"Porcine menisci transcriptome multi-approach NGS study: investigations on zonal cell composition, human resemblance, and potential applications in xenotransplantation"

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The meniscus, a fibrocartilaginous tissue crucial for stabilizing the knee joint and distributing load, consists of three distinct zones—red, white, and intermediate—based on its blood supply, extracellular matrix (ECM) composition, and healing capabilities. Current therapies of meniscal injuries such as repair and surgical meniscectomy have shown unsatisfactory success rates. Given its susceptibility to tears, particularly under heavy loads and shear pressures, and limited repair capacity development of new treatment options is crucial. To preserve the mechanical properties of the meniscus, innovative strategies, including tissue engineering (TE) and xenotransplantation, are being explored, with domestic pigs identified as a promising source due to their similarity to humans in physiology and organ structure.

In the proposed project we intend to discover the cellular makeup of porcine meniscus, and check if it mirrors that of humans. Proving resemblance to humans is of great importance since porcine menisci might become valuable biological model for studying new therapies and become a source of biomaterial for TE. To accurately replicate meniscus characteristics in TE, a comprehensive understanding of the cellular architecture of porcine meniscus is essential. Porcine menisci may also serve as a source for xenotransplants. However, immune rejection remains a concern, and genetic engineering involving the removal of specific antigens is considered. Understanding the transcriptomic makeup of swine meniscus is crucial for future genetic editing to enhance xenotransplant survivability.

Implementing advanced sequencing techniques will facilitate creating porcine menisci single cell atlas. Single-cell approaches and short and long-read sequencing, will be employed. Integrating these data will generate a detailed reference transcriptome for pig menisci, encompassing full-lenght transcripts with unique splicing variants. Comparative analyses with publicly available human data will focus on divergent zonal compositions, cell interactions, and chondrocyte and epithelial cell types and functions. Spatial transcriptomics will unveil the internal organization of cells and identify spatial locations of those involved in expressing epitopes that could trigger the immune system in xenograft recipients.

Pig models play a pivotal role in advancing medical research, and this study aims to provide valuable insights into the genetic makeup of pig menisci. The collected data will contribute to understanding the zonal composition, healing potential, and resemblance to humans, facilitating precise gene editing, drug testing, and the development of new therapeutic strategies in TE and xenotransplantation for orthopedic research.