HÉMA-QUÉBEC

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A Monthly Newsletter Summarizing Important Advances in Transfusion

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Human immunoglobulin production in bovine species

The demand for intravenous immunoglobulins (IVIg), a human plasma fractionation product used in the treatment of several autoimmune diseases, keeps increasing. A team led by James M. Robl from Hematech, LLC, (Westport, CT, USA) designed genetically modified bovine calves capable of synthesizing human immunoglobulins. Kuroiwa et al. relied upon a new type of genetic vector that allows transfer of an entire segment of a human chromosome into bovine embryos. Robl's team succeeded in obtaining seven « transchromosomic » calves capable of producing human immunoglobulins in their blood. Although human immunoglobulin blood levels were low, the technology could eventually lead to large-scale IVIg production at very competitive costs.

Kuroiwa, Y., et al., **Cloned Transchromosomic Calves Producing Human Immunoglobulin**, Nat Biotechnol 20 (9) : 889-894 (2002) (doi : 10.1038/nbt727).

Hematopoietic stem cell plasticity: The controversy continues

Several studies published in the past few months suggested that hematopoietic stem cells are able to differentiate into diverse cell types (muscle cells, endothelial cells, neurons, etc.). Irving L. Weissmann's group at Stanford University (Stanford, CA, USA) just published results that challenge this view. Wagers et al. designed a murine experimental model allowing to follow the fate of a single hematopoietic stem cell grafted into a recipient mouse. Genetic labeling of the grafted cell using a fluorescent protein gene enabled to trace back daughter cells of the original grafted cell. A thorough analysis of several tissues from single cell-grafted mice revealed very few fluorescent non-hematopoietic cells, suggesting that hematopoietic stem cells' transdifferentiation potential is more limited that originally thought.

Wagers, A., et al., **Little Evidence for Developmental Plasticity of Adult Hematopoietic Stem Cells**, Science 297 (5590) : 2256-2259 (2002) (doi : 10.1126/science.1074807).

Culture of human embryonic stem cells: A technical advance

The potential of stem cells for medical applications such as tissue reconstitution and therapeutic cloning remains a hot topic in both the scientific literature and mainstream media. So far, preserving the undifferentiated state of human embryonic stem cells in culture required the use of animal-derived supplements (murine stromal feeder cells, bovine serum). In the context of a regulated environment, the risk of transmission of animal pathogens to humans is a matter of concern. To circumvent this drawback, Ariff Bongso's team, working at the National University of Singapore, succeeded in maintaining the undifferentiated state of human embryonic stem cells without animal-derived material, whether feeder cells or culture additives. This technical advance is a step forward in the application of human embryonic stem cells for therapeutic use.

Richards M., et al. **Human Feeders Support Prolonged Undifferentiated Growth of Human Inner Cell Masses and Embryonic Stem Cells**, Nat Biotechnol 20 (9) : 933-936 (2002) (doi : 10.1038/nbt726).

A new hypothesis supporting the therapeutic efficacy of IVIg

Despite the increasing number of clinical indications for which intravenous immunoglobulins (IVIg) are recommended, the mechanism of action of this plasma fractionation product is still being debated. Ryan J. Hansen and Joseph P. Balthasar (University at Buffalo, The State University of New York, Buffalo, NY, USA) designed an animal model of autoimmune disease induced by infusion of an antiplatelet antibody and responding to IVIg treatment. The results indicate that IVIg accelerates autoantibody clearance, which is consistent with the observed therapeutic efficacy of IVIg in this animal model.

Hansen, R. J. and Balthasar, J. P., **Effects of Intravenous Immunoglobulin on Platelet Count and Antiplatelet Antibody Disposition in a Rat Model of Immune Thrombocytopenia**, Blood 100 (6) : 2087-2093 (2002).

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