Methods in Neurobiology – Case Study 1 Module 2 – Vanessa Libera

Question/Biological Problem (10 points)

Hemophilia A is a recessive X-linked coagulation disorder that causes a delay in blood clotting, which results in excessive blood loss due to internal bleeding. Factor VIII, also referred to as antihemophilic factor (AHF), is a glycoprotein procofactor that is essential for blood clotting. Factor VIII is encoded by the F8 gene, and defects in this gene lead to Hemophilia A. Factor VIII production occurs in vascular, glomerular, tubular endothelium and sinusoidal cells in the liver. [5] Additional complications of Hemophilia A include a higher risk of deep vein thrombosis and pulmonary embolisms, which may be life-threatening. [6]

Aim: To use a primary sinusoidal cell culture obtained from the liver of a donor patient with non-defective F8 gene. Then, purifying Factor VIII out of the culture to inject directly into the diseased individual's veins as a treatment regimen.

Research Plan/Model (10 points)

- Identify a willing donor to obtain a very small chunk of their healthy liver.
- Mince the piece of liver and disaggregate by the use of an enzyme.
- Innoculate the cells in a Roux culture bottle supplied with fresh culture growth medium, such as Hepatic growth medium. [2]
- Cell will produce Factor VIII, which will be isolated from the media and purified.
- Factor VIII therapy will include injection of the product directly into the blood steam in the hand or arm. To maintain the appropriate amount of the clotting factor in the body, a patient with severe Hemophilia A will need to receive the therapy via infusion regularly. [1]
- I chose this model because most therapies focus on recombinant DNA technology, and perhaps the body would respond well to this method. Scientists will be able to observe the treatment and gain a better understanding of the role that Factor VIII plays in blood clotting. [4]
- Liver cell culture may be fairly simple, and even once a part of the liver is removed from a patient, it will regrow and function correctly within a few months, so the donor patient will not be put in harm's way and the recipient of the isolated Factor VIII will be able to have enough clotting factors in their body.

Sources:

[1] Hemophilia a. National Hemophilia Foundation. (n.d.). Retrieved September 13, 2021, from https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-a.

[2] Hepatic cells. Zen. (n.d.). Retrieved September 13, 2021, from https://www.zen-bio.com/products/cells/hepatocytes.php.

[3] Products licensed in the US. National Hemophilia Foundation. (n.d.). Retrieved September 13, 2021, from https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/products-licensed-in-the-us.

[4] SI;, C. (n.d.). *Factor viii: Structure and function in blood clotting*. American journal of hematology. Retrieved September 13, 2021, from https://pubmed.ncbi.nlm.nih.gov/6424437/.

[5] Uppangala, N. (n.d.). *Recombinant Clotting Factor VIII, Erythropoietin and Hepatitis B Vaccine*. Recombinant clotting factor viii, erythropoietin and hepatitis b vaccine. Retrieved September 13, 2021, from https://www.biotecharticles.com/Biotechnology-products-Article/Recombinant-Clotting-Factor-VIII-Erythropoietin-and-Hepatitis-B-Vaccine-387.html#:~:text=In%20humans%20clotting%20factor%20VIII%20is%20encoded%20by,amount%20of%20blood%20loss%20due%20to%20internal%20bleeding.

[6] Wikimedia Foundation. (2021, August 29). *Factor viii*. Wikipedia. Retrieved September 13, 2021, from https://en.wikipedia.org/wiki/Factor_VIII.