“Blood connects us all” is the theme for the WHO’s World Blood Donor Day, taking place on June 14, 2016. This event celebrates those who have saved lives through blood donation and motivates healthy individuals who have yet to donate. Blood is an extraordinary tissue that performs a huge array of vital functions within the body. Red blood cells (RBCs) contain hemoglobin (Hb) that transports oxygen to tissues. White blood cells (WBCs) make up the immune system that protects the body against infectious diseases, and platelets are able to clot blood vessels during injury. Blood supplies the body with nutrients and hormones found in the plasma, removes waste and regulates acidity and temperature. Given these vital functions, when one or more of blood’s components fail to work as it should, or if it is lost in sufficient quantities, serious disorders can arise.

Approximately one-third of the world’s population has some form of anemia (abnormally low Hb levels), making this range of disorders the most common clinical problem worldwide. Within the European Union alone, the economic burden of hematologic disorders has been estimated at €23 billion per year. A global challenge of this magnitude must be dealt with strategically. At the beginning of 2016, the European Hematology Association (EHA) published a consensus document bringing together experts to identify unmet clinical and scientific needs to facilitate hematology research. This EHA roadmap breaks down hematology into several categories depending on the nature of the condition. Specific priorities within each field are assigned and accompanied by research proposals and anticipated impact.

Transfusion medicine is one of the highlighted areas. Blood transfusions are commonly used to reduce maternal mortality, treat patients with blood disorders and enable major surgery including organ transplantation. According to WHO figures, the total number of blood donations collected globally has increased by 25% over the last decade to around 108 million. Although encouraging, the rate of blood donation in low-income countries is 0.39% of the population, compared to 3.7% in high-income countries, creating a disparity in available blood. Socio-economic factors also reflect the way blood is utilized: in low-income countries, approximately 65% of blood transfusions are given to children under 5 years of age, whereas over 75% of blood transfusions in high-income countries are given to patients over 65 years old. It is therefore essential to ensure that blood supply adequately meets the healthcare system’s needs.

Having sufficient access to blood is not the only challenge. Particularly in under-resourced countries another problem is determining the quality of donated blood. Transfusion-transmissible infections (TTIs) such as HIV and hepatitis B/C are prevalent in countries that do not implement sufficient blood screening. The most common reason is insufficient access to test kits, and the issue is compounded by a lack of external quality assessment schemes. Although TTIs are less of a problem in richer countries, there is demand for blood from specific communities. This requires recruitment drives to attract donors from different ethnic backgrounds and individuals with desirable blood types.

Considerable effort is being spent in trying to develop artificial blood in order to alleviate the risk of TTIs and enable sufficient quantities of matched blood products. Various types of stem cell (SC), including hematopoietic stem cells (HSCs), human embryonic SCs and induced pluripotent SCs have already been used to derive cultured red blood cells, although producing sufficient numbers of suitable cells has been a major hurdle. An alternate approach being explored is to immortalize cell lines using viral vectors. At the RIKEN institute in Japan, Yukio Nakamura and colleagues have described the first immortalized human erythroid progenitor cell lines that are able to produce functional enucleated RBCs. Creating blood constituents ex vivo is a rapidly evolving field and according to the UK’s NHS Blood and Transplant, laboratory-produced RBCs are set to enter early-phase clinical trials in humans by 2017.

Besides immortalizing cell lines to generate transfusable RBCs in bulk, viral vectors have been engineered to ectopically express genes that compensate for non-functional versions in hematologic disorders. This approach was recently applied to treat a preclinical model of pyruvate kinase deficiency (PKD). PKD is a monogenic metabolic disorder caused by mutations in the pyruvate kinase, liver and RBC (P Kyle) gene, which affects the survival of RBCs. Murine HSCs were infected with a lentiviral vector driving the expression of PKLR cDNA, and transplanted into a PKD mouse model. Mice transplanted with modified HSCs displayed a normalized RBC compartment with no adverse effects, underscoring its therapeutic potential.

In contrast to the random genomic insertion of viral vectors, targeted gene therapy using nuclease technology such as CRISPR/Cas systems has enabled researchers to insert exogenous DNA into specific regions of the genome. Depending on the genetic etiology of the disease, a mutated region can be replaced, or a therapeutic transgene can be inserted into a ‘genomic safe harbor’, to restore cellular phenotype with minimal disruption of endogenous genes. While the feasibility of this approach has been demonstrated preclinically in, for example, Fanconi anemia (FA), issues such as how gene-modified cells behave after transplantation need careful investigation. Nevertheless, new early phase clinical trials are being initiated daily with the hope that otherwise incurable blood disorders can be tackled using gene and cell therapy.

It is vitally important that hematology research does not get overlooked when health budgets are allocated because this is the life-blood of safer and more effective treatments. EBioMedicine endeavors to capture the critical role blood has in diagnosing, treating and understanding disease. In this current issue alone, the journal features studies...
on proliferative disorders of the blood (acute lymphoblastic leukemia), aberrant cell number (FA and sarcoidosis) and infections (HIV). We will be attending the American Society for Hematology Annual Meeting taking place in San Diego (USA) at the end of 2016 to gain a better understanding of the diversity of translational research in hematology. In the meantime, we should collectively embrace World Blood Donor Day and consider rolling up our sleeves to save a life.