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A Monthly Newsletter Summarizing Important Advances in Transfusion

Volume 1, Number 3

A cellular model of cancerous transformation by horizontal transfer of apoptotic bodies

Apoptotic bodies are made up of genomic DNA-protein particles formed from the death of precancerous cells. Some *in vitro* models have previously demonstrated the horizontal transfer and the acquisition of genes from apoptotic bodies by healthy living cells. The latest results from Lars Holmgren's team (Cancer Center Karolinska Hospital, Stockholm, Sweden) provide support for this model, by demonstrating the *in vitro* transformation through transfer of apoptotic bodies carrying activated oncogenes.

Bergsmedh, A., et al. (2001) **Horizontal transfer of oncogenes by uptake of apoptotic bodies**. Proc Natl Acad Sci USA 98: 6407-6411.

Immunomodulatory effects of red blood cells

Before the era of universal leukoreduction of blood components, it was thought that the immunomodulatory effects of blood transfusion were mediated by leukocytes (white blood cells). Recent results from a team led by Fernando A. Arosa (Institute for Molecular and Cell Biology, Porto, Portugal) suggest that red blood cells could contribute to host defense mechanisms, by facilitating T lymphocyte activation, while simultaneously slowing down apoptotic death of these same T cells.

Fonseca, A. M., et al. (2001) **Red blood cells inhibit activation-induced cell death and oxidative stress in human peripheral blood T lymphocytes**. Blood 97: 3152-3160.

Inhibition of the immune response against factor VIII

To compensate for their hereditary deficiency in factor VIII, hemophilia A patients are treated with factor VIII concentrate derived from either human plasma or from genetically engineered *in vitro* production. However, almost a third of treated patients eventually develop neutralizing antibodies against factor VIII. Dorothea Scandella's group at the American Red Cross (Rockville, MD, USA) tested an animal model of tolerance induction based on the infusion of antibodies against CD154, an important costimulatory molecule of the immune system. Treatment with anti-CD154 antibodies prior to factor VIII infusion, and sustained treatment with anti-CD154, resulted in long-term tolerance to factor VIII in 12 of 22 treated mice.

Rossi, G., et al. (2001) **Long-term induction of immune tolerance after blockade of CD40-CD40L interaction in a mouse model of hemophilia A**. Blood 97: 2750-2757.

Hengjun Chao and Christopher E. Walsh, from the University of North Carolina (Chapel Hill, NC, USA) reached a similar goal through the use of a viral vector bearing the gene for human factor VIII targeted for liver-specific expression. The low and sustained expression of human factor VIII succeeded in inducing specific tolerance to this coagulation factor.

Chao, J. and Walsh, C. E. (2001) **Induction of tolerance to human factor VIII in mice**. Blood 97: 3311-3312.

Identification of susceptibility genes for transmissible spongiform encephalopaties (TSE) in the mouse.

John Collinge's team, from the Imperial College School of Medicine at St Mary's (London, UK), report on the identification of three loci in the mouse genome which would presumably encompass genes influencing TSE predisposition and incubation time.

Lloyd, S. E., et al. (2001) **Identification of multiple quantitative trait loci linked to prion disease incubation period in mice**. Proc Natl Acad Sci USA 98: 6279-6283.

Some traces of bacteria in the blood of healthy individuals?

The blood of healthy individuals is considered to be a sterile environment. However, recent results from Simo Nikkari and coworkers (Stanford University School of Medicine, Stanford, CA, USA) suggest that the blood of healthy individuals might contain very low levels of bacteria.

Nikkari, S., et al. (2001) **Does blood of healthy subjects contain bacterial ribosomal DNA?** J Clin Microbiol 39: 1956-1959.