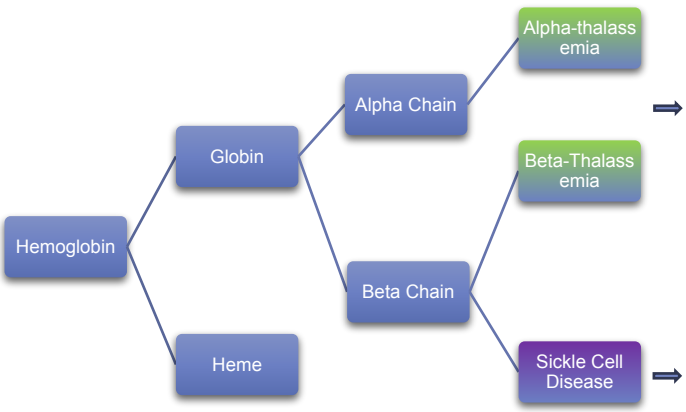
HEMOGLOBINOPATHIES

Hemoglobinopathies are characterized by quantitative and qualitative defects of globin chains.



QUANTITATIVE DEFECT:

An imbalance of α or β globin chains from 1 or more missing or diminished globin chains:

- **Alpha-Thalassemia** – combination of deletions of the 4 α chain genes on chromosome 16
- **Beta-thalassemia** – mutations of the 2 β chain genes on chromosome 11 leading to absent "βO" or diminished "$\beta+$" production

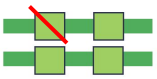
QUALITATIVE DEFECT

Mutation in β globin gene causing structural abnormalities:

- **HbS** – Glutamate to valine mutation
- **HbC** – Glutamate to lysine mutation

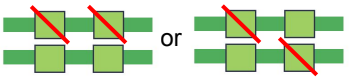
ALPHA-THALASSEMIA

One deletion (Trait):



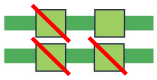
Asymptomatic

Two deletions (Trait):



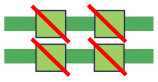
Mild anemia: Cis deletion carry higher risk of severe thalassemia in offspring

HbH disease:



Moderate-severe anemia: β chains form HbH tetramers

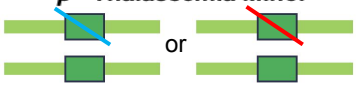
α –Thalassemia Major:



Lethal in utero: γ chains form Hb Barts

BETA-THALASSEMIA

β –Thalassemia Minor



Heterozygosity ($\beta/\beta+$) or (β/βO)

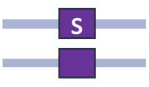
β –Thalassemia Intermedia and Major

Homozygosity of ($\beta+/\beta+$) or (βO/βO) or compound heterozygosity (βO/$\beta+$)

Of note: Intermedia is non-transfusion-dependent and major is transfusion-dependent

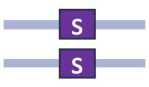
SICKLE CELL DISEASE

Sickle cell trait (HbAS)



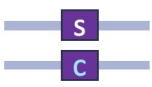
Asymptomatic carrier

Sickle Cell Disease (HbSS)



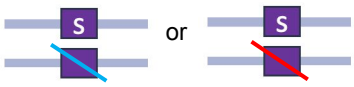
Severe anemia and vaso-occlusive disease

HbSC disease



Moderate-severe anemia and vaso-occlusive disease

Sickle β-thalassemia



Severity is determined by β-globin chain production (mild sickle → severe sickle)

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