In silico prediction of new minor histocompatibility antigens.

Dmitry Malko, Nadia Bykova

National Research Center for Hematology, Novy Zykovski lane 4a, Moscow, Russia

dmitry.malko@gmail.com, n.bykova@blood.ru

The number of allogeneic bone marrow and stem cell transplantations (allo-HSCT) is increasing worldwide. The alloreactive immune response during the transplantation depends on the genetic mismatches between a donor and a recipient. Even if a transplant donor and recipient are identical with respect to their major histocompatibility complex (MHC) genes, variant peptide products from other polymorphic genes, known as minor histocompatibility antigens (MiHA), can be recognized by donor T cells as foreign antigens; this mechanism underlies both beneficial graft-versus-leukemia (GvL) effect and detrimental graft-versus-host disease (GvHD) [1]. MiHAs encoded in hematopoietically restricted genes can be viewed as specific markers of recipient hematopoietic system, that is meant to be completely depleted and replaced by healthy donor cells. In this way, hematopoietically restricted MiHAs are now considered as potential targets for allo-HSCT related immunotherapy, and discovery of novel MiHAs is of very high interest. MiHA identification pipelines, consisting in the detection of recipient specific peptides caused by SNPs or frameshift mutations followed by evaluation of their immunogenicity, could form the basis of personal immunotherapy against MiHAs relevant for a specific donor-recipient pair [2].

We attempted to create a comprehensive multifunctional tool that focuses specifically on the MiHA identification problem. One part of the program functionality is focused on the personal approach and allows to find variant peptides in a donor-recipient pair on the basis of exome data, while the other considers the problem of potential variant peptides in the specific genes of interest. Our implementation significantly outperforms the existing tools in the case where numerous adjacent variations are found in a gene.

1. Goker H. et al. (2001), Acute graft-vs-host disease Pathobiology and management, *Experimental Hematology*, **29**(3): 259-77.

2. Van Bergen C. A. et al. (2010), High-throughput characterization of 10 new minor

histocompatibility antigens by whole genome association scanning, *Cancer Res*, **70**(22):9073-9083.