Factors influencing immune response after in vivo retrovirus-mediated gene transfer to the liver.

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Résumé en anglais	**BACKGROUND:** Highly efficient retrovirus-mediated gene transfer into hepatocytes in vivo triggers an immune response directed against transduced hepatocytes. This effect may be due either to spreading of retroviral vectors in the blood stream with subsequent infection of antigen presenting cells (APCs) or to cross-presentation of the transgene product present as a contaminant in the viral stock. In order to decrease immune response, we evaluated the effect of asanguineous perfusion of the liver as well as purification of the viral stock on long-term transduction of hepatocytes using the nls-lacZ marker gene. **METHODS:** Animals were divided in four groups. In group 1, the viral supernatant was perfused in the regenerating liver after complete vascular exclusion of the organ. In group 2, using the same strategy, animals received retroviral supernatant that was passed through a beta-galactosidase affinity column to reduce beta-galactosidase contamination. In two control groups (respectively groups 3 and 4) the corresponding viral supernatants were delivered via peripheral injection. **RESULTS:** In group 1, 23.1% of animals had no immune response 2 months after gene delivery vs. 33.4% in group 2, 4.3% in control group 3, and 0% in control group 4. Statistical analysis of the results demonstrated that only the difference between groups 2 and 3 was statistically significant. This indicated that both asanguineous perfusion together with passage through an affinity column were required to decrease significantly immune response. **CONCLUSIONS:** Our present results suggest that both supernatant contamination and viral spreading contribute to immune response after retrovirus-mediated gene delivery to the liver.
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Liens

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