GENDX

KIR allele level genotyping of a Japanese healthy individual cohort

The importance of matching or mismatching of the Killer Immunoglobulin-like Receptor (KIR) genotypes between transplantation donor and patient is getting more and more attention in the field. Especially during hematopoietic stem cell transplantation, it seems that KIR matching of certain gene groups may have a beneficial effect on transplantation outcome. On the other hand, mismatching of KIR and their ligands can benefit the treatment of certain leukemia's[2,3]. The full extent of the effect that KIR genotypes have on transplantation, requires knowledge on the exact allelic genotype of each donor and patient.

Materials & Methods

Allele level genotyping information of a healthy Japanese cohort was generated and compared with an experimentally obtained presence/absence dataset to confirm amplification results. KIR genotype was determined for 11 genes (KIR2DL1, KIR2DL2, KIR2DL3, KIR2DL4, KIR2DL5, KIR2DS2, KIR3DL1, KIR3DL2, KIR3DL3, KIR3DS1 and KIR3DP1) with 5-digit resolution and for some cases up to 7 digits. Amplification was performed with NGSgo-AmpX KIR and data analysis was done with NGSengine, applying KIR database 2.9.0.

Results

In total 35 individuals were genotyped, resulting in the detection of maximally 70 alleles for each KIR gene. In this set, 11 new alleles were identified, based on the novel base call information that the sequence provided (Figure 1). Comparing the alleles that were detected with the alleles that are most frequent in Caucasian populations[4], some striking differences are observed. The alleles that are present with a very high frequency in Caucasian populations are not necessarily the high frequent alleles in the Japanese panel. There are some alleles that are not detected in Caucasians at all, or at a very low rate. The main differences are observed for KIR3DL1, KIR3DL2 and KIR3DL3, where the most frequent alleles in the Japanese panel, are hardly present in Caucasians at all (Figure 2).

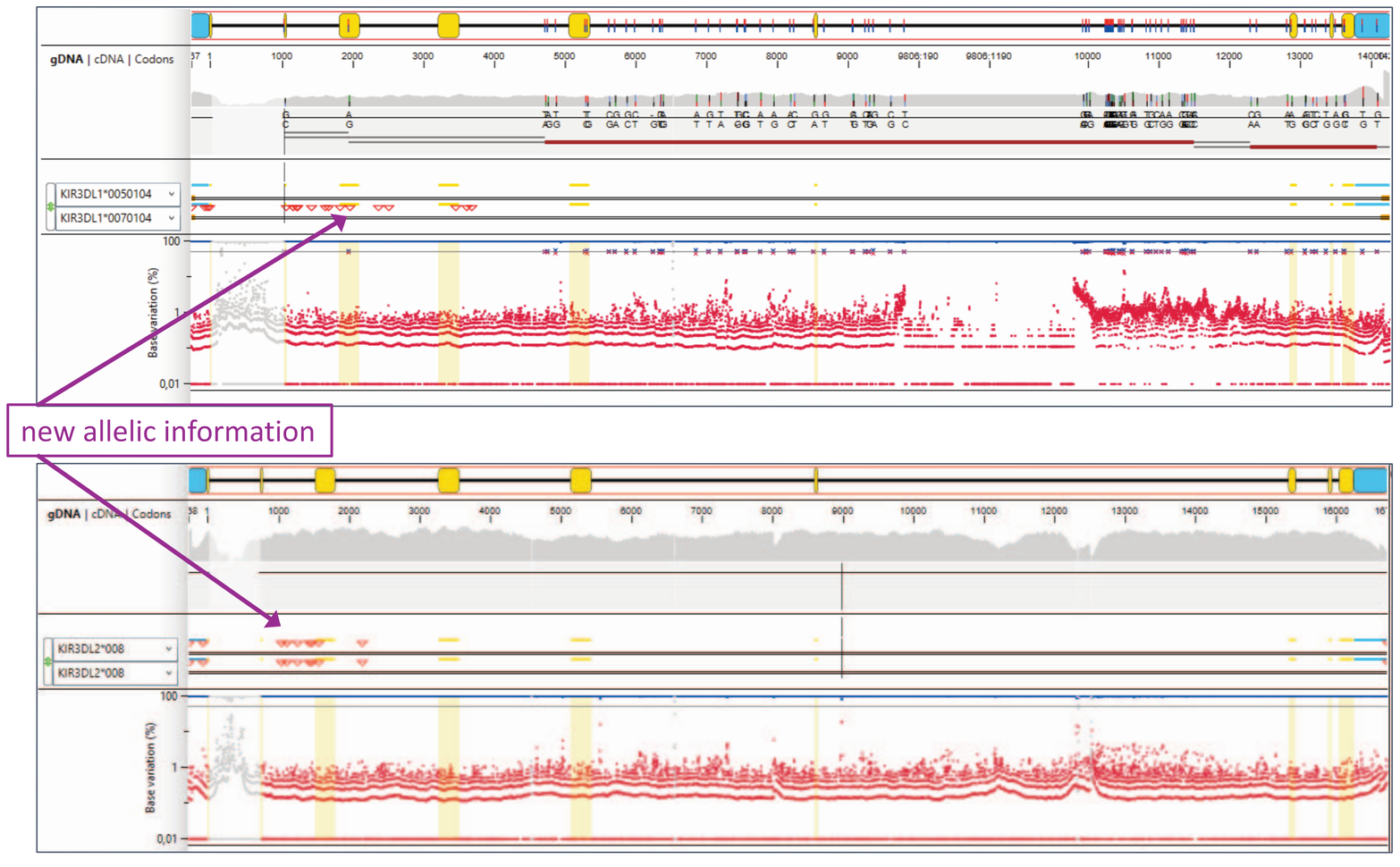
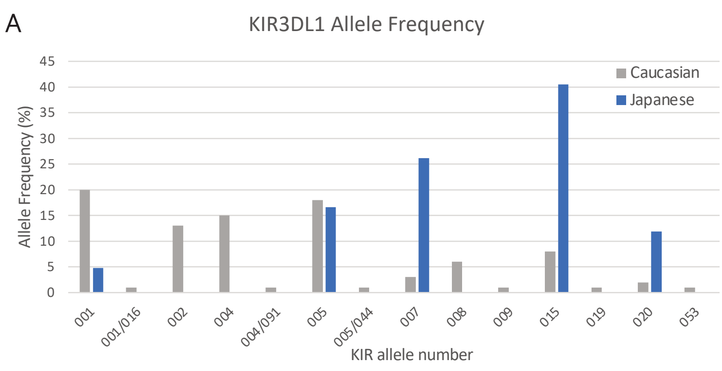
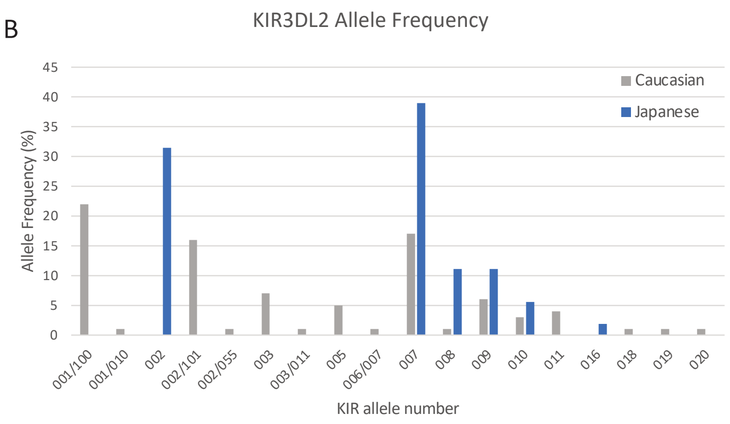


Figure 1. eleven new alleles identified





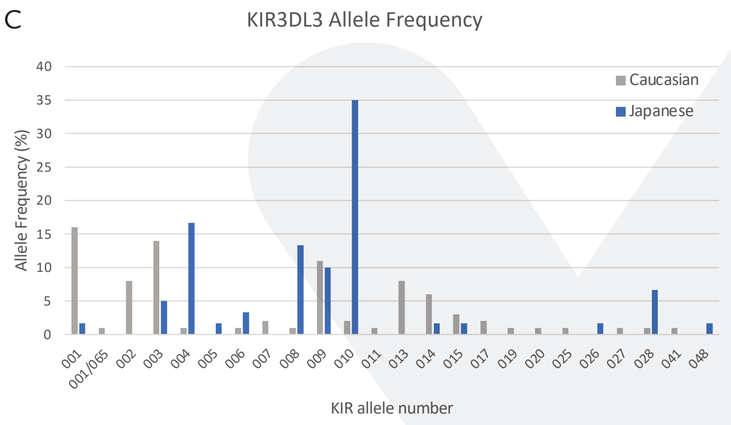


Figure 2. KIR3DL allele frequencies found in Japanese population panel.

Conclusion

Although determined in a small cohort, the differences between the Caucasian and Japanese population are quite striking. Also, the number of new alleles that were found for this small cohort, indicates that there is still a lot of allele data missing in the current database. A more elaborate study on a much larger panel is required to clearly identify the frequent alleles for the Japanese population and to create a complete overview of the alleles that are present.

Population studies like these will contribute to the general understanding of KIR allele distribution and impact on disease and transplantation settings.

References

1. McQueen, et al.; Human Immunology (2007)
2. Cooley, et al.; Journal of Immunology (2014)
3. Ruggeri, et al.; Frontiers in Immunology (2016)
4. Wagner et al.; Frontiers in Immunology (2018)

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Seik-soon Khor[2], Loes A.L. van de Pasch[1], Sanne Vendelbosch[1], Helma H.M.E. de Bruin[1], Katsushi Tokunaga[2], Erik H. Rozemuller[1]

1 GenDx, Utrecht, the Netherlands
2 Genome Medical Science Project, National Center for Global Health and Medicine, Tokyo, Japan

experts in transplant diagnostics