OBA News

News from the NIH Office of Biotechnology Activities

June 15, 2009

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Clonal Population of Cells Detected in a Clinical Human Gene Transfer Trial Using a Lentiviral Vector - The National Institutes of Health Office of Biotechnology Activities (OBA) has been informed that a "relative clonal dominance" was detected during follow-up of a subject who is participating in a French human gene transfer trial being conducted for individuals with β-Thalassemia Major and Sickle Cell Anemia. The clinical trial, sponsored by Genetix France, used hematopoietic stem cells transduced by a self inactivating (SIN) HIV-1 lentiviral vector containing the gene for β-globin under the control of the β-globin promoter. The subject received the gene modified cells in June 2007.

This clonal dominance appears to result from the integration of the vector in the gene encoding for the HMGA2 protein, which is associated with both benign and malignant tumors. The clone however has been stable for five months and the subject remains in good health. In fact, although the subject required almost monthly blood transfusions during the 11 months prior to the gene transfer intervention, the subject has not since required a blood transfusion.

The investigators involved in this trial will be performing further studies to evaluate the consequences of this integration and its capacity to proliferate. Until these studies are completed and another review is performed by the French Medicine Agency, AFSSAPS, no other subjects in this study will receive the gene modified cells.

On June 10, OBA sent a memorandum to inform OBA-registered investigators who are using or propose to use lentiviral or retroviral vectors in hematopoietic or other stem cells. OBA is currently seeking additional information regarding this event such as the specifics of the vector used, the dose of the cells, transduction conditions, and the clinical course of the first subject treated in this trial. OBA will organize a discussion at a meeting of the NIH Recombinant DNA Advisory Committee (RAC) when this information is available.