# The South African Bone Marrow Registry – role in providing unrelated donors for allogeneic stem cell transplantation

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## History

The South African Bone Marrow Registry (SABMR) was established in 1991 in Cape Town, as a non-profit organisation at the initiative of professors Ernette du Toit and Peter Jacobs, to provide human leukocyte antigen (HLA) matched unrelated donors (MUDs) for South African (SA) patients.

Allogeneic bone marrow and now peripheral blood stem cell transplantation has come a long way since the work of E Donall Thomas in Seattle in the early 1950s.[1] These studies showed that by using HLA-matched sibling donors it was possible to cure certain haematological and metabolic diseases. These include acute and chronic myeloid leukaemia, myeloid dysplasia, lymphomas, multiple myeloma, aplastic anaemia, haemoglobinopathies, thalassaemia, Fanconi's anaemia and storage diseases.

Only some 25% of patients requiring haematopoietic stem cell (HSC) transplantation have an HLA matched family donor. Thus, the need for MUD registries became evident and led to the establishment of donor registries of unrelated individuals worldwide. Each registry, including the SABMR, has a database of HLA typed volunteers who are prepared to donate stem cells, anonymously and without payment, for the benefit of the sick anywhere in the world. Today, there are 19 million unrelated donors and cord blood units, in 67 linked registries.

## Structure and function

The SABMR is the hub centre for South Africa, registered as a non-profit organisation, responsible for formulating the national policies and donor recruitment strategies, as well as for the provision of a national database of potential HSC donors. The SABMR facilitates appropriate donor recruitment, obtaining consent from and counselling of potential HSC donors and arranging for the collection and transport of stem cells by human couriers for identified and adequately matched recipients.

The registry is responsible for the well-being of its own donors (with a 5-year post-donation follow-up), and for payments to local as well as foreign service providers.

The SABMR donor database of ±65 000 HLA typed individuals is also listed on Bone Marrow Donors Worldwide (BMDW). BMDW maintains a database of HLA typed donors and provides an 'Internet search engine' to identify possible donors for a particular patient anywhere in the world. While the SABMR maintains the national database, the Sunflower Fund recruits donors on behalf of the SABMR. The SABMR is also a member of the World Marrow Donor Association (WMDA) which provides guidelines for the collection and transfer of stem cells and donor safety.

## HLA matching and sourcing

The degree of HLA matching required is critical for the selection of the best donor. The relative importance of the various HLA loci and the resolution level at which they are matched have been analysed by many.[2,3] It is now accepted that high-resolution HLA matching at a DNA (molecular level) is associated with the best clinical outcome.[4] While the theoretical chance of an HLA match in a family is 1/4, the chance of a MUD is 1/100 000. Because of the extreme variability of the HLA system within and between populations and the need for very close matching, no country is self-reliant.

The sources of stem cells are peripheral blood stem cells (PBSC), bone marrow and cord blood. The majority of patients in SA receive PBSC.

## The procedure

The SABMR recruits healthy volunteers between the ages of 18 and 45 years. All donations are anonymous. An independent physician ensures that the donors are healthy and is responsible for the donor's general well-being, including post-donation follow-up.

The discovery of haematopoietic growth factors, such as granulocyte colony-stimulating factor (G-CSF) had a major impact on bone marrow transplantation. G-CSF is used to mobilise HSCs into the peripheral blood and has now almost totally replaced bone marrow harvesting as a means of obtaining stem cells for transplantation. Stem cells are harvested from the peripheral blood via a cell separator, making general anaesthesia, to aspirate bone marrow, unnecessary. Donors are given a 5-day course of 5 - 10 µg/kg G-CSF subcutaneously prior to harvesting PBSCs. The procedure takes 4 - 6 hours (if necessary on 2 consecutive days), for sufficient cells to be harvested for successful engraftment.

## Statistics

Since 1991 the SABMR has conducted preliminary searches for >1 000 patients. Of these, between 1997, when the first MUD transplant took place and March 2012, a total of 254 SA patients received HSC transplants from MUDs (Fig.1). This included patients from other countries on the African continent who were treated in

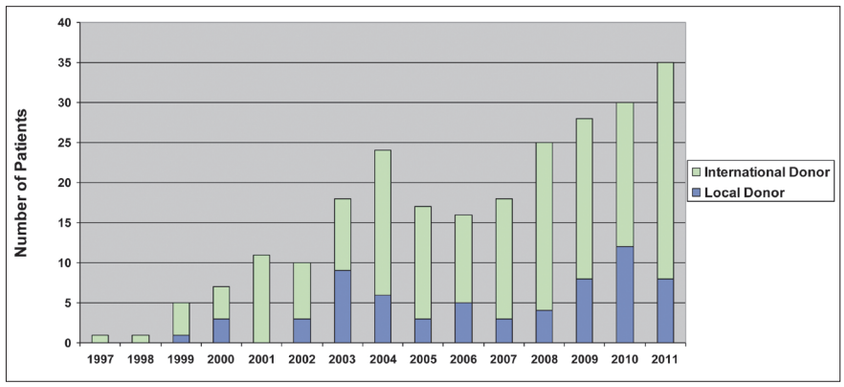


*Fig. 1. Matched unrelated donor bone marrow transplantation in South Africa – first transplants only.*

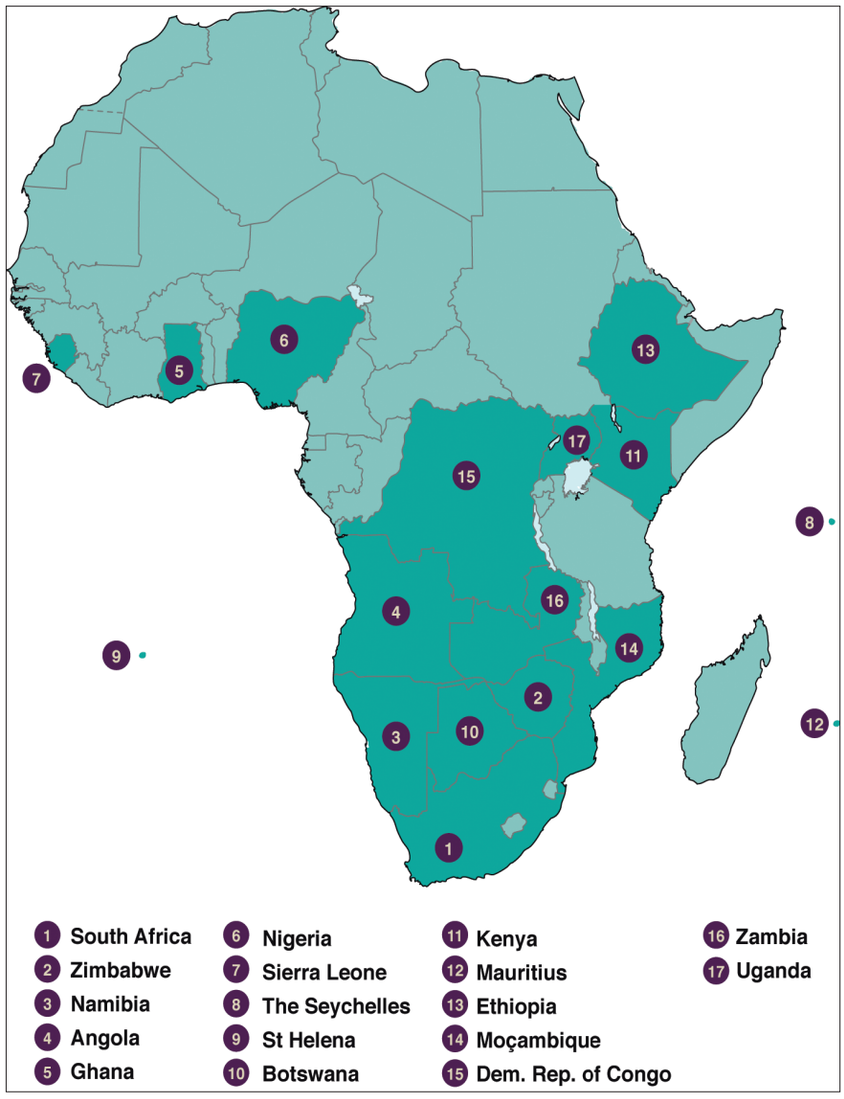


*Fig. 2. Preliminary search requests for patients referred for treatment in South Africa from African countries.*

SA (Fig. 2). The SABMR has also provided HSCs for foreign patients.

The 2010 WMDA report states that all stem cell registries together provided 12 822 bone marrow and peripheral blood stem cell products in 2010. It should also be noted that over 45% of these products involved a transplant from a donor in a country that was different from the patient's. To date, only 25% of patients transplanted in SA received HSCs from local donors and 75% from international donors. The reasons for this are due partly to the lack of HLA-A, -B, -DR typed donors in the SABMR and partly to the lack of donors, for patients of African and Asiatic ancestry, in the registry.

Cord blood banks have a very important role to play, as the product is readily available to the patient. There are limitations in that a single cord blood unit is usually only suitable for children and small adults. In addition, establishment of a cord blood bank needs more finance than a donor registry as the cord blood unit has to be collected, processed and stored with all the attendant expenses of HLA typing, infectious disease marker testing, etc., including quality management.

The number of unrelated cord blood units provided per year increases annually. In 2010 all cord blood banks together reported that 4 054 cord blood units were provided for transplantation. To date the SABMR has imported 19 cord blood units for SA patients.

## Conclusion

The SABMR renders a highly specialised service, currently to the 3 centres offering allogeneic unrelated bone marrow transplantation in SA, as well as international registries.

This service includes liaising between the patient's doctor and local donors, or international donor registry as well as assisting the transplant centre with the selection of the best HLA matched donor at a DNA level.

**References available at www.cmej.org.za**