

# Single-cell sequencing reveals the role of *IL-33*<sup>+</sup> endothelial subsets in promoting early gastric cancer progression

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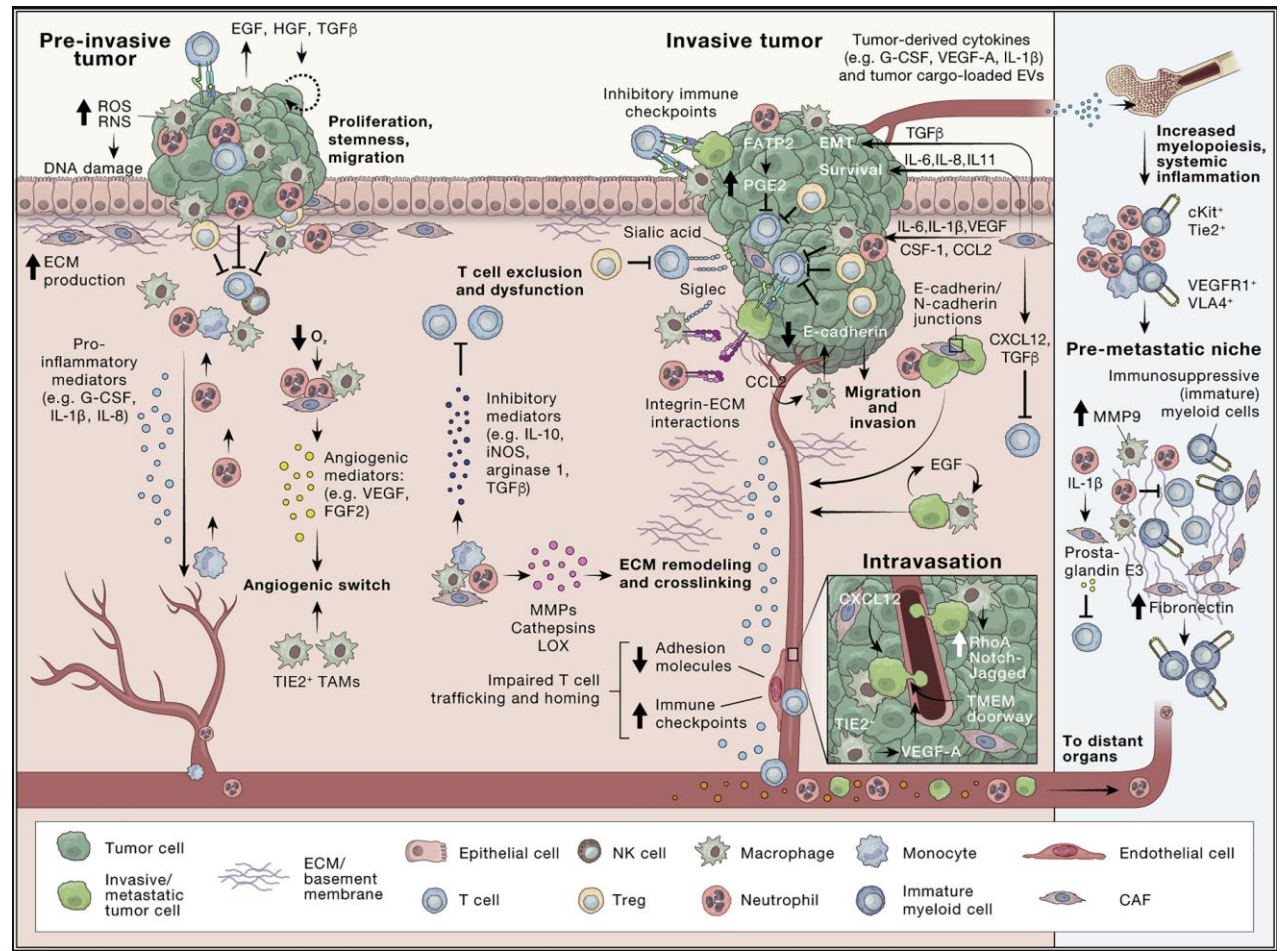
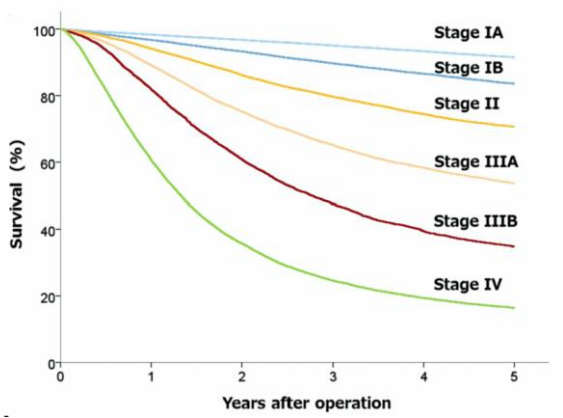
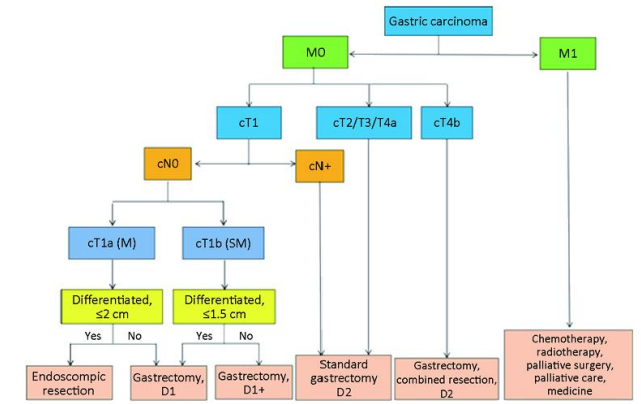
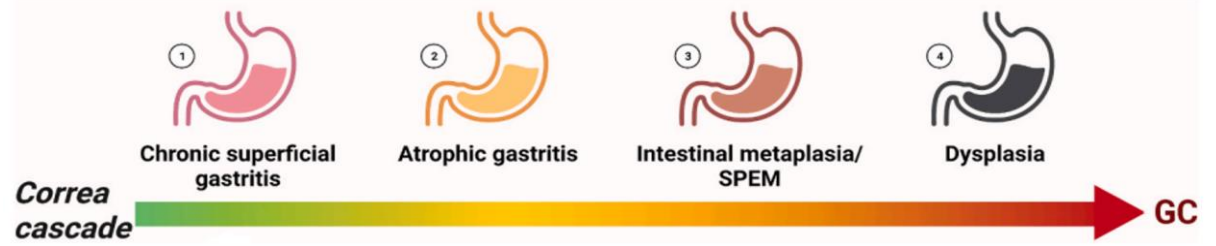
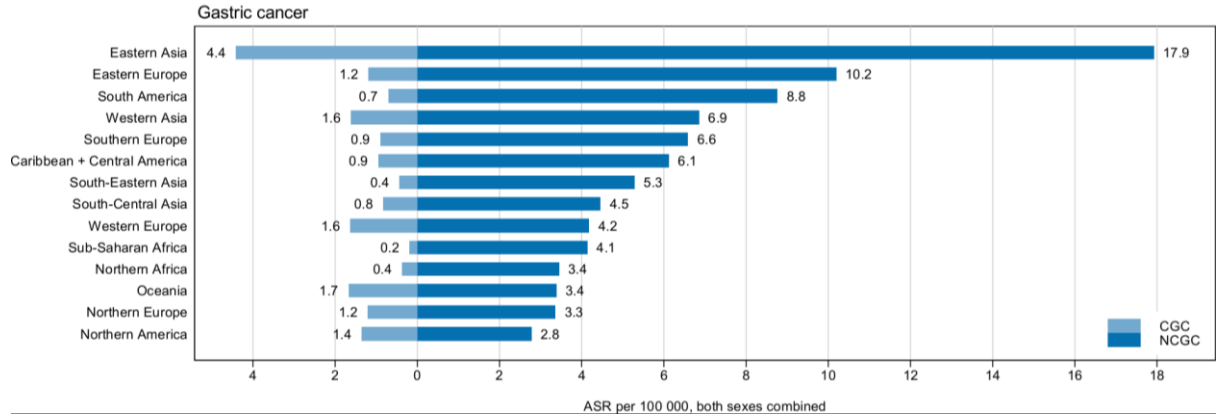
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Li Zhou, Mei Yang, Chao Deng, Song He, Zhihang Zhou. 2025. Single-cell sequencing reveals the role of *IL-33*<sup>+</sup> endothelial subsets in promoting early gastric cancer progression. *iMeta* 4: e70050. <https://doi.org/10.1002/imt2.70050>.

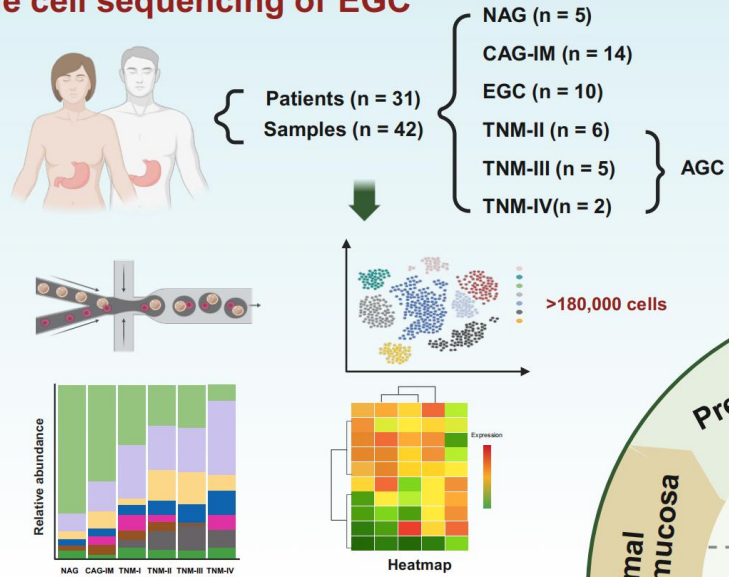
# Introduction



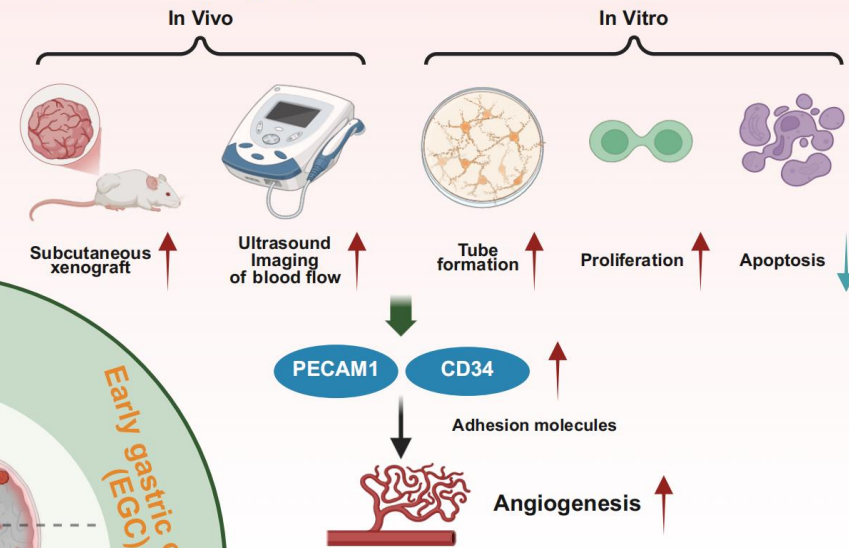
Early gastric cancer (EGC); Advanced gastric cancer (AGC).

# Highlights

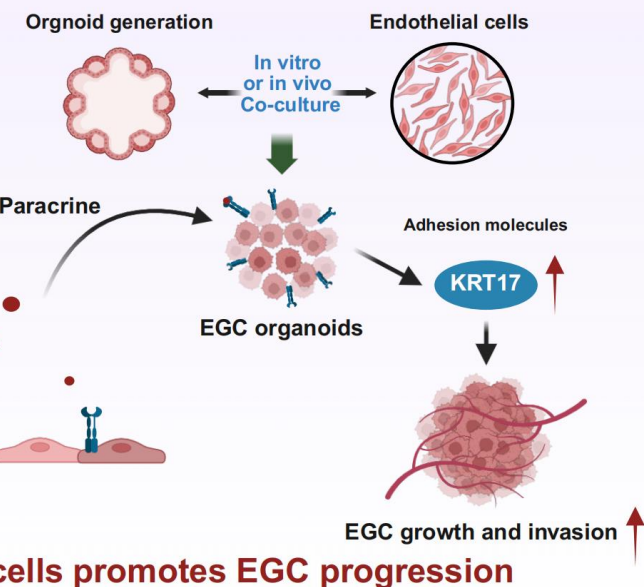
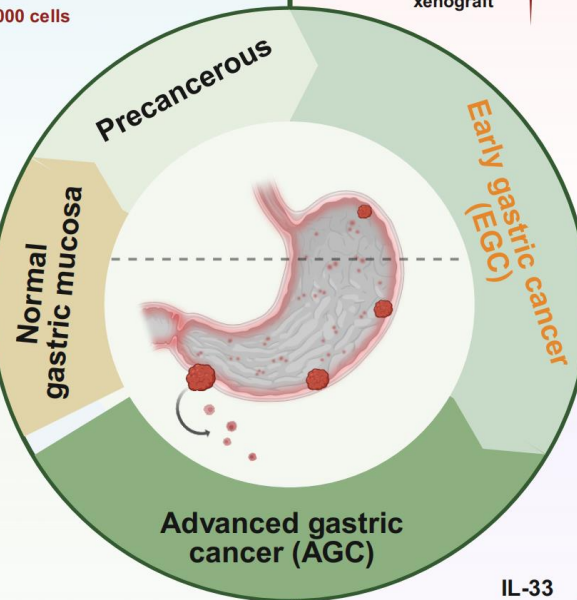
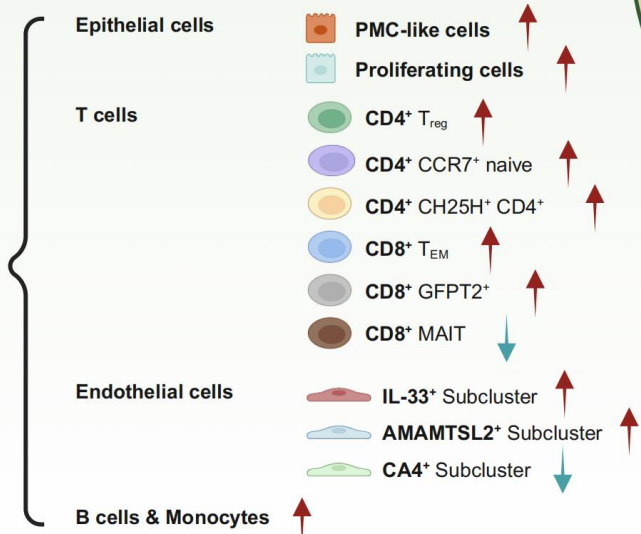
## Single cell sequencing of EGC



## IL-33 promotes angiogenesis



## Altered subpopulations in EGC



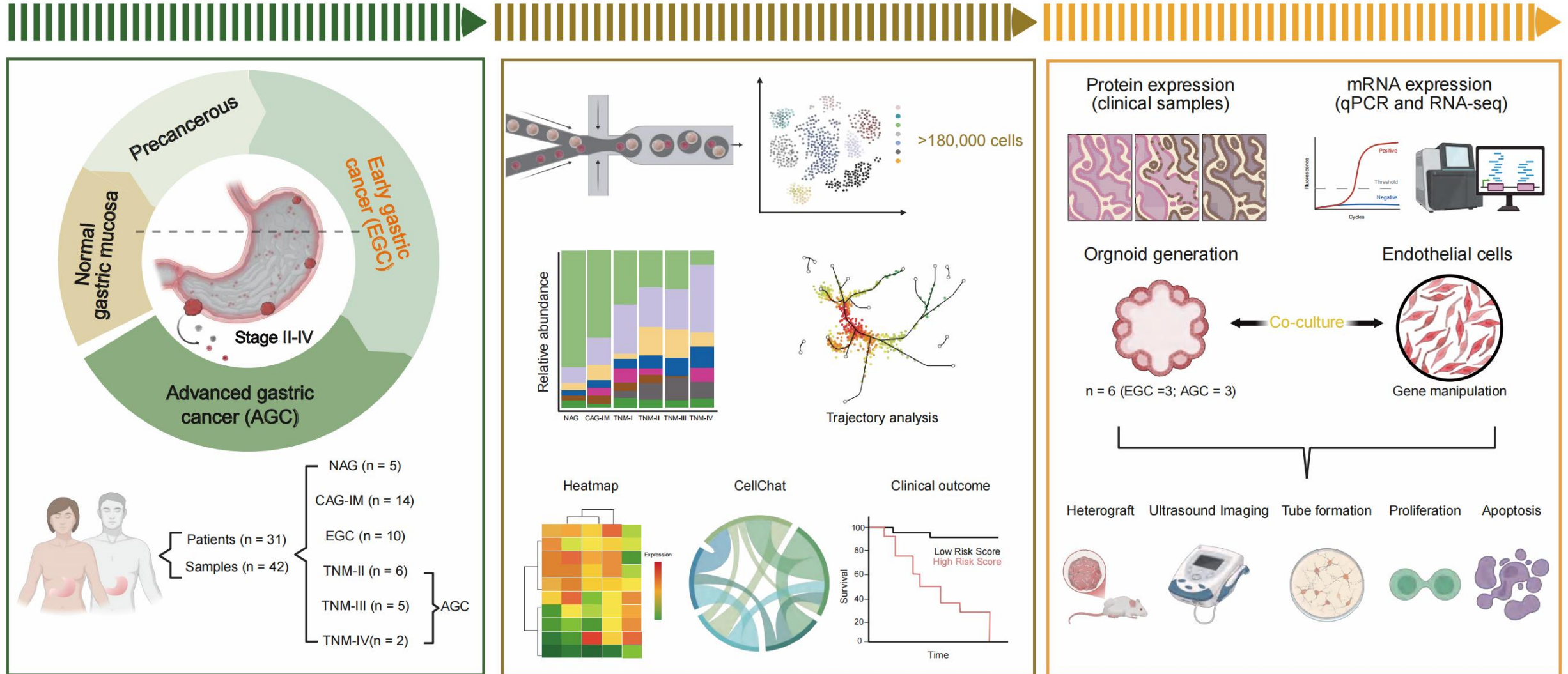
# Overview of study design

(A)

Multi-stage sampling

10X scRNA-seq

Characteristic validation & clinical associations



# A single-cell atlas of the progression from gastritis to GC

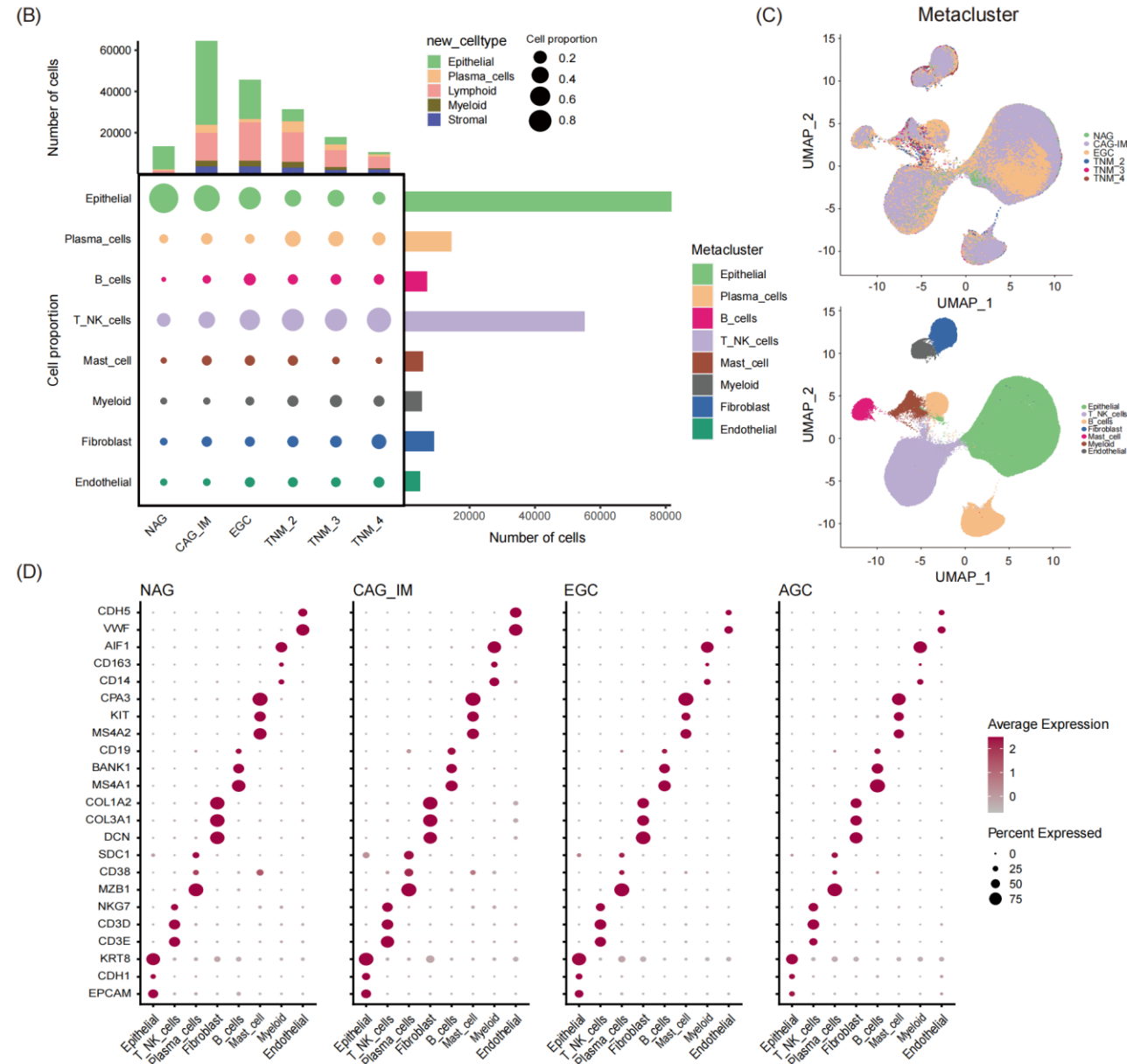


Figure 1. A single-cell atlas of the progression from gastritis to gastric cancer (GC).

# The number of PMC-like and PC subclusters among epithelial cells increased in EGC

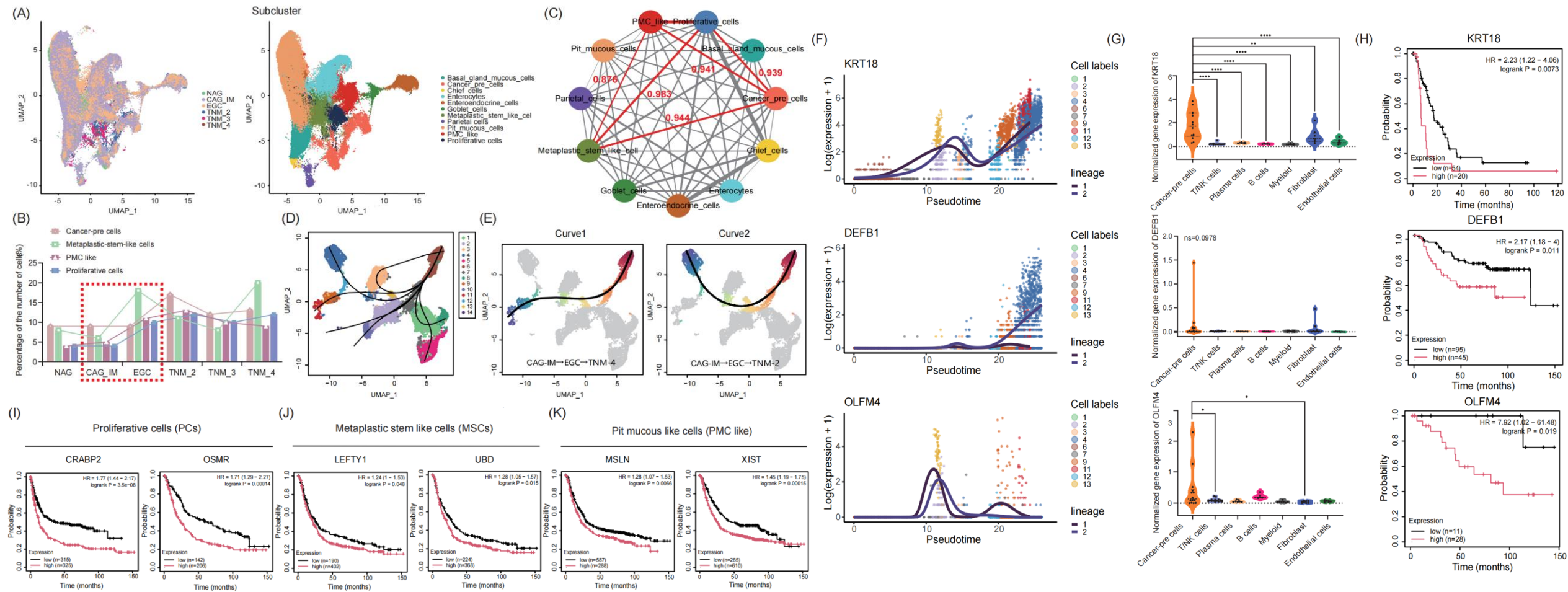


Figure 2. The number of pit mucous-like cells (PMC-like) and proliferating cell (PC) subclusters among epithelial cells increased in early gastric cancer.

# $T_{reg}$ , $CCR7^+$ naive, $CH25H^+$ $CD4^+$ , $T_{EM}$ $CD8^+$ , and $GFPT2^+$ $CD8^+$ T cells increased, whereas MAIT $CD8^+$ T cells decreased in EGC

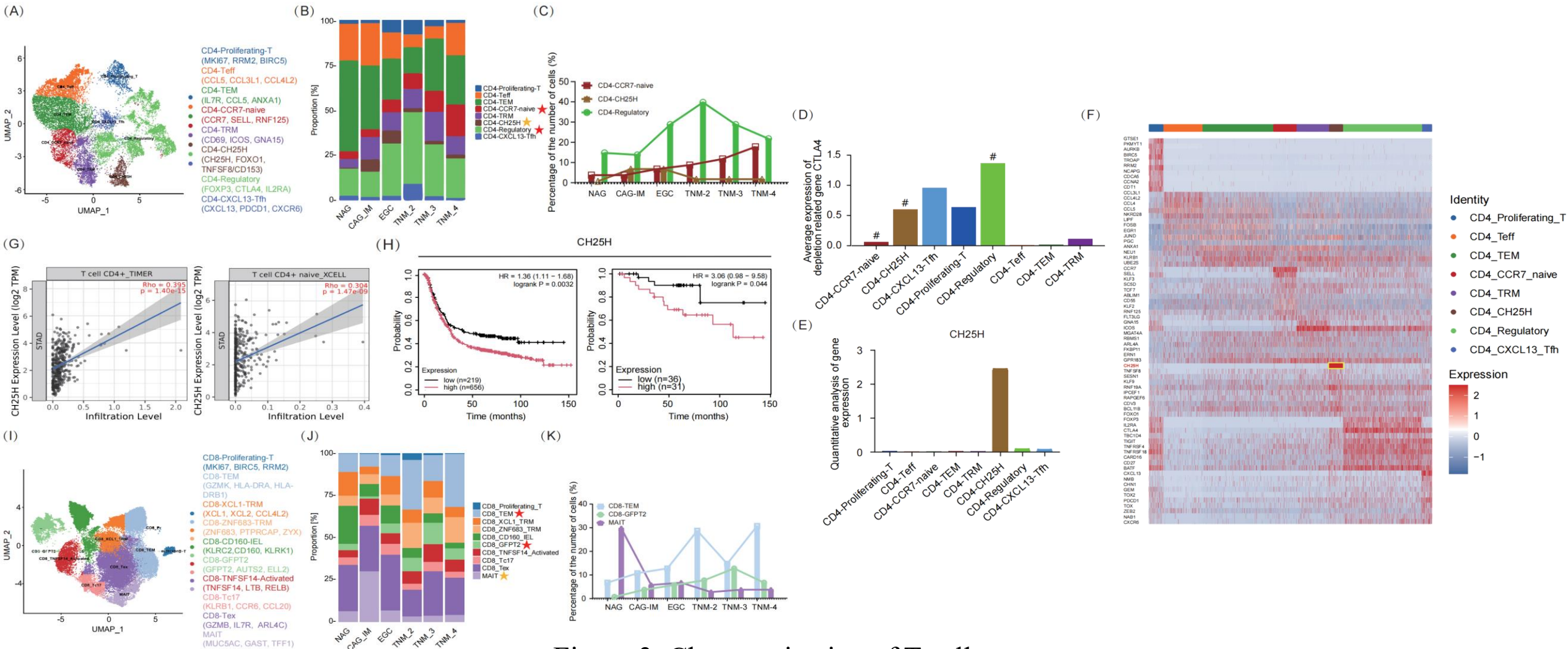


Figure 3. Characterization of T cell states.

# Fibroblasts remain stable in EGC

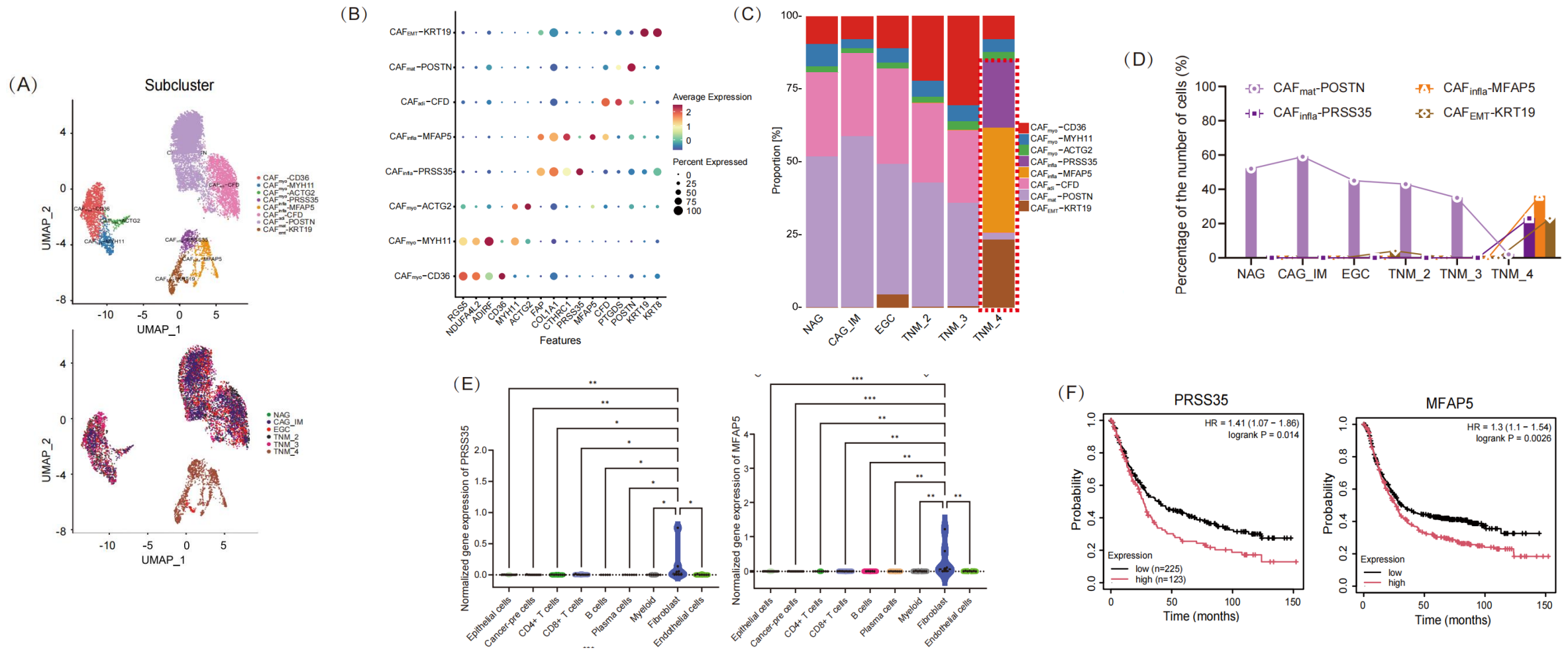


Figure 4. Stromal cell remodeling in GC progression.

# The proportions of *IL-33*<sup>+</sup> Venous-1 and *ADAMTSL2*<sup>+</sup> Artery-2 increased, whereas those of *CA4*<sup>+</sup> Capillary-2 dramatically decreased in EGC

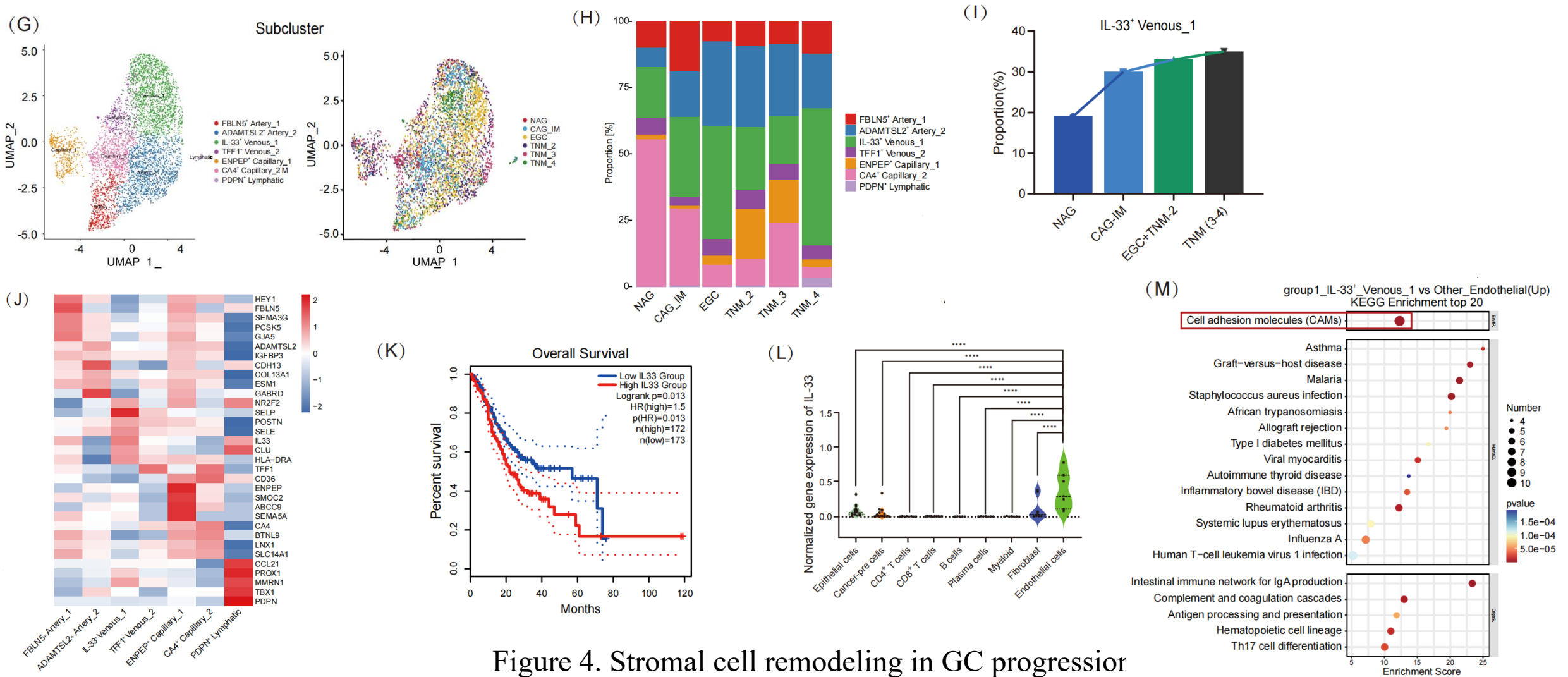


Figure 4. Stromal cell remodeling in GC progressior

# IL-33 enhances angiogenesis, and *IL-33*<sup>+</sup> endothelial cells promote the growth of both EGC and AGC organoids *ex vitro*

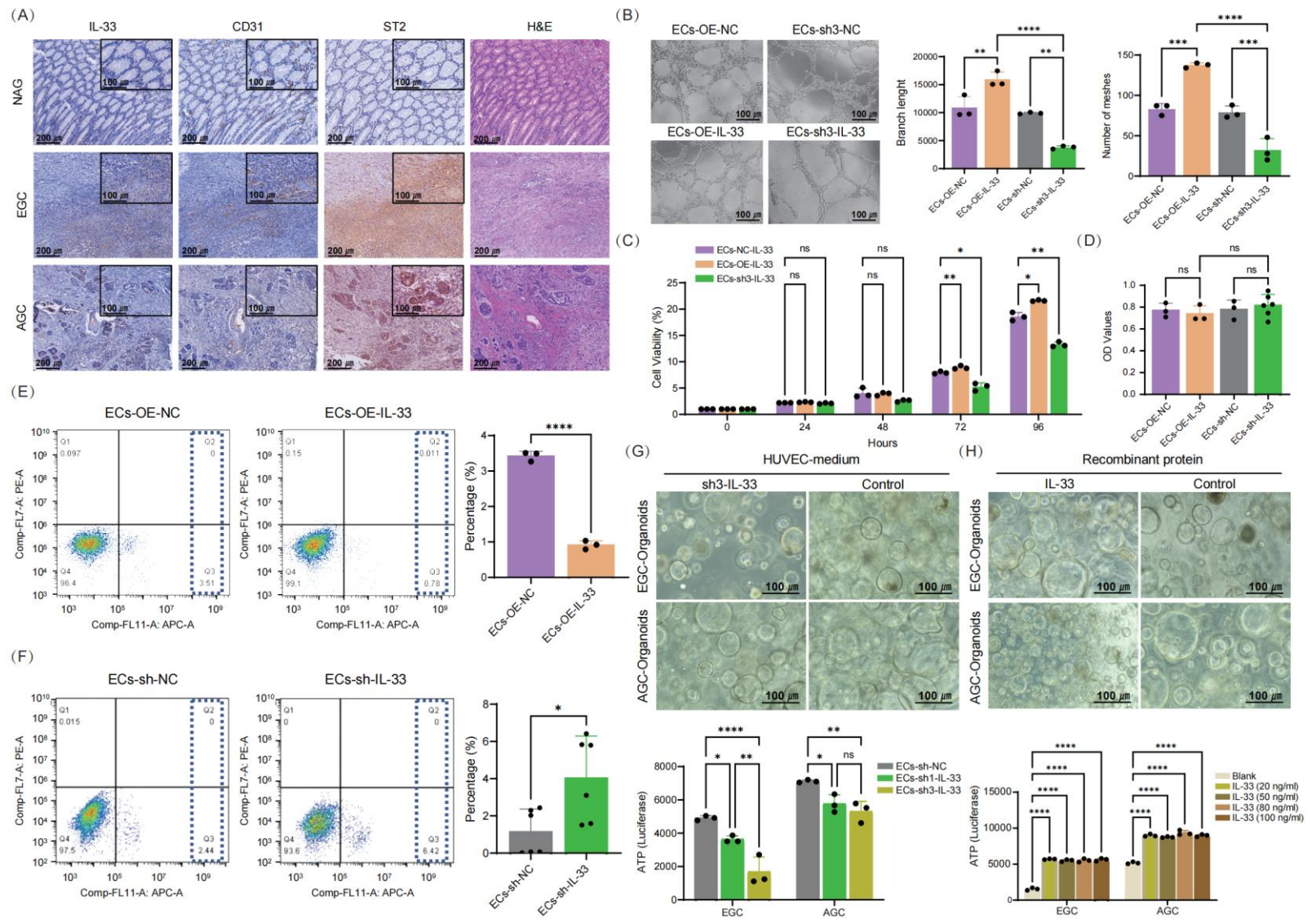


Figure 5. IL-33 drives endothelial angiogenesis, and *IL-33*<sup>+</sup> endothelial cells (ECs) promote EGC and AGC growth *ex vitro*.

# IL-33 enhances angiogenesis, and *IL-33*<sup>+</sup> endothelial cells promote the growth of both EGC and AGC organoids *in vivo*

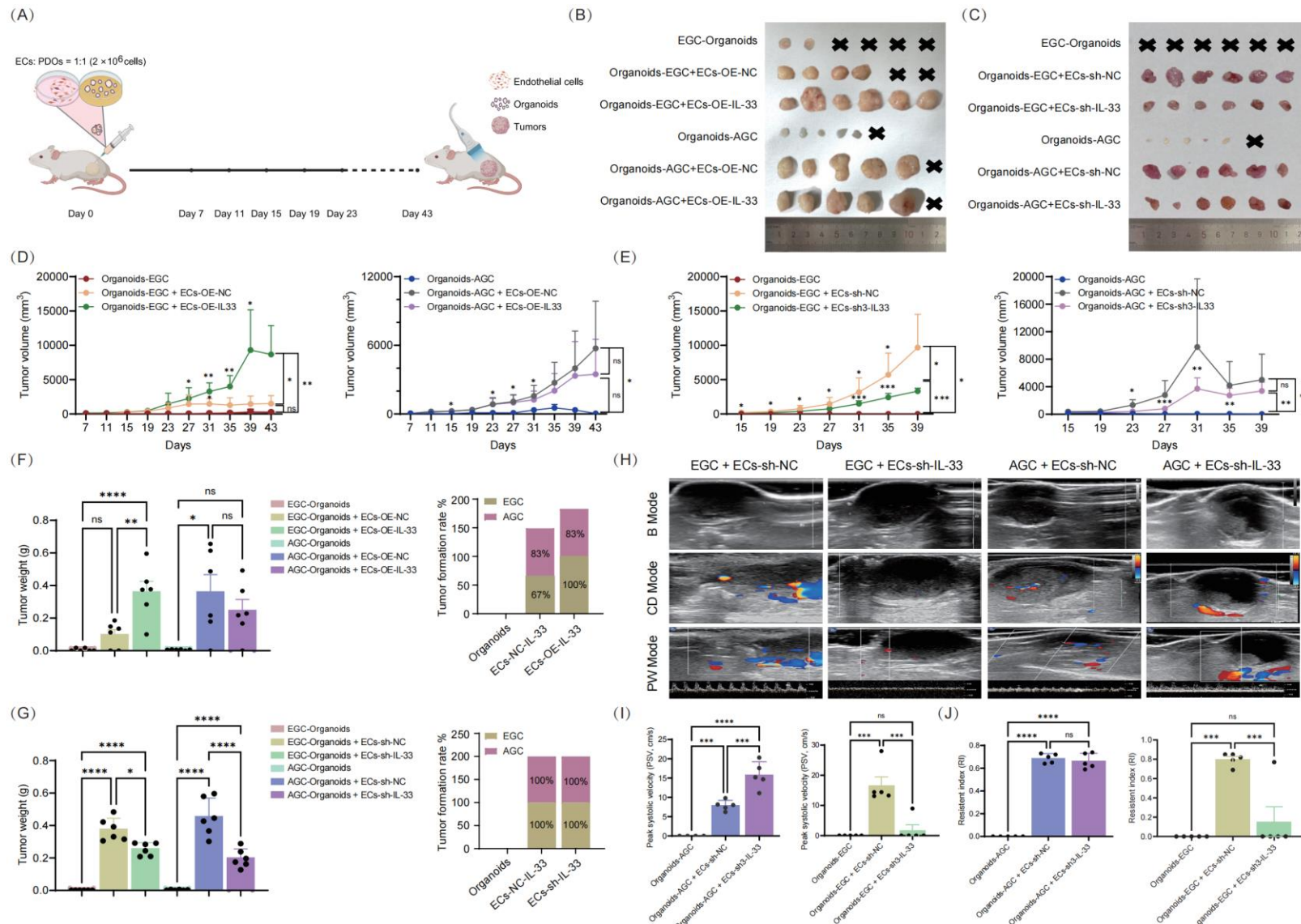


Figure 6. *IL-33*<sup>+</sup> ECs promote EGC and advanced gastric cancer angiogenesis and growth *in vivo*.

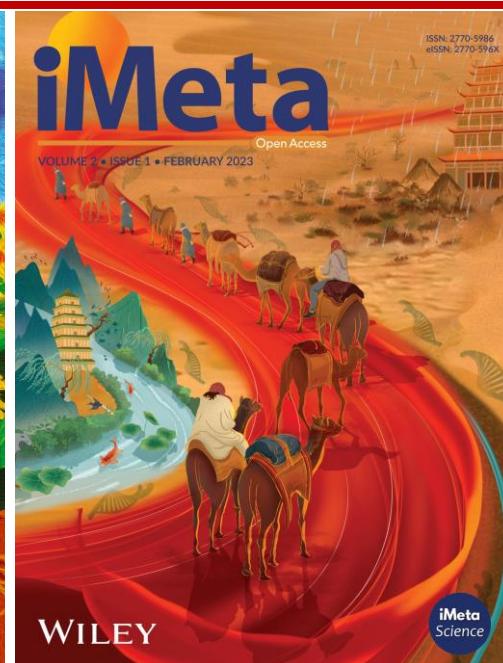




# Summary

- ❑ As one of the most comprehensive single-cell sequencing studies to date for EGC, our study provides a unique resource for generating novel biological insights into tumor cell types, subtype-based TME compositions, and cell–cell interactions in EGC.
- ❑ Mechanistically, IL-33 enhances the survival and angiogenesis of endothelial cells by upregulating the adhesion proteins PECAM1 and CD34. Endothelial-derived IL-33 could also promote the growth of EGC organoids through increasing KRT17 expression.
- ❑ Notably, we also found that high expression of IL-33 was positively correlated with the depth of invasion and malignancy of EGC in the clinic.

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