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Stem cell therapy for bleeding disorder

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Hemophilia A is an X-linked recessive bleeding disorder caused by the deficiency the clotting Factor V-III. Currently, treatment of hemophilia consists of factor replacement using fresh frozen plasma, cryoprecipitate, or Factor VIII concentrate.

The transdifferentiation of bone marrow cells (BMCs) into hepatocytes has created enormous interest in applying this process to the development of cellular medicine for degenerative and genetic diseases. The cellular origin of factor VIII synthesis is controversial. Liver transplantation cures hemophilia A, demonstrating that the liver is a major site of factor VIII synthesis. We hypothesize that the partial replacement of mutated liver cells by healthy cells in hemophilia A (HA) mice could ameliorate the severity of the bleeding disorder. We perturbed the host liver with acetaminophen to facilitate

the engraftment and hepatic differentiation of lineagedepleted (Lin⁻) enhanced green fluorescent protein (eGFP)-expressing BMCs. Immunohistochemistry experiments with the liver tissue showed that the donorderived cells expressed the markers of both hepatocytes (albumin and cytokeratin-18) and endothelial cells (von Willbrand factor). The results of fluorescent in situ hybridization and immunocytochemistry experiments suggested that differentiation was direct in this model. The BMC-recipient mice expressed FVIII protein and survived in a tail clip challenge experiment. Furthermore, a coagulation assay confirmed that the plasma FVIII activity was maintained at 20.4 \pm 3.6% of normal pooled plasma activity for more than a year without forming its inhibitor. Overall, this report demonstrated that BMCs rescued the bleeding phenotype in HA mice, suggesting a potential therapy for this and other related disorders.

Biography

Dr. Neelam Yadav has completed her Ph.D from Industrial Toxicology Research Centre, Lucknow and postdoctoral studies from Stem Cell Biology Laboratory of National Institute of Immunology (NII) New delhi, India. She is Assistant Professor in Department of Biochemistry, at Dr. R.M.L. Avadh University, Faizabad, India. Dr. Neelam has published many papers in reputed international journals and filed one patent.

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