

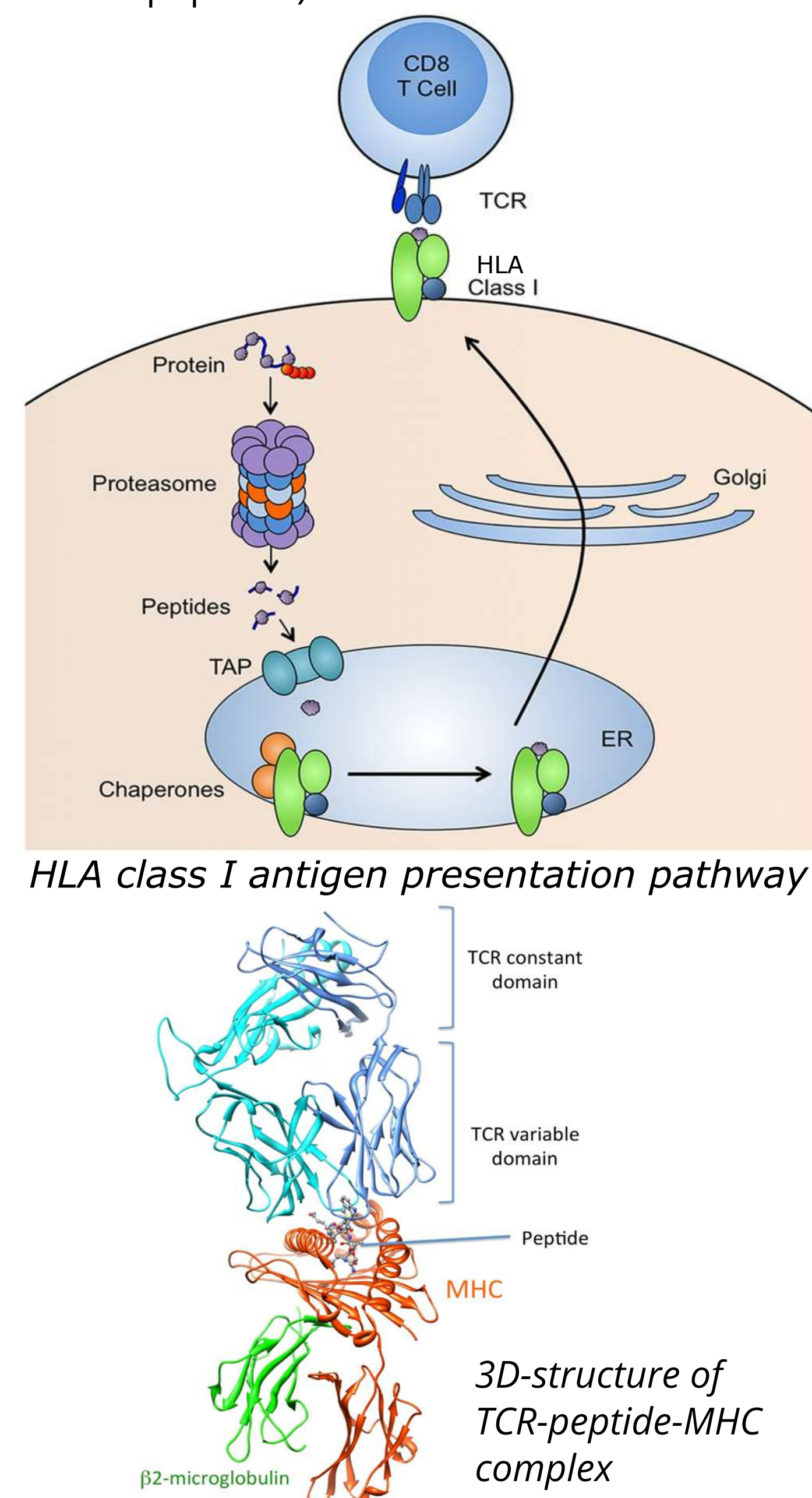
Variability of immunologically significant regions of HLA class I proteins

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Introduction

- Human leukocyte antigen (HLA) proteins are key components of the immune system
- HLA class I proteins bind peptides derived from degraded intracellular proteins and present them on the cell surface for inspection by T-cell receptors (TCR) of T-cells
- TCR interacts both with HLA and peptide
- TCR recognition of pathogenic peptide presented by HLA triggers adaptive immune response
- HLA class I genes are HLA-A, HLA-B and HLA-C
- HLA genes are the most polymorphic in the genome (>10000 variants, presenting different sets of peptides)



Aims

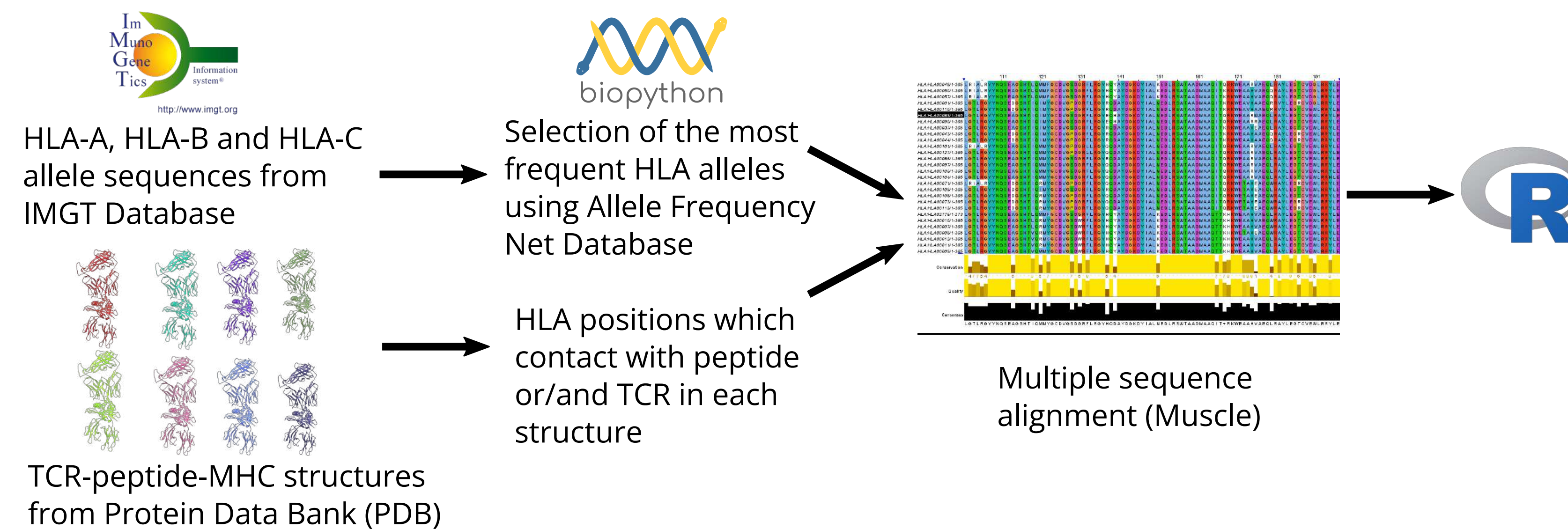
- To analyse the variability of TCR- and peptide-contacting regions of HLA.
- To investigate variability within HLA-A, -B and -C groups of alleles.
- To search for evolutionary conservative sequences of peptide- or/and TCR-contacting positions.

Conclusions

- Peptide-contacting positions are more polymorphic than TCR-contacting ones. Non-contacting positions are conservative.
- HLA-A alleles differ mostly in TCR-contacting positions, HLA-B - in peptide-contacting ones.
- We found a conservative sequence of TCR-contacting residues in a set of HLA-B alleles which may be evolved convergently.

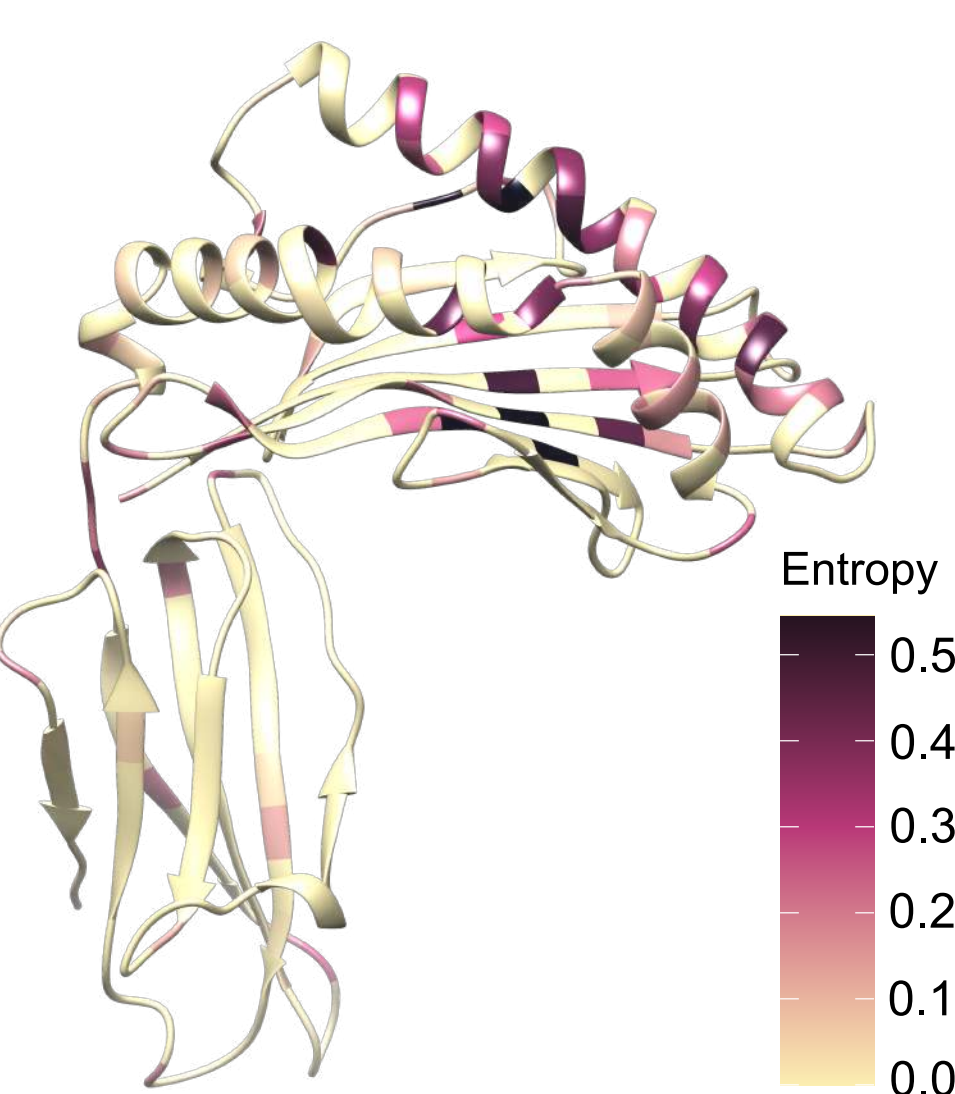
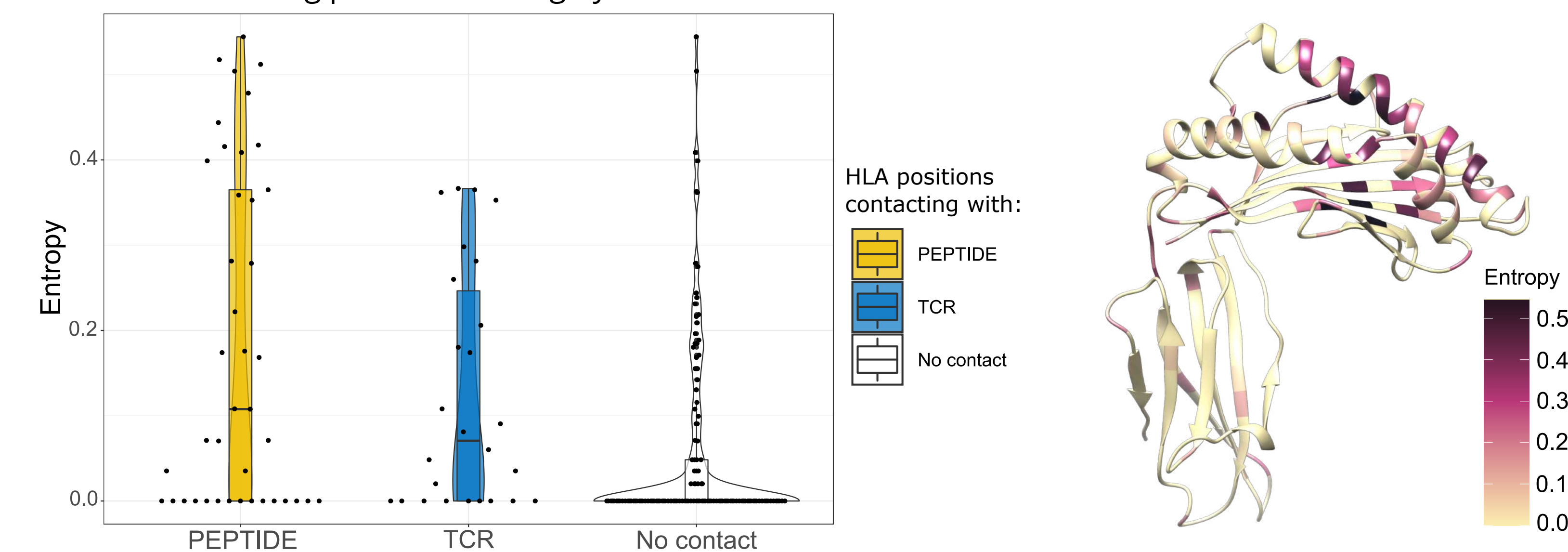
Results

1. Identification of peptide- and TCR-contacting regions of HLA



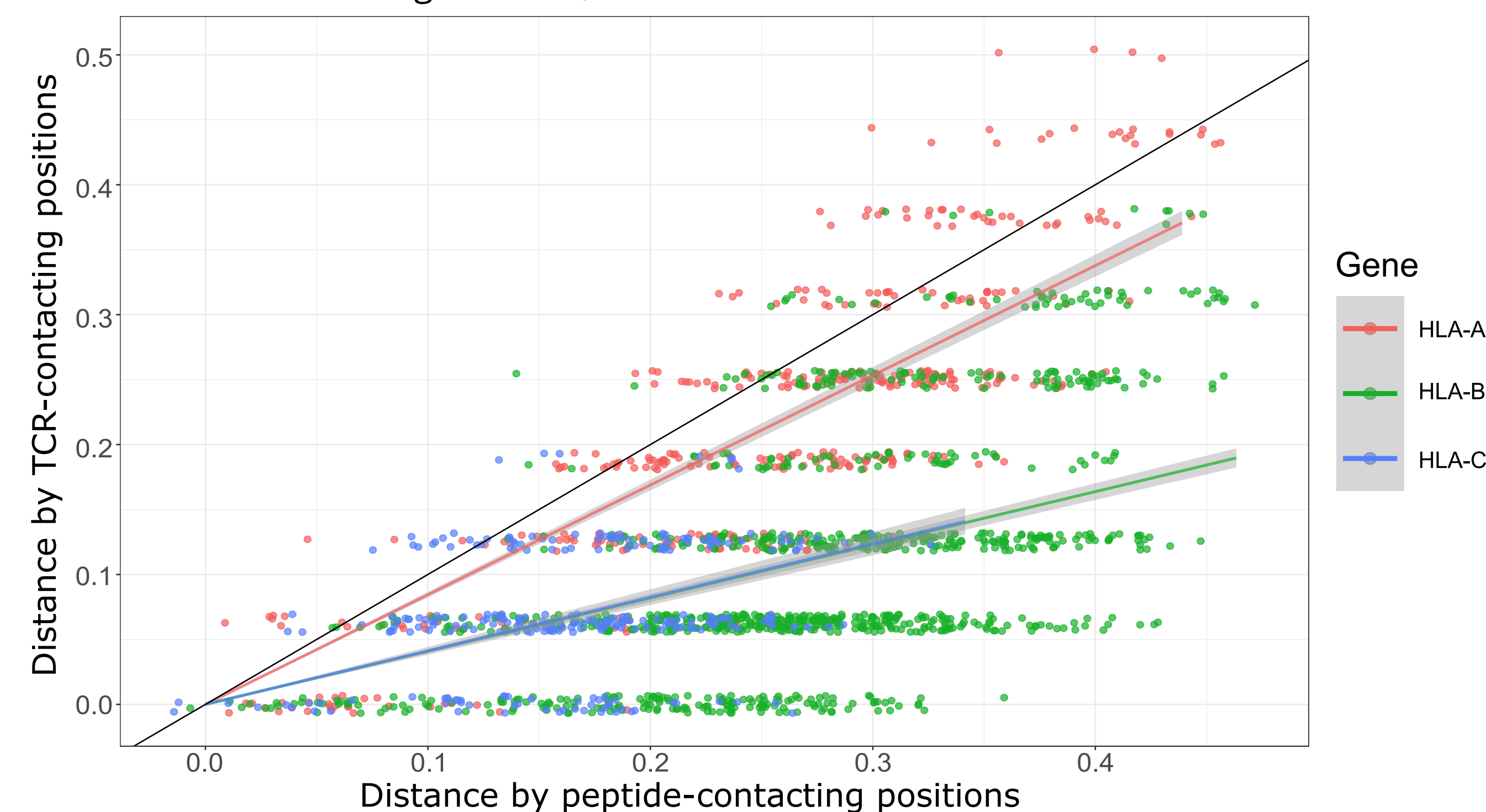
2. Variability of TCR- and peptide-contacting positions

Peptide-contacting positions are more variable than TCR-contacting ones. Most non-contacting positions are highly conservative.

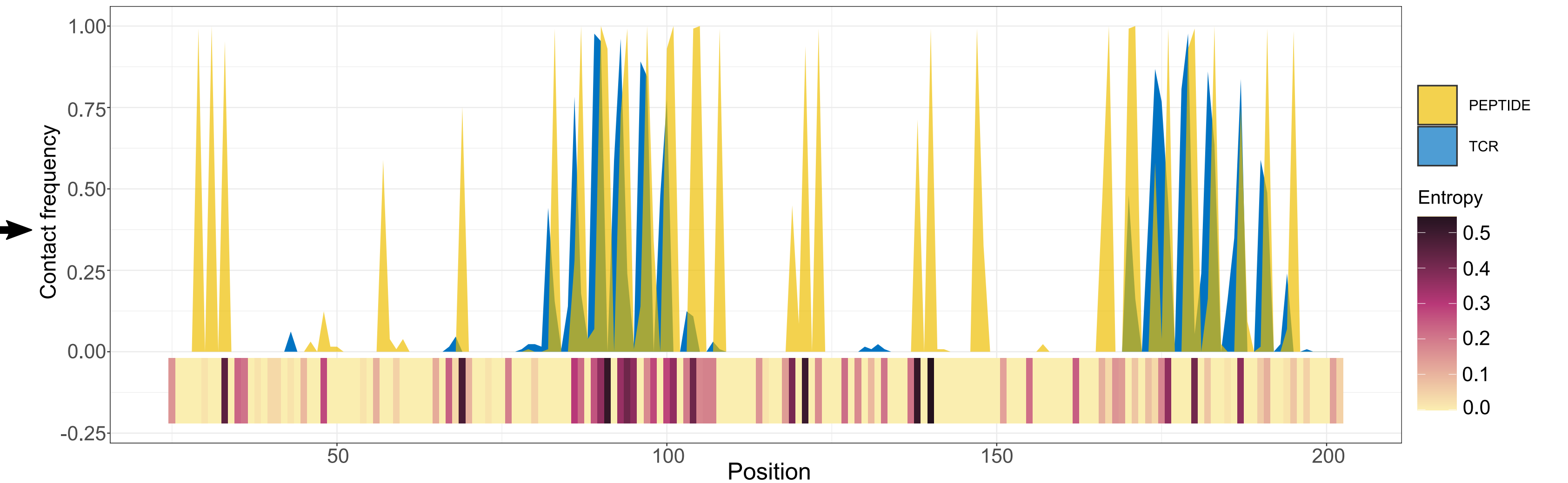


4. Similarity of TCR- and peptide-contacting regions of different alleles

A set of variants with a significant difference in peptide-contacting residues have identical TCR-contacting residues, while the inverse situation is not observed.

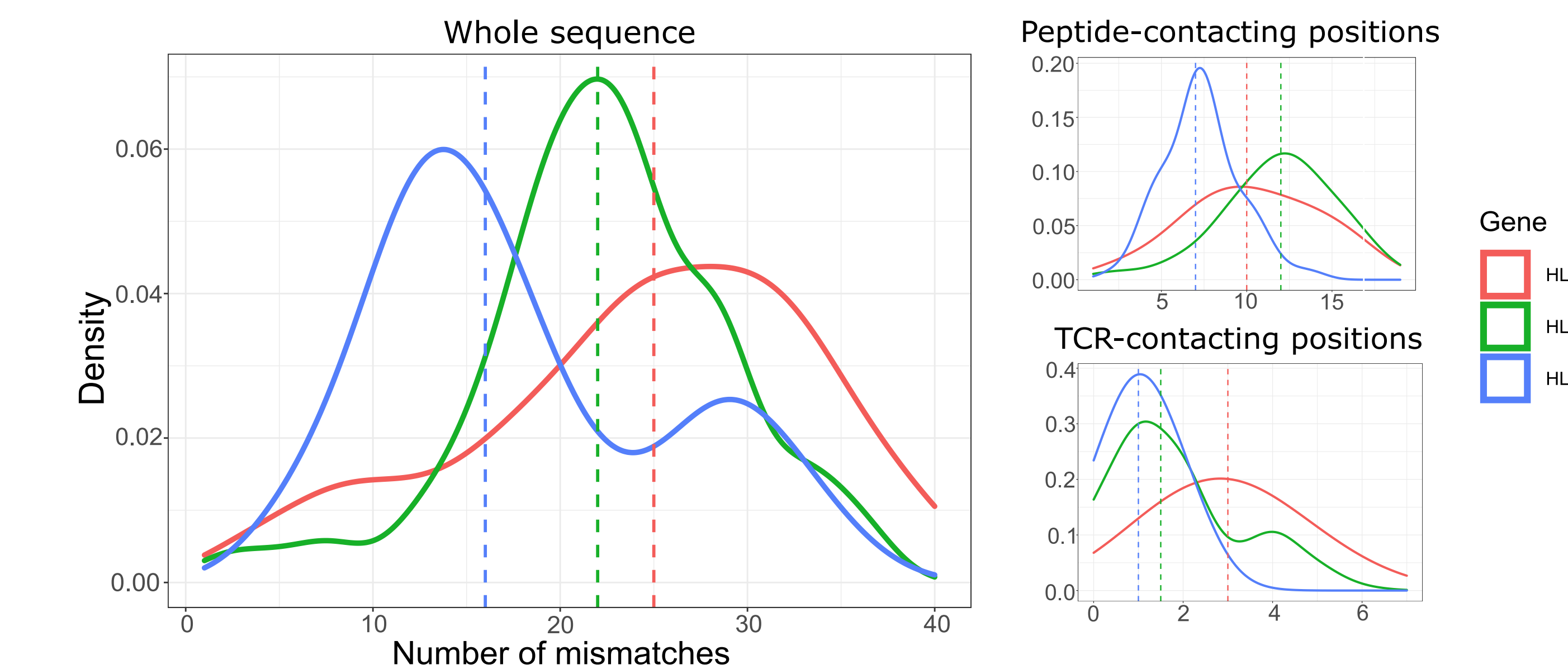


Regions with a higher degree of variability coincide with TCR- and peptide-contacting regions.

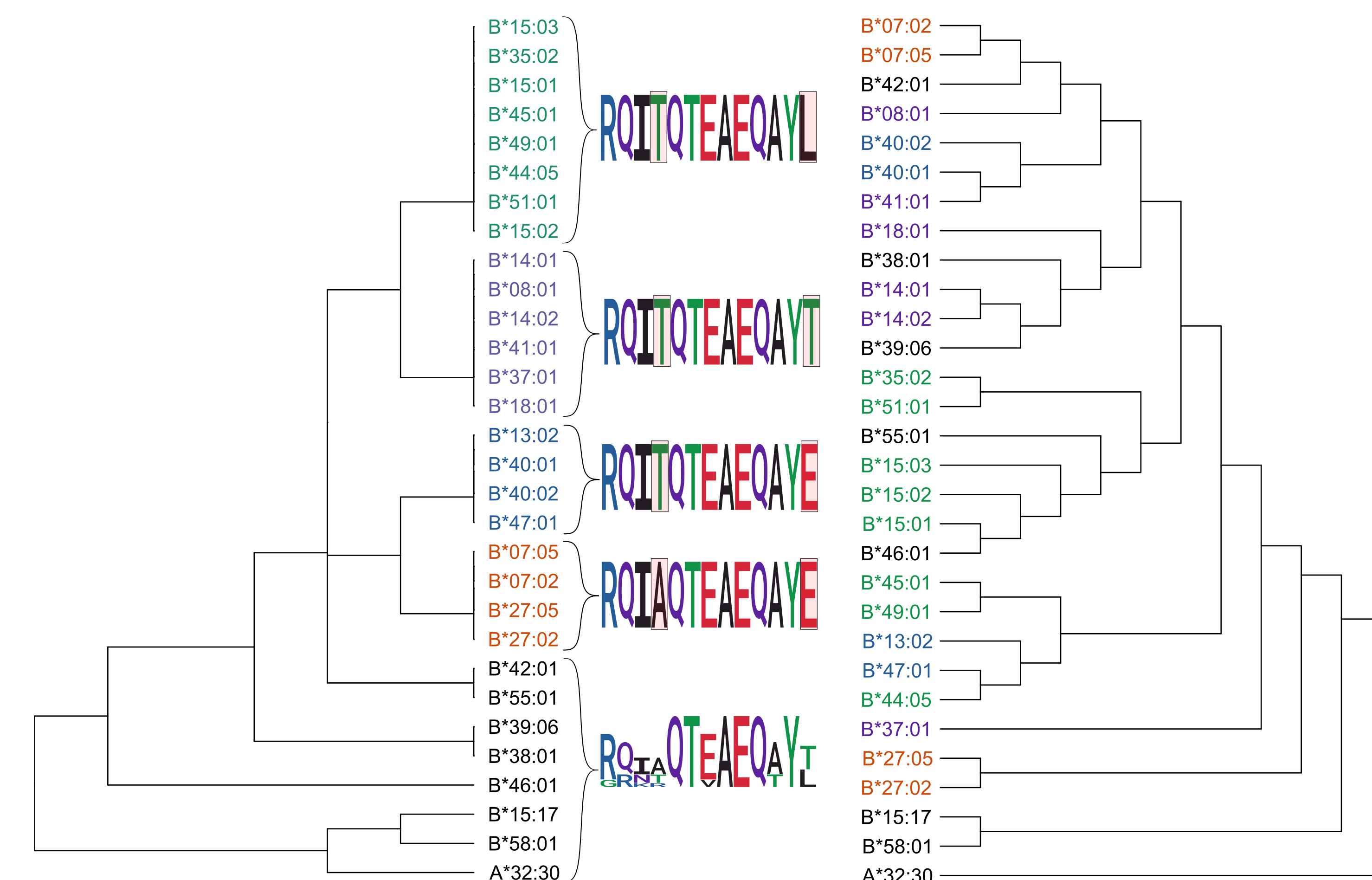


3. Sequence variability within HLA-A, HLA-B and HLA-C alleles

HLA-A alleles are more variable in TCR-contacting region compared to HLA-B and -C. While HLA-B are the most variable in peptide-contacting region. HLA-C are less variable compared to HLA-A and HLA-B.



5. Evolutionary origin of conservative sequence of TCR-contacting residues



Alleles sharing same TCR-contacting motif are spreaded into different clades on the evolutionary tree, suggesting independent developing of TCR-contacting motif. The homology of different HLA variants in the TCR contacting region may indicate the optimal structure of this region for interaction with a wide range of TCR variants formed during VDJ recombination.