# Prospecting the MHC

**PROPOSITIONS**

belonging to the dissertation entitled:

**Prospecting the MHC**
**A Bioinformatic View of HLA Polymorphism and Gene Organization**

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1. Ultimately, matching of HLA for SCT will evolve from gene- and allele-level matching to SNPs, haplotypes, and functional epitopes.

2. Typing of an individual SNP or epitope is useful but not sufficient, biological function may be determined by multiple polymorphisms in linkage disequilibrium or by the interaction of distant amino acids, which may even be located on separate proteins in a heterodimer.

3. Polymorphism in the 5′ and 3′ UTR regions affect protein expression by regulating mRNA transcription and protein translation, which defines differences in the biological behavior between cell types.

4. HLA alleles are distinguished by any polymorphism, regardless of frequency, but determining major and minor polymorphism gives context to allele differences. Accurate definitions of major and minor polymorphism can only be accomplished by considering a wide variety of populations.

5. Although allele groups are defined by exon homology, this does not imply they belong to the same ancestral gene. Evolution may direct HLA towards increasing diversity, but it may also conserve immunological relevance.

6. Every SNP is important.

7. When associating SNPs with disease, it can be hard to tell the "spurious" from the "surious."

8. Research projects must be hypothesis-driven, and a hypothesis must be concise and clear. "If you cannot express your line of thought in 1500 words, 20 references, and a 150-word unstructured summary, it is not a hypothesis." (Lancet Information for Authors)

9. We are greater than the sum of our parts. International collaborations and community-based efforts allow us to combine our specializations, share and reinterpret data, and maximize the impact to the HLA community.

10. DNA is like Taco Bell: The same four ingredients in an endless number of unique functional arrangements.