Hepatocellular Carcinoma is a High-risk Side Effect of Thalassemia Disease

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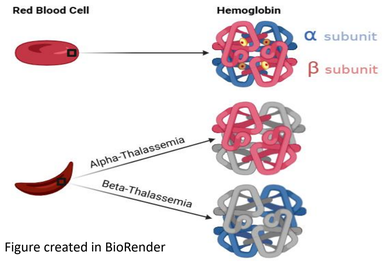
INTRODUCTION



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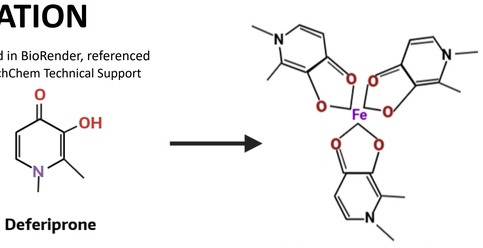
THALASSEMIA

- Partial to null loss of function due to a point mutation in several known sites of the HBB and HBA1 and 2 genes, which code for hemoglobin
- Thalassemia has two types:
  1. Alpha: point mutation causes a loss of function of the alpha subgroups on the hemoglobin protein
  2. Beta: point mutation causes a loss of function in the beta subgroup of the hemoglobin protein.
- Diagnosed based on the severity group in two categories:
  1. Intermediate: severity is in the median range, and most patients are non-transfusion dependent
  2. Major: highest severity, and patients are always transfusion dependent to maintain baseline hemoglobin levels for survival

CHELATION

Figure created in BioRender, referenced from the BenchChem Technical Support Team. 2026.

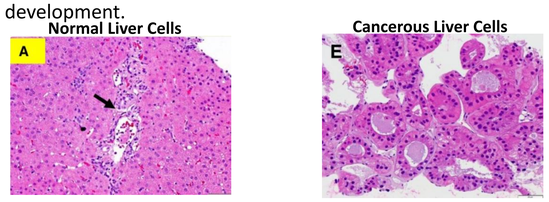


Deferiprone **Deferiprone Iron Complex**

- Deferiprone is one of several possible supplements taken by transfusion-dependent patients as a type of therapy for iron overload.
- The complex molecule binds to excess iron for excretion through urine and stool.
- Found to be highly effective in releasing excess iron during transfusion to decrease iron overload from transfusion therapies.
- Deferiprone is just one example of what a chelation therapy molecule looks like and how the iron is bound for transportation out of the liver.

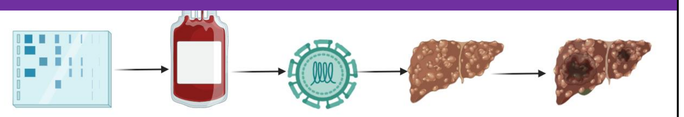
HEPATOCELLULAR CARCINOMA

- Hepatocellular carcinoma is one of the most common forms of cancer, which arises from mutations in hepatocytes, the main functioning cells in the liver.
- Free iron is implicated in causing malignant proliferations due to the generation of reactive oxygen species, causing peroxidation of the cell membrane fatty acid properties of the liver.
- Hepatitis C and liver disease are confounders that increase the risk of development.



Panel A shows the morphology of normal liver cells and panel E shows the morphology of cancer liver cells. (Figure from Jiang et al., 2018)

METHODS



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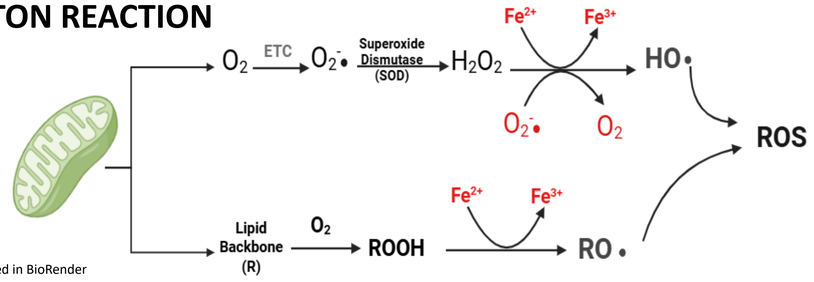
- Review of gene editing experiments
  - seeing if the disease is reversible. Comparison of non-transfusion and transfusion-dependent patients.
  - Analyzing the difference in side effects and their correlation to hepatocellular carcinoma.
- How hepatitis C is developed within thalassemia treatment or lifestyle.
  -Hepatitis C can be developed through life choices as well as developed in transfusion treatments within systems of low evaluation of blood-borne pathogens
- Review of several variations of liver disease and how they can add to the significance of developing secondary hepatocellular carcinoma
  -Fibrosis: excessive amount of collagen derived from the activation of hepatic stellate cells, causing hepatic-portal scarring
  -Cirrhosis: advanced distortion of normal liver architecture
- What is hepatocellular carcinoma, and how can it relate to a disease such as thalassemia that impacts the liver?

RESULTS

FENTON REACTION



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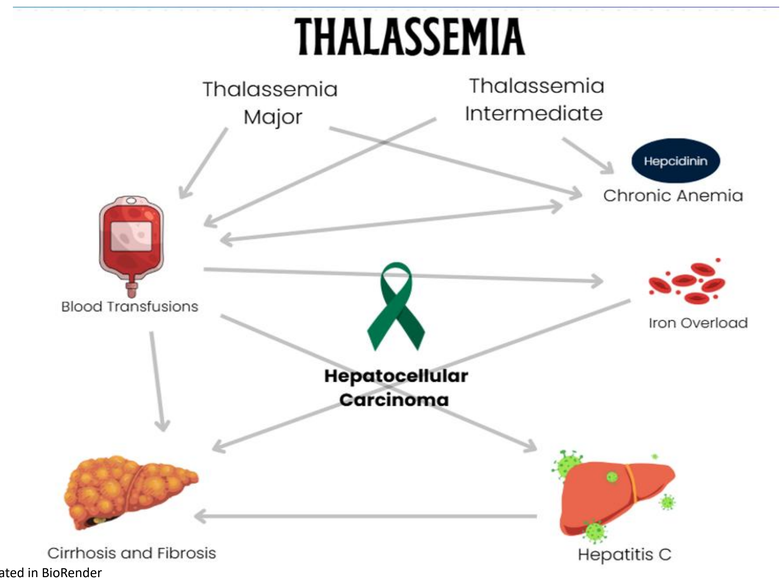
Fenton reaction is a reaction in environments of excessive amounts of iron to produce highly reactive oxygen species (ROS) that cause damage in liver tissue cells. Thalassemia patients have a high risk of problems with excessive oxygen levels

1. Thalassemia Major patients get transfused with about 20-40 units of blood a year; each unit contains about 200mg iron per unit.
2. Thalassemia Intermediate patients get transfusions, but even without the additional iron being transfused, they do not have the machinery to get rid of the iron produced by the body.



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- Hypothetical progression map of what the diagnosis would be if all side effects were in place: In a sense, a thalassemia patient who is transfusion-dependent and has acquired Hepatitis C viral infection from the transfusion, causing fibrosis scarring in the liver because of the viral attachment, resulting in enough cell damage to produce malignancy.
- Thalassemia patients during treatment have an increased risk of developing hepatocellular carcinoma from several additional confounders, including transfusion volume, history of or development of liver disease, and Hepatitis C.
- There is no straight line between these elements, and each patient's journey is individualized through genetic expression and personal life choices (alcohol, drug use, and hygiene).
- Age has a major effect on the development of liver cancer, as it is seen mainly in adults older than 55 years of age
  - Children with thalassemia are under close watch for malignancy because they have a longer period for a mutated cell to form because of treatment or side effects.

REFERENCES

KEY TAKE AWAYS

- Thalassemia is diagnosed in terms of loss of function of the beta or alpha hemoglobin proteins
- Chelation is a therapy for patients to discard unneeded iron
- There is not straight path from thalassemia to hepatocellular carcinoma
- Fenton reaction has a major role in the side effects of thalassemia
- Lifestyle has a big effect on the outcome of hepatocellular carcinoma