

Recombinant SLA Class I and II Molecules for Xenotransplantation Diagnostics

Background

Recent advances in xenotransplantation are rapidly transforming the organ replacement therapy landscape, offering new hope in addressing the global shortage of donor organs. Pigs are frequently used as organ donor organisms. Recent examples of pig-to-human transplantations include heart, kidney, islet cells, and skin grafts. Especially for highly immunized patients, xenografts are considered as an option to overcome restrictions in organ availability. One of the major concerns in xenotransplantation is antibody-mediated rejection (AMR). It has been shown that swine leukocyte antigens (SLA) are also targets of AMR. However, we are only starting to understand the extent to which human recipients of pig organs develop anti-SLA antibodies and how anti-human leukocyte antigen (HLA) antibodies cross-react with SLA molecules.

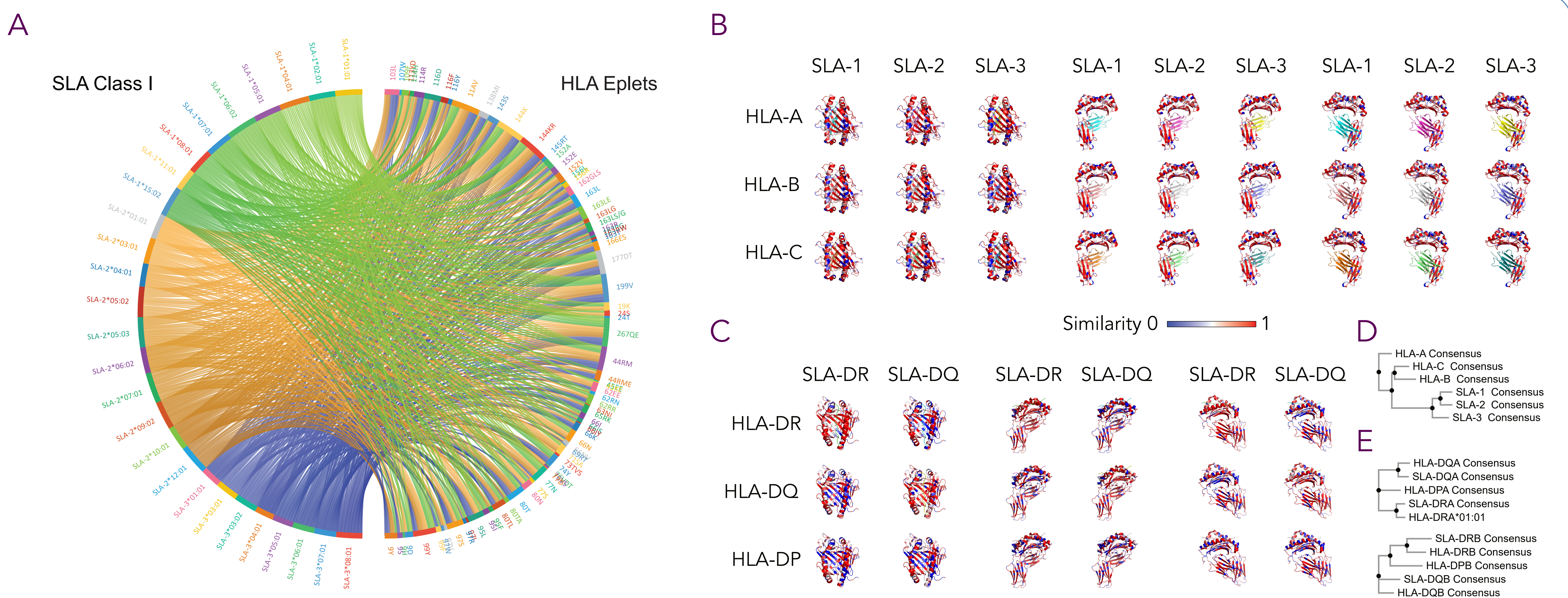


Figure 1. Eplet and Similarity Analysis of SLA in Comparison to HLA.

(A) Sequence-based analysis of the occurrence of HLA eplets in SLA class I sequences. Connecting lines are green for SLA-1, yellow for SLA-2, and blue for SLA-3. Position-wise similarity of (B) HLA versus SLA class I and (C) class II loci, respectively. Phylogenetic trees of consensus sequences of (D) SLA and HLA class I and (E) class II, respectively.

Results

We produced recombinant soluble SLA class I and II. We identified HLA eplets in the sequence of SLA, analyzed the similarity between SLA and HLA proteins (Figure 1), and found anti-HLA sera that were reactive against SLA (Figure 2). By adsorbing antibodies onto SLA molecules, we were able to alter mean fluorescence intensity (MFI) patterns in single antigen HLA bead assays, indicating the direct binding of anti-HLA antibodies to SLA (Figure 3).

