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Influence of Donor Clonal Hematopoiesis in Allogeneic Hematopoietic Stem Cell Transplantation

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This research project aims to analyze the production of genetically identical blood cells (clonal hematopoiesis) in elderly donors, in order to evaluate the outcome after transplantation.

The production of all blood cells (hematopoiesis) is a complex biological process which mainly takes place in the bone marrow. All important blood cells develop during hematopoiesis (red blood cells, white blood cells, platelets etc.). All blood cells originate from hematopoietic stem cells.

Clonal hematopoiesis occurs when a change in the genome of those cells (mutation) changes the activity of one or more genes. This one mutated cell (clone) can proliferate and produce its own cell population, all carrying the mutation(s). These mutation(s) are acquired over time and are called somatic mutation(s). The cell populations have the potential to replace other (healthy) cell populations in the blood, causing clonal hematopoiesis.

Clonal hematopoiesis is a common phenomenon in older healthy individuals, since it occurs in the peripheral blood of at least 15% of individuals older than 60 years of age. At present, caution is needed when predicting clinical consequences from the gene mutations in healthy individuals.

In the context of allogeneic stem cell transplantation, it is unknown whether the presence of such mutations in hematopoietic stem cells of eligible stem cell donors may affect the transplantation. Some mutations influence specific characteristics of the stem cells, such as increased self-renewal. Therefore, it is conceivable that mutated stem cells may lead to stronger effects of graft-versus-leukemia (GVL) and could also be associated with an increased risk of donor cell leukemia (DCL).

This research project therefore proposes to analyze over 650 elderly donors for clonal hematopoiesis, in order to evaluate the outcome after transplantation.