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A Monthly Newsletter Summarizing Important Advances in Transfusion

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A gene therapy trial for hemophilia A treatment

David A. Roth (Beth Deaconess Medical Center, Harvard Medical School, Boston, MA, USA) et al. report the results of a phase I gene therapy trial for hemophilia A. For four of the six treated patients, a reduced number of bleeding episodes and lower dependence on exogenous factor VIII were noted. However, these therapeutic benefits had faded one year post-treatment.

Roth, D. A., et al. (2001) **Nonviral transfer of the gene encoding coagulation factor VIII in patients with severe hemophilia A**. N Engl J Med 344: 1735-1742.

Immunological tolerance induction *in utero*

Starting from the fact that the fetal stage of development is conducive for the induction of immunological tolerance, Nam D. Tran, Christopher D. Porada (Veterans Affairs Medical Center, University of Nevada, Reno, NV, USA) and coworkers were able to show that exposure of fetal lambs to a model antigen allows to induce long-term, antigen-specific immunological tolerance.

Tran, N. D., Porada, C. D., et al. (2001) **Induction of stable prenatal tolerance to β-galactosidase by in utero gene transfer into preimmune sheep fetuses**. Blood 97: 3417-3423.

Therapeutic efficacy of an EPO dimer

Erythropoietin (EPO) is naturally produced by the body to stimulate the production of red blood cells by the bone marrow. A research team led by Emmanuel Payen, from Hôpital Saint-Louis in Paris, has evaluated the biological properties of a recombinant EPO produced as a dimer, whereby a single dimer molecule is formed by the combination of two EPO molecules. The activity of the dimeric form was found to be substantially improved relative to the monomer. In addition, Payen's team succeeded in *in vivo* controlling the production of dimeric EPO in mice through a gene therapy approach.

Dalle, B., et al. (2001) **Dimeric erythropoietin fusion protein with enhanced erythropoietic activity in vitro and in vivo**. Blood 97: 3776-3782.

Efficacy of immunological reconstitution after hematopoietic stem cell transplantation

Jan Storek (Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA) and coworkers compared the relative efficacy of immunological reconstitution after hematopoietic stem cell transplantation using bone marrow *vs*. peripheral blood as stem cell source. The results reveal an enhanced cell-mediated immunity in peripheral blood stem cell recipients compared to bone marrow recipients. This finding translated into a lower infection rate among peripheral blood stem cell recipients.

Storek, J., et al. (2001) **Immune reconstitution after allogeneic marrow transplantation compared with blood stem cell transplantation**. Blood 97: 3380-3389.

In vitro amplification of pathogenic prion

A team headed by Claudio Soto, from the Serono Pharmaceuticals Research Institute (Geneva, Switzerland), devised a method for *in vitro* PrP^{Sc} amplification. The process is based on successive cycles of ultrasound pulses and incubations, leading to substantial improvements in the sensitivity of current detection methods.

Saborio, G. P., et al. (2001) **Sensitive detection of pathological prion protein by cyclic amplification of protein misfolding**. Nature 411: 810-813.

Genetic susceptibility to prion diseases

A new linkage study, undertaken by Ian J. Jackson (Western General Hospital, Edinburgh, Scotland, UK) and his team, identified 4 additional prion disease susceptibility loci in the mouse genome. In addition, the data shed light on environmental factors as contributing elements in the pathogenesis of prion diseases.

Manolakou, K., et al. (2001) **Genetic and environmental factors modify bovine spongiform encephalopathy incubation period in mice**. Proc Natl Acad Sci USA 98: 7402-7407.