1 Bone Marrow Reconstitution

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1 Introduction

An observation 50 years ago – rescue of mice from lethal irradiation by shielding the spleen – rapidly led to the clinical use of bone marrow transplantation (BMT). It was observed that reconstitution of the bone marrow took place from cells that could be found in the non-irradiated spleen. Shortly thereafter it was shown that bone marrow taken from one mouse could reconstitute the bone marrow in a lethally irradiated mouse. These observations and further canine experiments led to the clinical concept of BMT (Thomas 1999a,b). The approach of using BMT for the treatment of severely ill patients was achieved before the cells responsible for the reconstitution of the bone marrow had been identified and characterised. Nevertheless, a rapid transition from animal experiments to clinical practice was necessary because the first use of BMT was in patients who had no other chance of cure. These were patients with relapsed or refractory leukaemia who would otherwise have died in a short time. However, it could be proved that by BMT some of these patients had a chance of being cured.
2 The Haematopoietic Stem Cell

The haematopoietic stem cell (HSC) is traditionally regarded as a cell that resides in the bone marrow and is able to reconstitute all cell lines involved in haematopoiesis (erythrocytes, thrombocytes, leukocytes and lymphocytes). In addition to its occurrence in the bone marrow as evidenced by the successful transplantation of bone marrow, the HSC has some unique properties that differentiate it from the other organ-related stem cells that are discussed at this meeting. The HSC is able to leave the bone marrow and repopulate the bone marrow at a site that is distinct from its original place of residence. As such, HSCs can be found in the circulating blood. It is well known that in the phase of regeneration following chemotherapy or after the application of haematopoietic growth factors, a dramatic increase of these stem cells can be observed in the circulation, making it possible to collect HSCs for therapeutic approaches (Tarella et al. 1995; Olavarria and Kanfer 2000). The HSC has been well characterised on morphological, immunological, functional and genetic grounds. Furthermore, a substantial body of clinical evidence and experience has been gained by using these stem cells in clinical transplantation for about 30 years.

2.2 Characterisation

The HSC has been characterised by several means within the last several years. Morphologically the stem cell resembles lymphocytes and can thus not be distinguished easily by microscopy. However, progress in the functional characterisation of the stem cell as well as the definition of a distinct phenotype by analysing the expression of surface antigens and the genetic repertoire has helped us substantially to understand the characteristics of the HSC.

2.3 Phenotype

It was recognised early that HSCs carry a distinct set of surface antigens. The most commonly accepted characterisation of HSCs includes the co-expression of CD34 and CD90 (Thy-1) together with the absence of