# Microbiota humanization drives human-like metabolic and immune transcriptomic shifts in pigs

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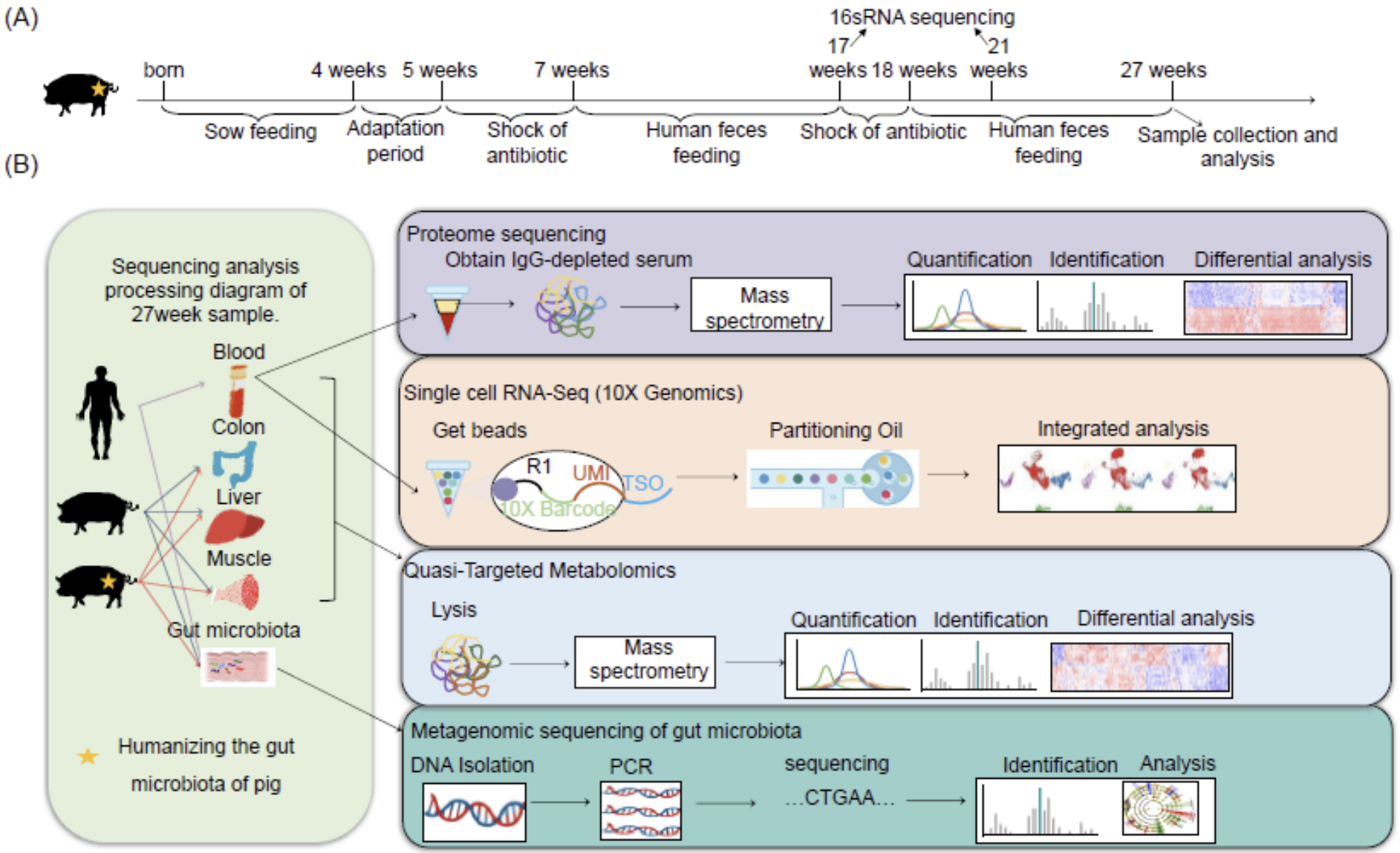
# Introduction

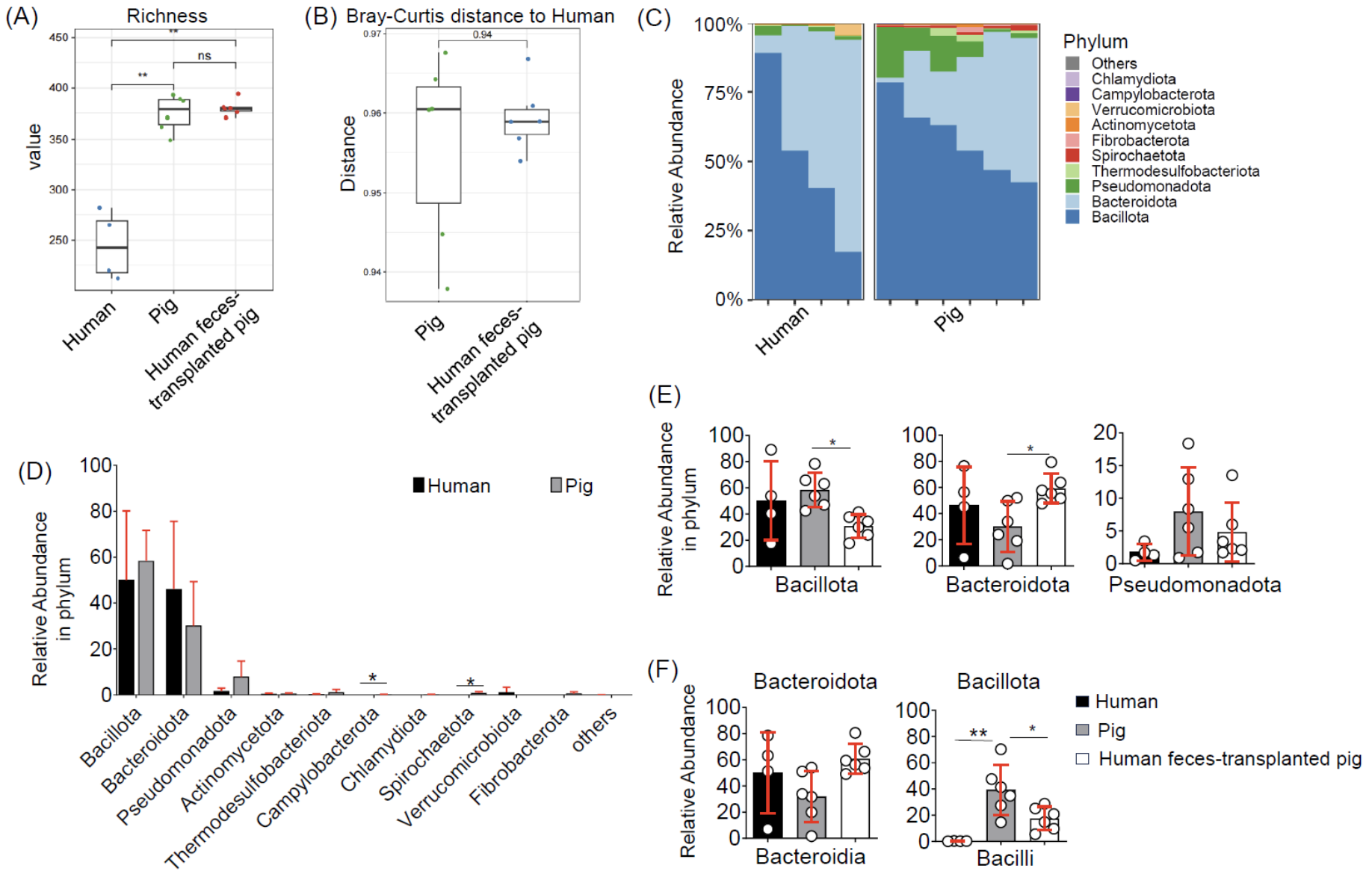


# Highlights

- Gut microbiota-humanized pigs were successfully established via of pigs with humanized gut microbiota.
- Human-like remodeling of serum metabolome was achieved in humanized pigs.
- Transcriptional reprogramming of immune cell subsets in humanized pigs revealed shifts toward human-like metabolic and biosynthetic activity.

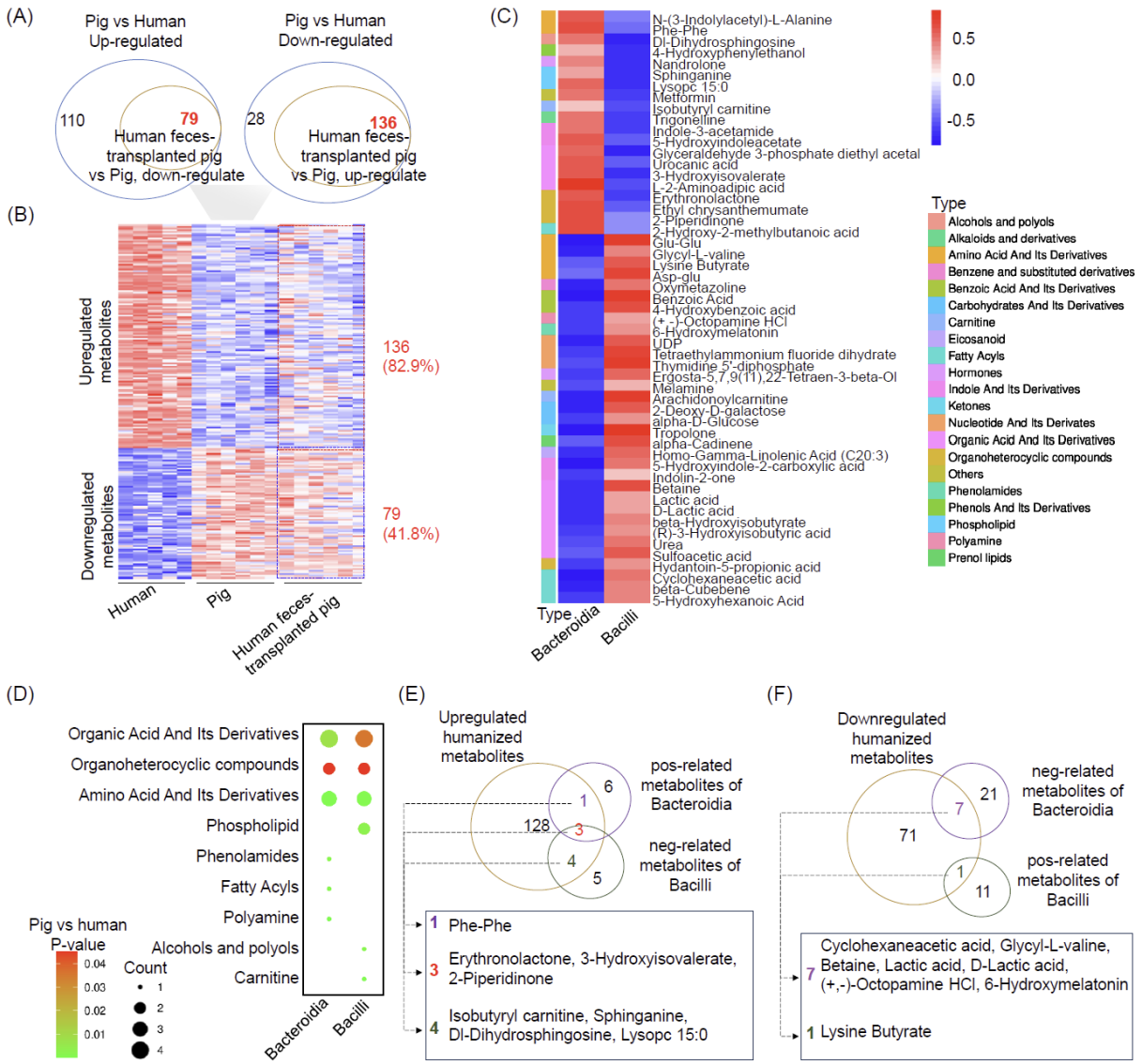
# Results

**Composition changes of the gut microbiome in the humanized pigs.**



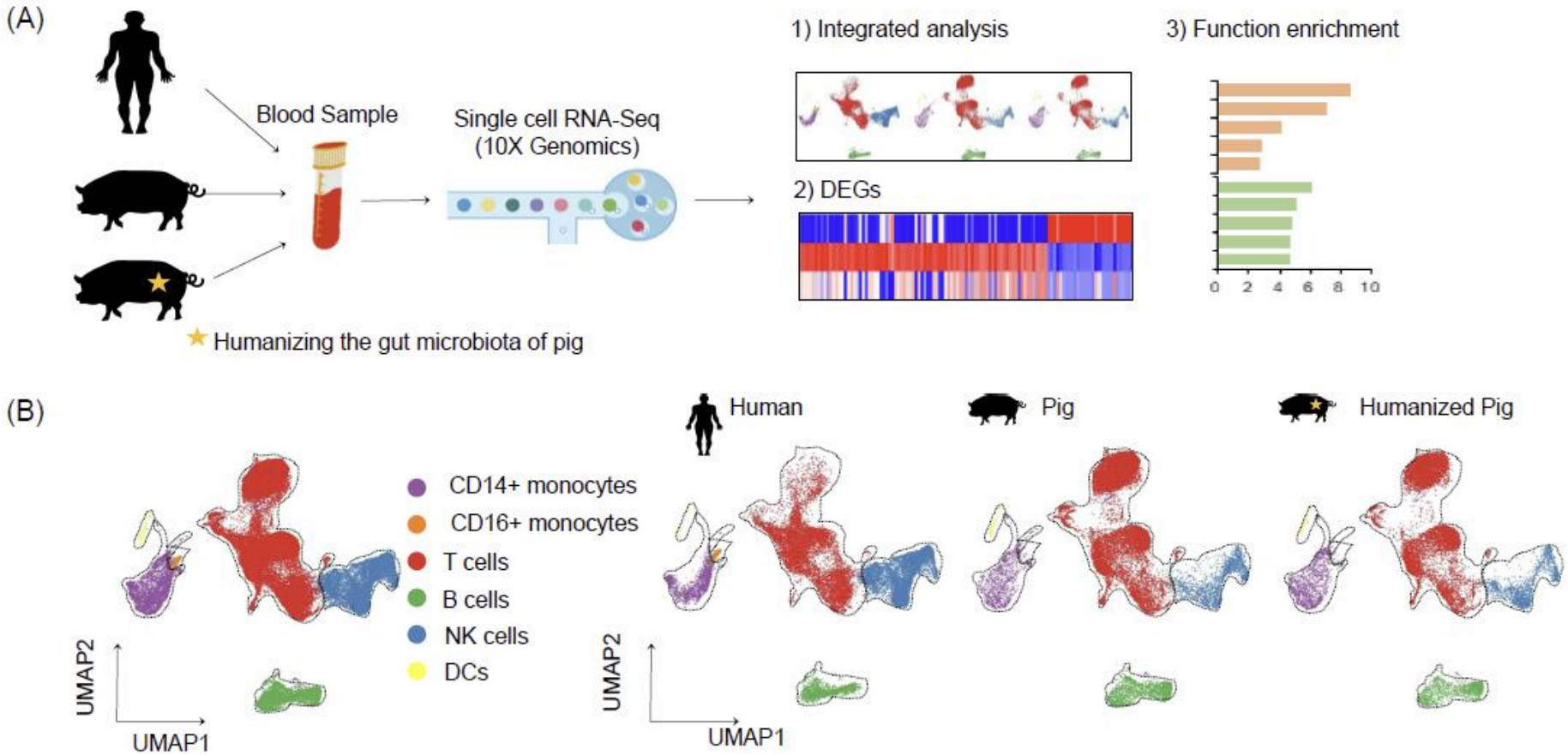
# Results

## Humanized gut microbiota alters the serum metabolite profile in pig



# Results

**Single cell transcriptome atlas of PBMCs in humans, pigs, and GMH pigs**



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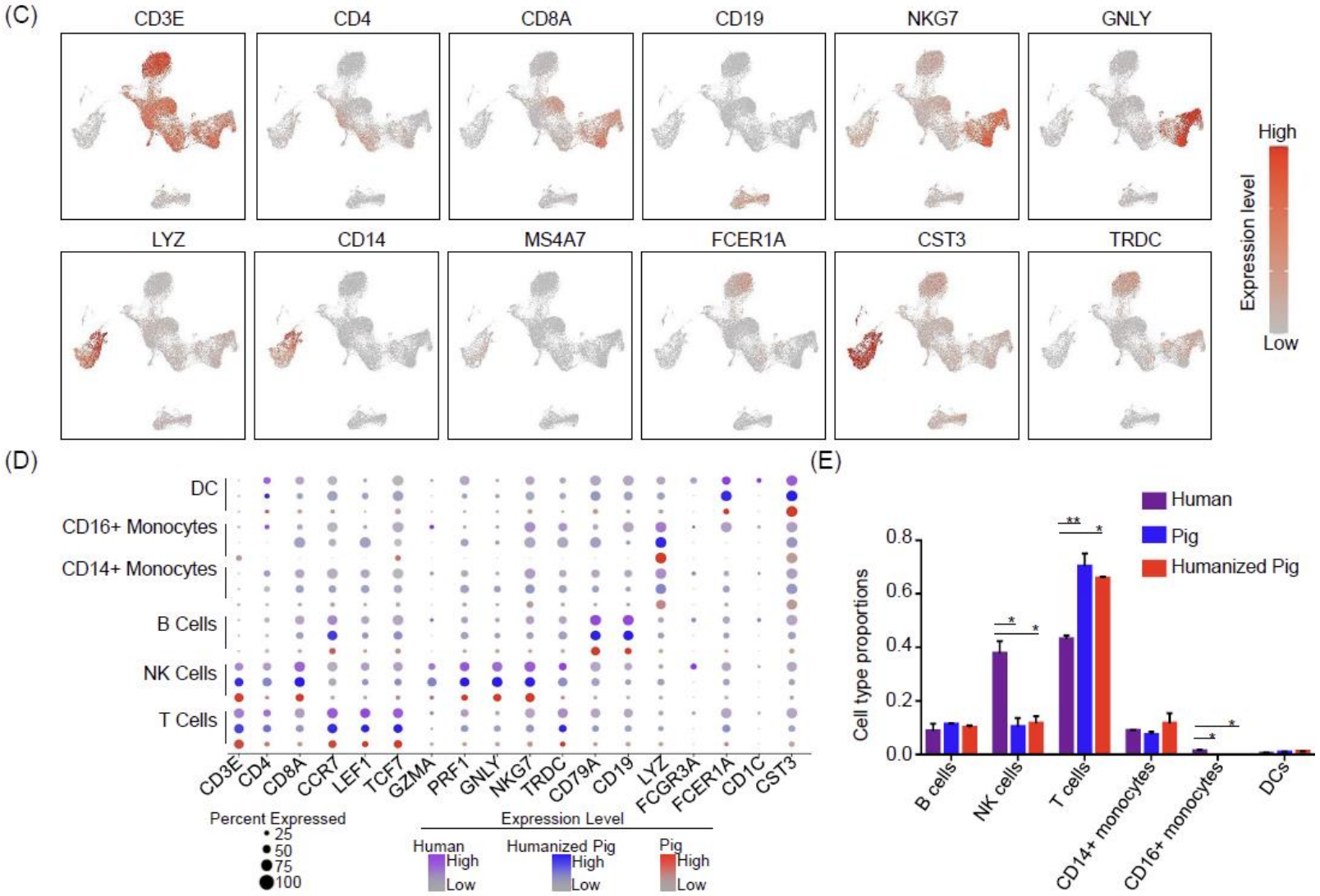
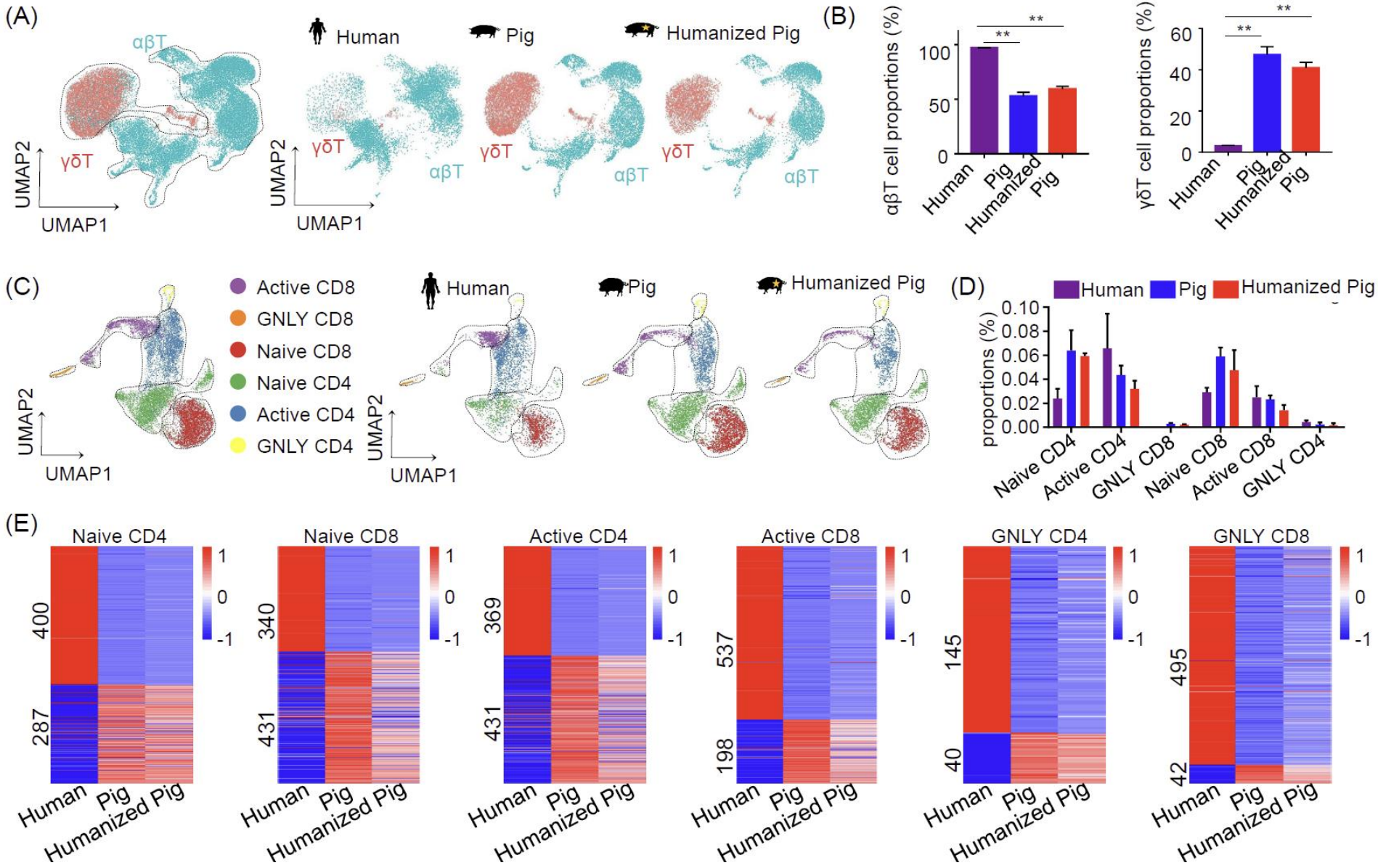


# Results

## Single-cell dissection of T cell subsets in humans, pigs, and GMH pigs



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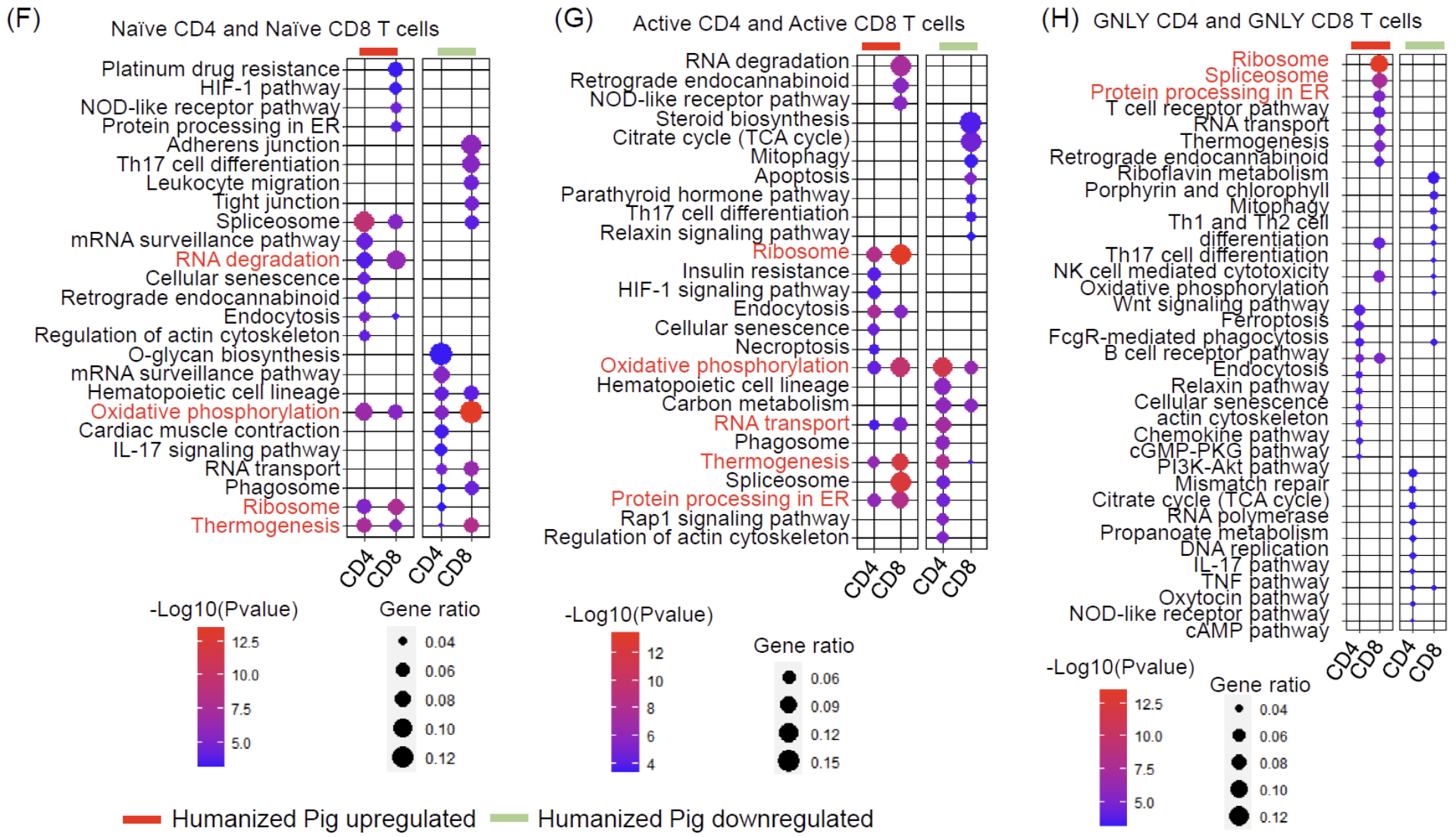
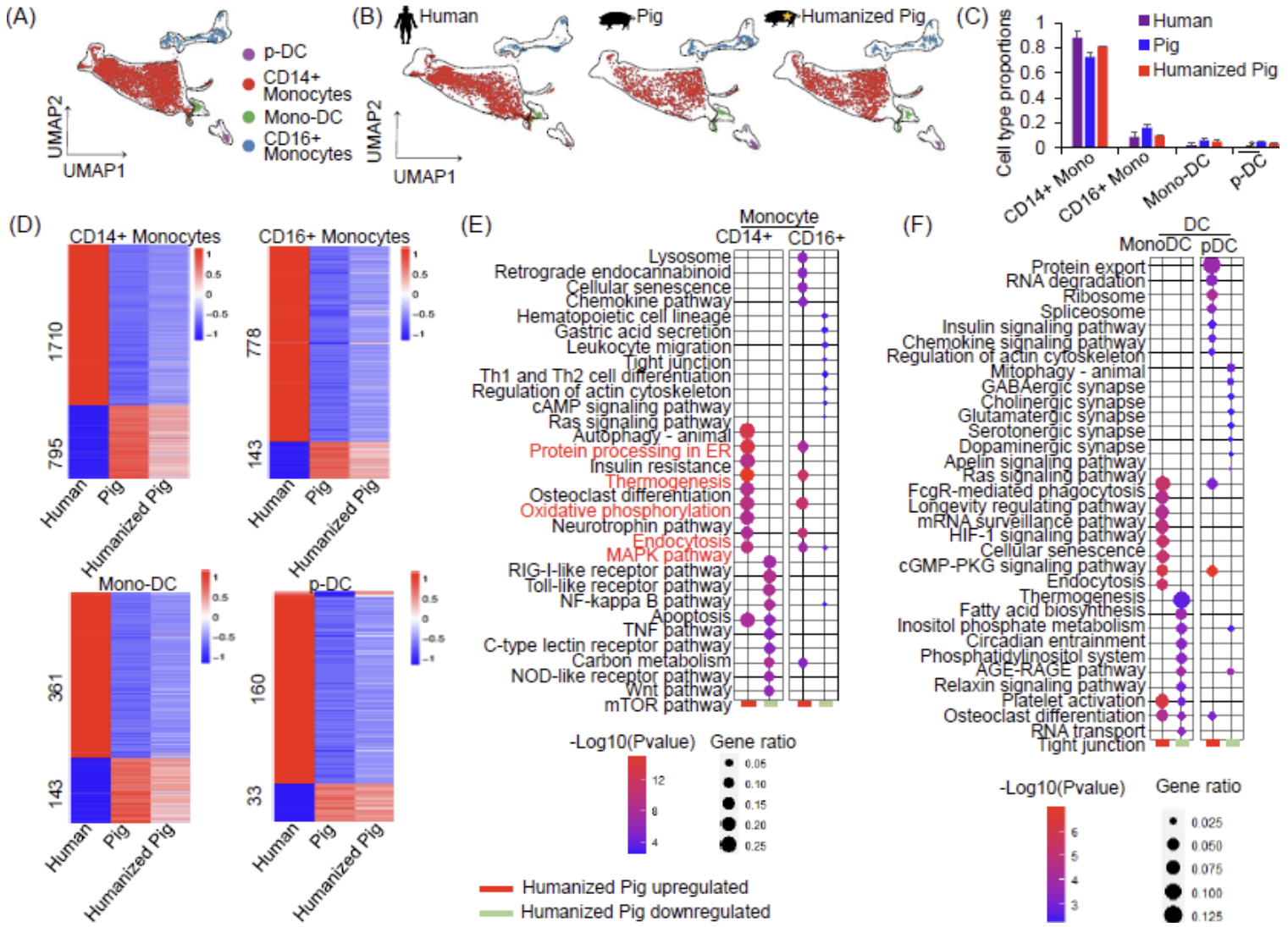


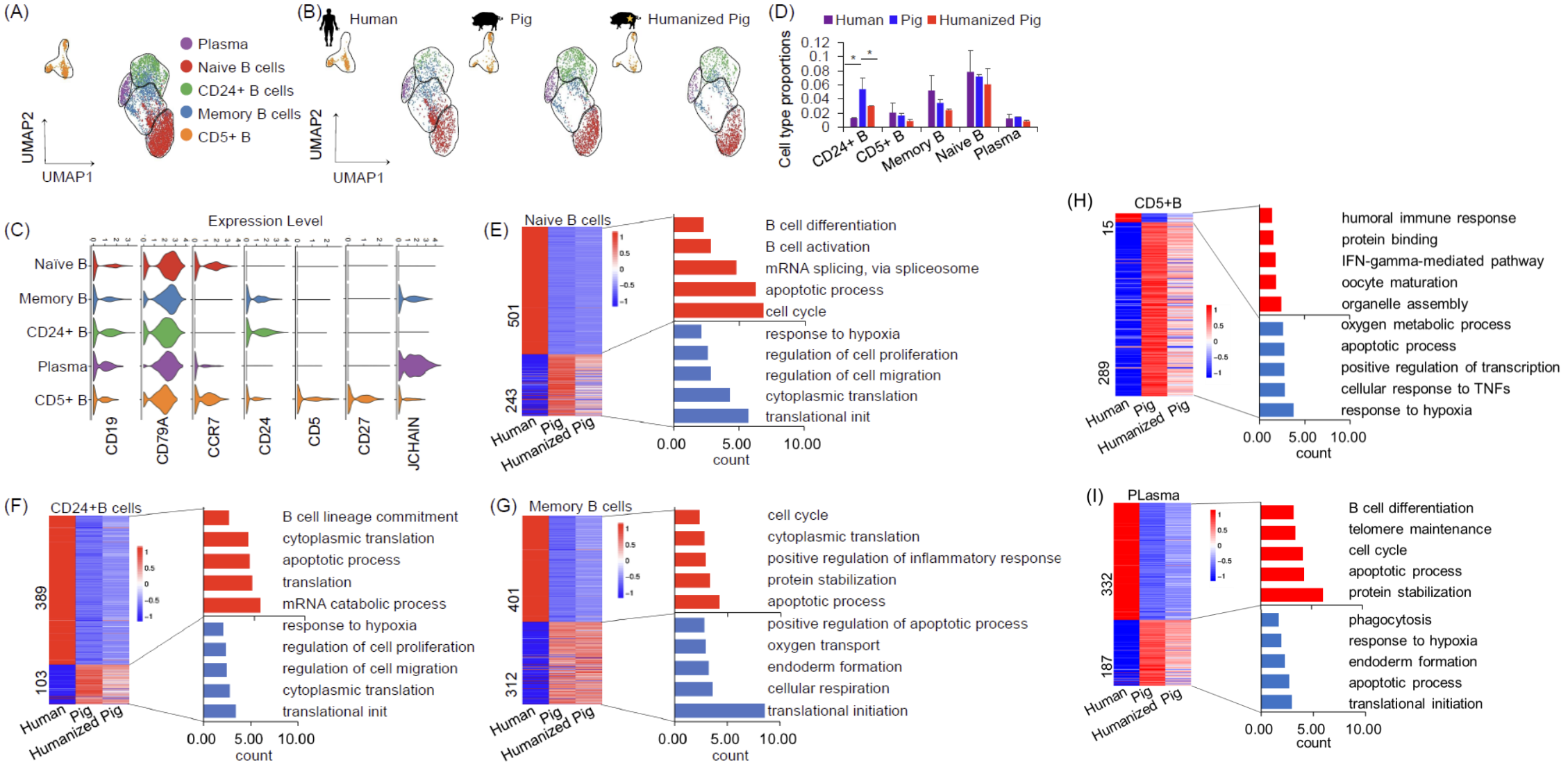
# Results

**Single-cell dissection of myeloid immune cell populations in humans, pigs, and GMH pigs**



# Results

## Human fecal microbiota transplantation modulates the composition and transcriptional profile of pig B cells



# Summary

- We successfully established a microbiota-humanized pig model by transplanting human fecal microbiota into antibiotic-treated pigs. This intervention led to substantial remodeling of the host microbial community and serum metabolome, with metabolite profiles shifting toward a human-like state.
- Concurrently, single-cell transcriptomic analysis further revealed that immune cell subset composition and gene expression profiles in peripheral blood were modulated by microbiota humanization, with enhanced signatures of metabolism and biosynthesis observed across multiple immune lineages. Collectively, these findings demonstrate that human gut microbiota can reprogram both systemic metabolism and immune cell function in a large-animal host.
- The resulting microbiota-humanized pig model provides a translationally relevant platform for investigating human microbiota-host interactions, microbiota-associated diseases, and the evaluation of microbiome-target therapies. Moreover, this model may hold future utility for xenotransplantation research and preclinical safety assessments.

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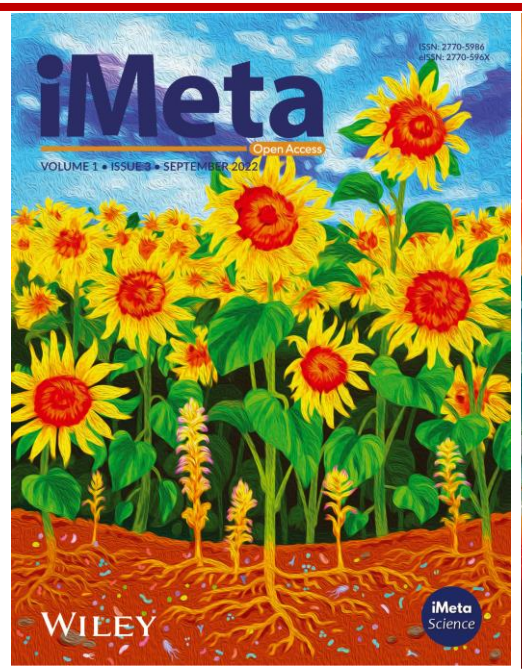


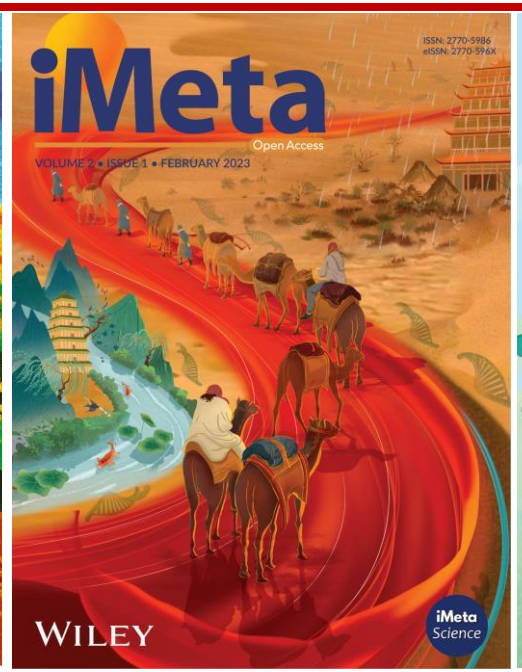


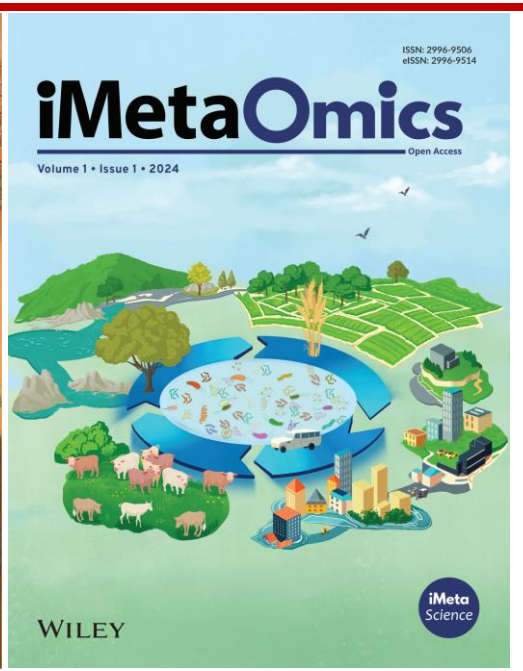



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