

# Fighting Cancer with the Immune System

Clinical Cooperation Group Hematopoietic Cell Transplants

Leukaemias are due to disturbed blood formation in the bone marrow, an excessive production of immature cells with no function. It is the aim of the therapy to destroy the degenerate cells in the bone marrow and replace them with healthy blood forming cells of a donor. In 1975 the current head of the Clinical Cooperation Group (KKG) "Hematopoietic Cell Transplants", Prof. Kolb, carried out the first successful bone marrow transplantation in Germany together with colleagues from the Munich Schwabing Hospital. T-cells which trigger a dangerous immune reaction of the donor against the recipient, can be removed from the donated bone marrow beforehand. Before the purged donor bone marrow can be transplanted, the patient's diseased bone marrow must be destroyed. This is done by radiation and chemotherapy.

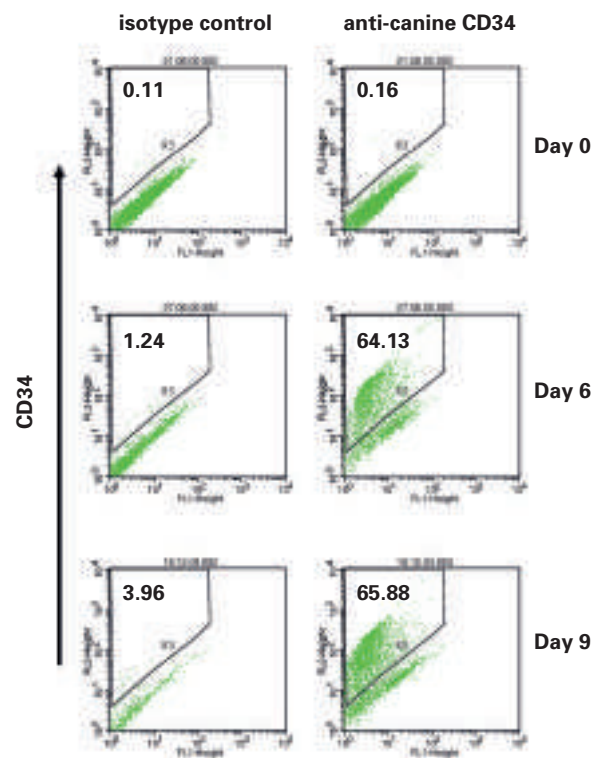
Unfortunately even after most intensive radiation and chemotherapy individual leukaemia cells are left in the organism, which means that the disease can flare up again (relapse), if the T-cells were removed. So there is a dilemma between the reaction against healthy organs of the patient on the one hand, a graft-versus-host reaction which can destroy the skin, the intestine and the liver and must,

therefore, be avoided, and the reaction against the patient's leukaemia, which is highly desirable. A solution to this dilemma was suggested by experiments on dogs, in which the blood formation of the recipient is switched off by the transfusion of lymphocytes of the donor 2 months and later after the transplantation of T-cell-deprived bone marrow, without triggering a graft-versus-host reaction.

This principle could be successfully applied in patients with relapsing leukaemia; as soon as chimerism and immune tolerance had been induced, donor lymphocytes could be transfused to treat the relapsed disease, without causing a severe graft-versus-host reaction. These donor T-cells recognise the leukaemia cells as being foreign cells and destroy them without the need for more radiation

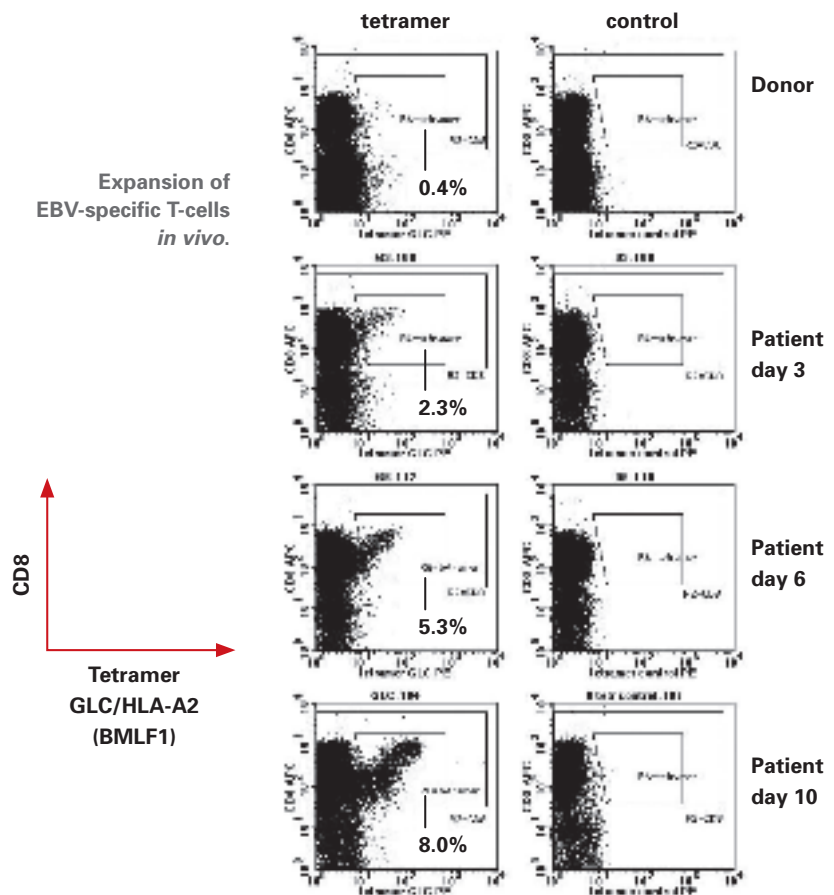
Production of hematopoietic stem cells from embryonic stem cells in dogs.

Expression of stem cell antigen CD34 after coculture with the mouse cell line OP9



or chemotherapy. Although chemotherapy and irradiation are still indispensable to the preparation of any bone marrow transplantation, the KKG could show that the quantity and thus the burden on the patient can be reduced considerably by subsequent adoptive immune therapy. The principle of immune therapy with T-cells from a healthy donor – after the establishment of the immune system of the donor from the stem cell transplantation – is also suitable for the treatment of other types of tumour diseases. However, the immune reaction against other types of tumour must be facilitated, since these are more difficult to recognise and attack than leukaemias. Tumour-specific antibodies and T-cells, but also T-cells armed with specific receptors by genetic therapy, can be used to destroy degenerate cells. Genetic therapy basically offers excellent possibilities for the treatment of leukaemia and malignant tumours, in the case of congenital diseases the disease gene can be replaced by a healthy gene in stem cells. But genetic therapy must also be further developed in animals similar to humans to reach a stage at which it can be applied to human patients effectively and without any severe complications.

Expansion of EBV-specific T-cells *in vivo*.



**Literature:**

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