Antigenic compatibility between blood products and transfusion recipients is critical for the clinical efficacy and safety of this common medical intervention. A total of 378 polymorphic blood antigens are known today, of which 345 have a known genetic basis. Since they are encoded in the genome, blood groups are inherited and demonstrate varying frequencies according to geographical ancestry. Although traditional blood typing is performed by serological techniques, research work during the past decade has demonstrated that genomic sequencing provides a more precise and comprehensive blood typing alternative. This lecture will review the genomic basis of blood groups, describe the application of genomic technologies to elucidate the blood phenotype diversity in Canadian blood donors and patients, and discuss the future applications of genomics in blood product characterization, allocation, and transfusion medicine practice.