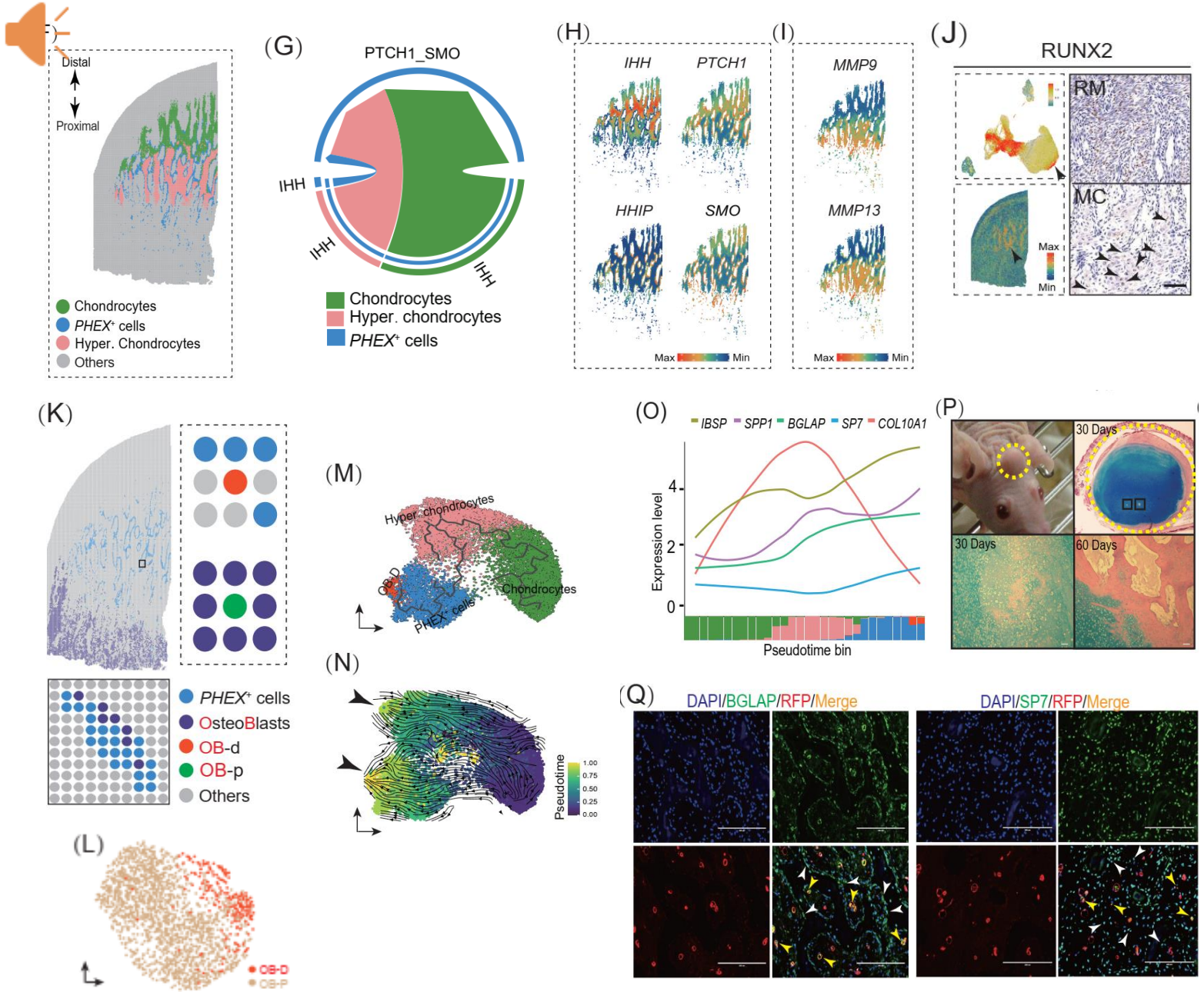
(B) Expression dynamics of key marker genes in snRNA-seq and Stereo-seq.

(C) AGC immunofluorescence showing blood vessel formation and mature vascular structures

(D) CytoTRACE2 activation levels of endothelial and perivascular cells across the five layers

(E) Scatter plot of TFs associated with activation or quiescence, showing TF expression versus CytoTRACE2 Pearson correlation, highlighting the top five TFs

PHEX⁺cells promote cartilage mineralization via Hedgehog signaling and may serve as intermediates in the direct conversion of hypertrophic chondrocytes to osteoblasts



(F) Spatial distribution of chondrocytes, hypertrophic chondrocytes, and PHEX⁺ cells

(G–H) Hedgehog (HH) signaling interactions among the three cell types and spatial expression of key HH pathway genes

(I) Spatial localization of MMP9 and MMP13.

(J) RUNX2 UMAP, spatial expression, and immunohistochemistry validation (positive in RM and MC)

(K–L) Spatial relationship between PHEX⁺ cells and osteoblasts (OB-p and OB-d).

(M–N) Differentiation trajectory: chondrocytes → hypertrophic chondrocytes → PHEX⁺ → OB-d, with endpoints at hypertrophic chondrocytes and OB-d

(O) Expression dynamics of marker genes along pseudotime

(P) Avascular cartilage transplantation model showing cartilage nodules and early osteogenesis at 30–60 days

(Q) Vascularized cartilage model (60 days) showing origins of OB-p and OB-d and participation of host RFP⁺ vascular cells in vessel formation

Conclusion

Deer antlers achieve extreme centimeter-scale daily bone growth through expanded stem/progenitor cell proliferation zones, low tumorigenicity, minimal mechanical load, and regenerative vascularization, combined with hybrid ossification via chondrocyte-lineage transdifferentiation into osteoblasts, whereas growth plates remain avascular, mechanically robust, and undergo terminal differentiation.

Future studies should explore whether these mechanisms can be harnessed to promote rapid regeneration and repair of human bone tissue in clinical settings.

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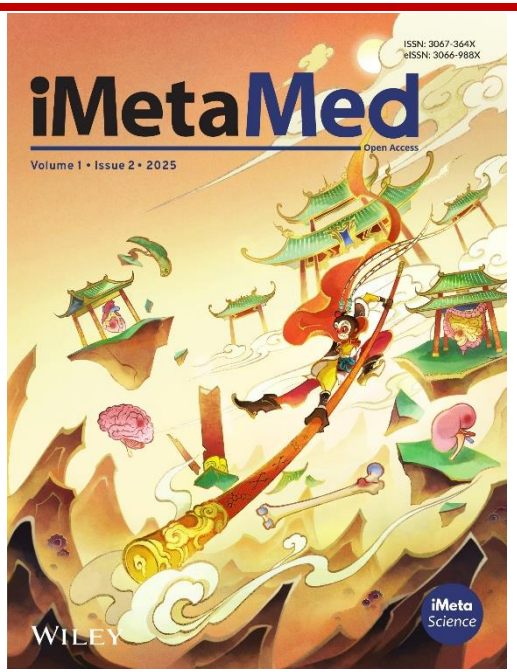

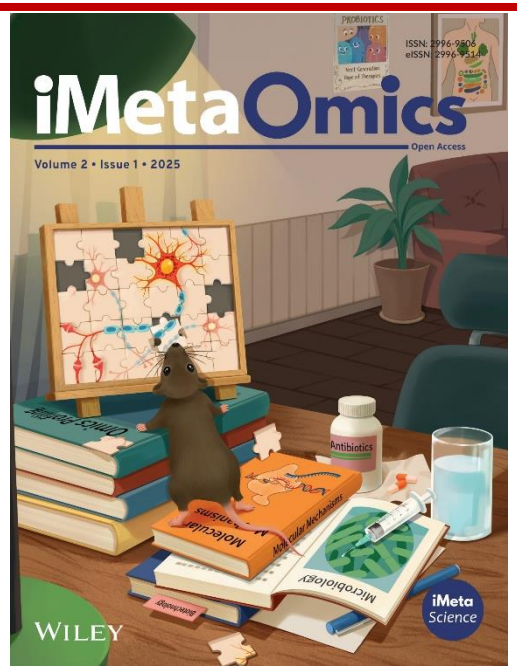

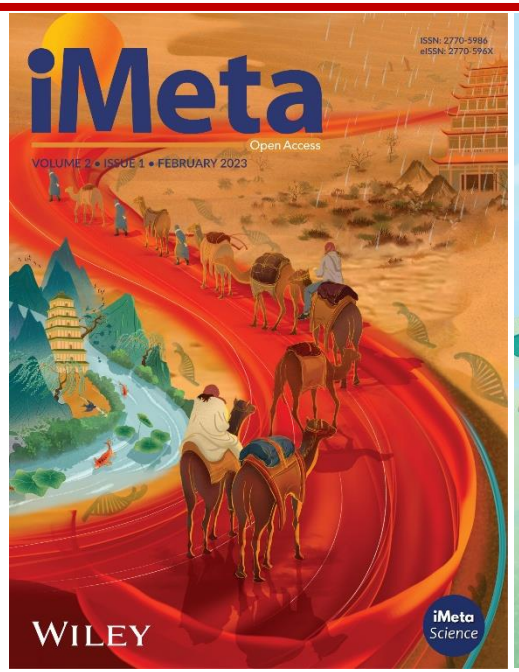

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