Dissection of HLA-C gene region to investigate its association with complex traits

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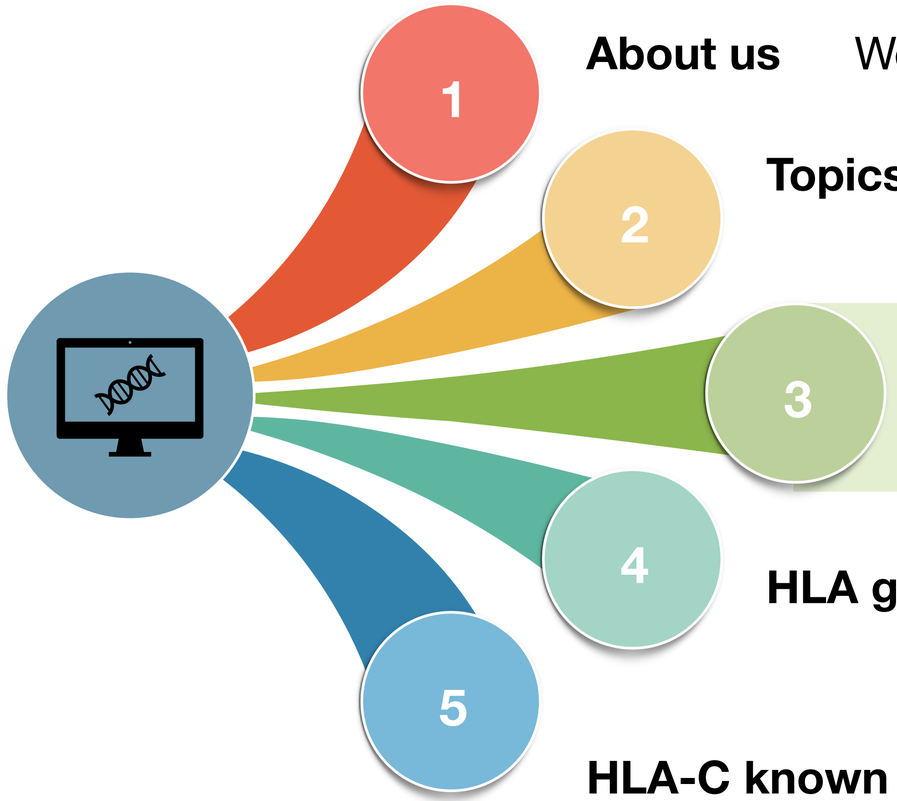
Background



About us We are a bioinformatic group of the University of Verona, in Italy.

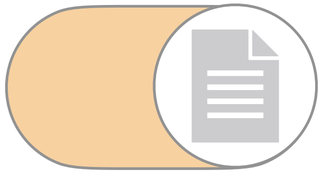
Topics covered Bacterial genomes, RNA-seq analysis, microbiome analysis, and association studies.

Project Focus on HLA-C gene and its variability.
Classification of the alleles.

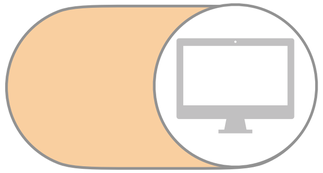
HLA gene The genomic region of HLA gene cluster (6p21.3) contains several highly polymorphic genes involved in the immune response.

HLA-C known alleles More than 3500 existing alleles.

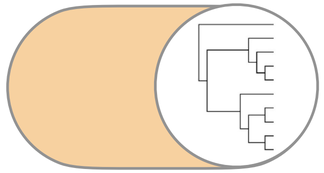
Methods



Data Collection:
We investigated more than 3500 known alleles of HLA-C gene (from IPD-IMGT/HLA database) that are grouped into 14 serogroups (e.g., C*01:02:01:01).



Data analysis:
All the sequences have been aligned against the human genome reference sequence (both versions; hg19 and hg38), highlighting more than 1500 SNPs.



Phylogenetic trees:
A clustering approach was used in order to understand how the alleles are evolutionarily connected.
Neighbor Joining algorithm to build phylogenetic trees.

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Results

Alleles of the same serogroup share strong identity in their sequence. Interestingly, as general rule, we observed that the main tree (figure 1) presents two branches, containing each a similar structure (relative distance between serogroups).

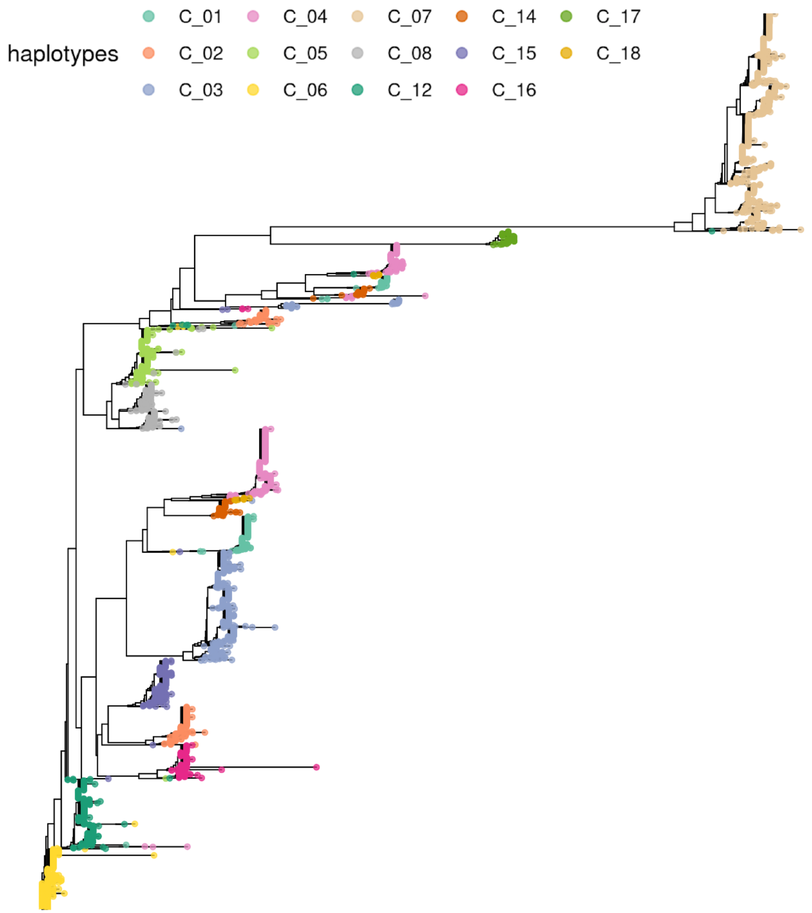

Figure 1. The entire set of HLA-C alleles

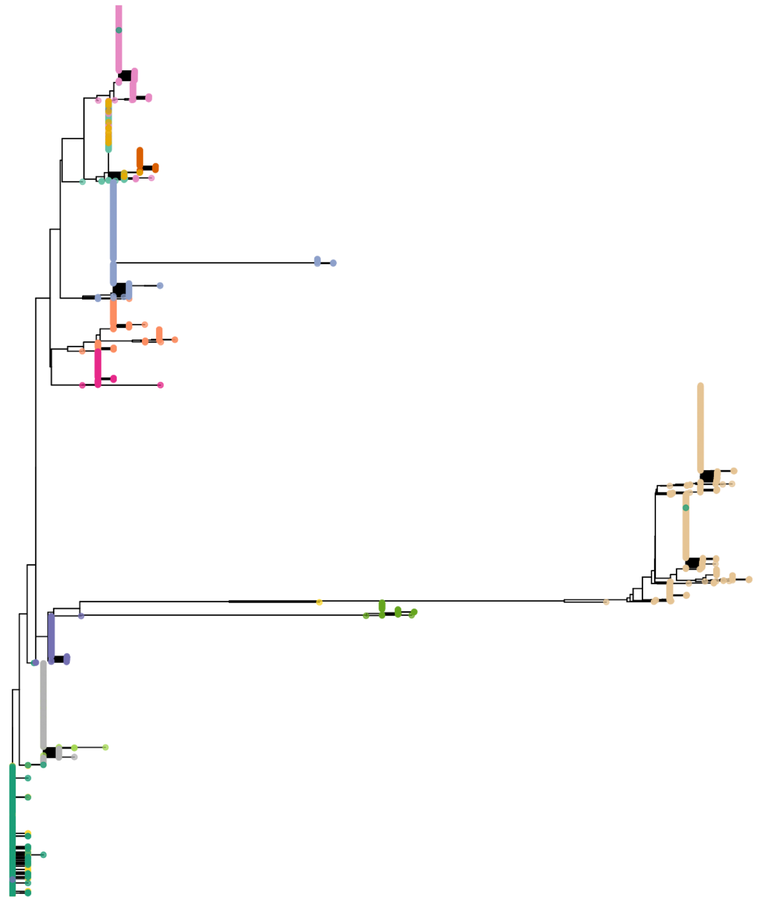

Figure 2. Alleles subsequences (from 1 to 2000 bp)

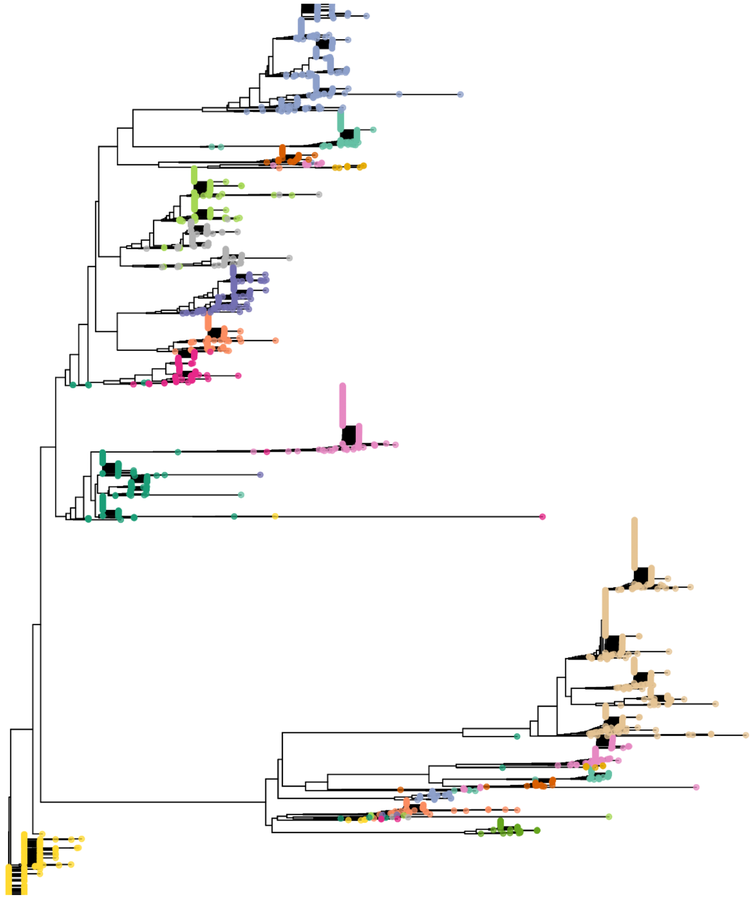

Figure 3. Terminal part of the sequences (from 2000 to 3000 bp)

Conclusions

- We used bioinformatic approaches to investigate the HLA-C gene and its many alleles, creating a phylogenetic tree to better understand the sequence similarities.

- We are studying the possible features that characterize these alleles, and which are the possible SNPs able to distinguish the several haplogroups of HLA-C gene.

- The study will go on by investigating the association of the HLA-C serogroup-SNP-based alleles with kidney related disease (INCIPE study) and Alzheimer's disease (NIAGADS database) in large cohorts of individuals.

References

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