Hematopoietic Growth Factors in Transfusion Medicine and Cellular Therapy – Part II

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On June 14, 2013, we all have celebrated the 10th anniversary of the world blood donor day with the slogan ‘give the gift of life’. This global campaign was initiated to thank all altruistically motivated donors for their life-saving and life-improving blood donations. The challenges of a safe and sufficient blood supply worldwide were outlined by the World Health Organization in March 2010:

‘Blood products contribute to the saving of millions of lives every year, improve dramatically life expectancy and the quality of life of patients suffering from life-threatening conditions, and support complex medical and surgical procedures. In many countries, demand outstrips supply, and blood services throughout the world face the daunting challenge of making sufficient supplies of blood products available, while also ensuring the quality and safety of these products in the face of known and emerging threats to public health. The health-related Millennium Development Goals of reducing child mortality, improving maternal health and combating HIV/AIDS, malaria and other diseases cannot be achieved unless significant attention is paid to the availability, safety and quality of blood’ [1].

In 2009, approximately 4.7 million RBCs, almost 500,000 platelet concentrates, and more than 1.1 million units of fresh frozen plasma were donated, manufactured, and consumed in Germany [2]. Until 2010, the hemovigilance data in Germany did not reflect a breakthrough in reducing the national demand of annual blood supply as the figures of transfused blood products remained nearly constant [3]. With respect to the serious adverse transfusion reactions stated in these both reports [2, 3], allogeneic blood transfusions still carry inherent risks. Even though the risk of transmission of various infectious diseases could be reduced significantly compared to ear-

lier years close to a near-zero risk, triggering of immunosuppressive mechanisms and immune reactive events associated with higher morbidity and mortality in transfused patients still pose a major challenge.

Alternatives to blood transfusions comprise fluid substitution in patients with acute blood loss by saline solutions or volume expanders such as albumin, hydroxyethyl starch or dextrans to keep the circulation going, or the application of hematopoietic growth factors such as erythropoietin, e.g., in anemic patients with chronic kidney disease. Surprisingly, the discovery of such growth factors and their marketing authorization in the last 2–3 decades did not push blood supply aside. In the current issue of TRANSFUSION MEDICINE AND HEMOTHERAPY which continues the special topic of the last issue we highlight the impact of hematopoietic growth factors in transfusion medicine and cellular therapy.

A major focus in this 2nd part is the potential replacement of allogeneic blood transfusions by endogenous stimulation of the patient’s own hematopoiesis by using erythropoietin or thrombopoietin analoga [4–6]. The rationale of these treatment options based on the knowledge that the intrinsic production of each growth factor is severely limited; however, a sufficient amount of ‘target cells’, e.g. multipotent hematopoietic progenitor cells, are still available in hematopoietic niches of the bone marrow for boosting and releasing into the blood stream after stimulation by ‘external’ growth factors. All hematopoietic growth factors clinically used are manufactured by recombinant protein expression technology bearing in principle the risk of alloimmunization and are associated with some side effects which should be carefully considered prior to clinical use.

Hematopoietic growth factors are naturally occurring, hormone-like substances with a high degree of pleiotropy and redundancy which orchestrates the complex formation of different blood cells [7]. In the meantime, a broad spectrum of di-

verse molecule families (FGF, TGF, hedgehog, wntless) was discovered, all acting to enhance cell proliferation and/or differentiation via interaction of each ligand with its specific transmembrane receptor. Upon binding, an intracellular signal transduction cascade activates or represses a set of genes responsible for growth behavior. The group of Maurer et al. [8] contributed original data of ex vivo expanded megakaryocytic progenitor cells which are generated from cord blood stem cells using a cocktail of growth factors.

Besides their impact on hematopoiesis, most of the so-called hematopoietic growth factors have other putative functions in embryogenesis, angiogenesis, tissue morphogenesis, or wound healing and might also contribute to accelerate

growth in specific cancer subtypes. In principle, platelets are a rich source of a huge variety of growth factors, cytokines and chemokines. This phenomenon is reflected in the paper of Bieback [9] addressing the safety and quality of human platelet lysate as a standardized source – comparable to fetal calf serum – in stimulating at least the expansion of mesenchymal stem cells in a GMP-compliant and xenogenic-free fashion. Last but not least, Burger [10] reviews the current knowledge about the biological function of IL-6 in normal hematopoiesis and the pathophysiology of human diseases (inflammation, sepsis) and hematological malignancies of B-cell origin such as Castleman's disease and multiple myeloma.

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