

Iron metabolism

5th week

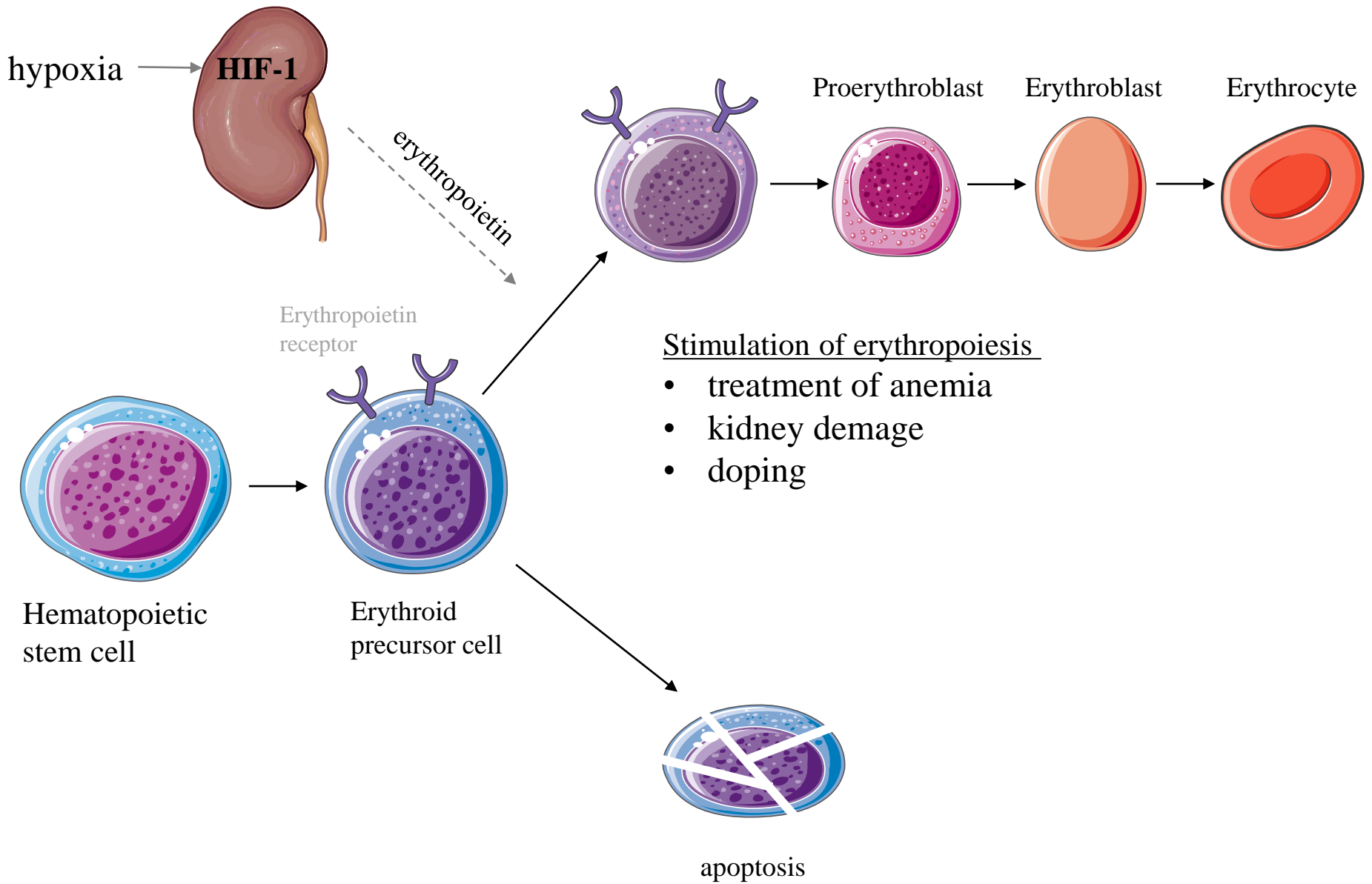
Distribution of iron:

Tissue	Form	% of iron
erythrocytes	hemoglobin	70,5
muscles	myoglobin	3,2
Stores – liver spleen	ferritin hemosiderin	26,0
Blood plasma	transferrin	0,1
other	cytochromes catalase peroxidase Fe - proteins	0,15

Chemical forms of iron:

Ferric (Fe^{3+}) iron: insoluble at physiological pH

Ferrous (Fe^{2+}) iron: dangerous if free, **forms free radicals**



Iron balance

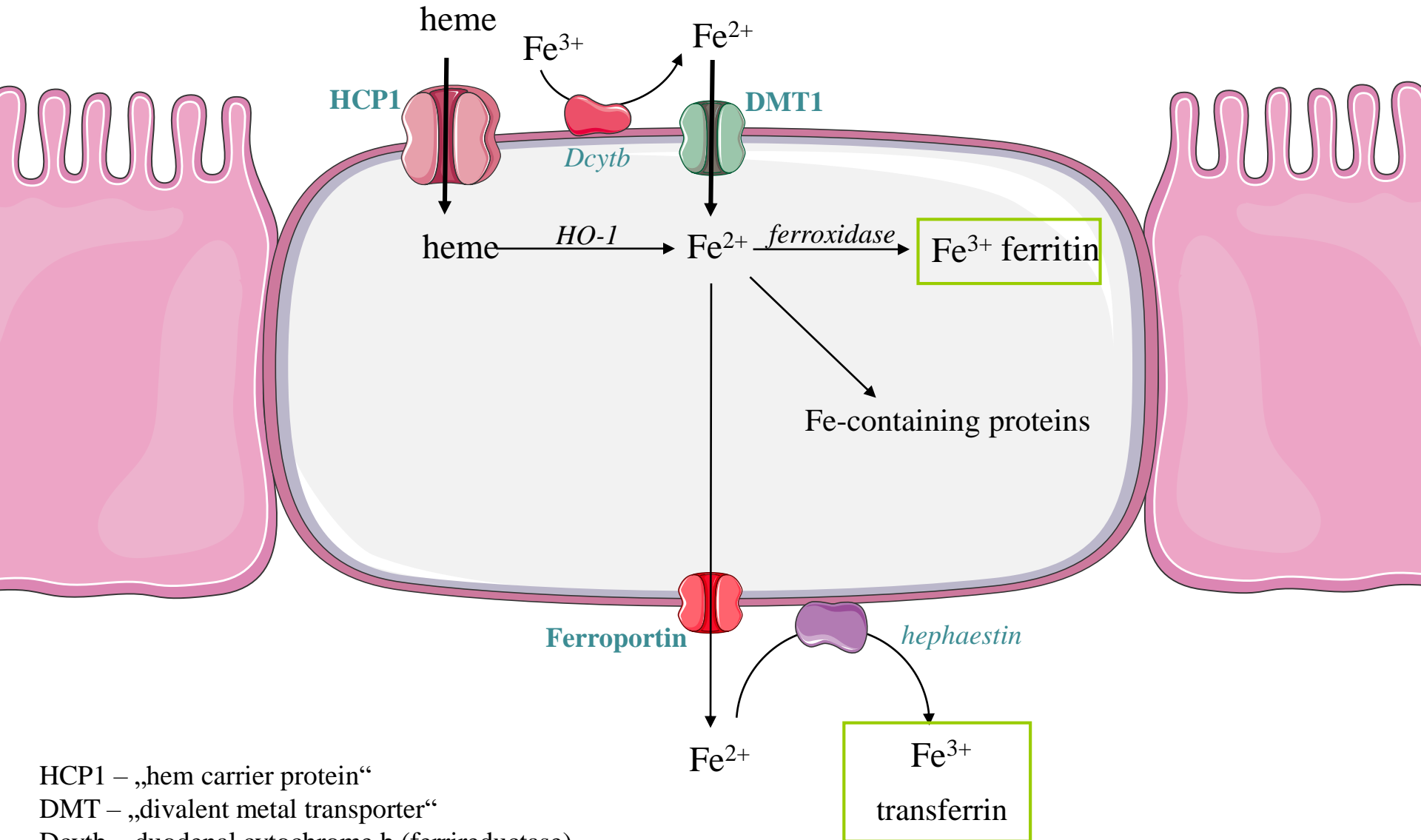
- Total body iron: 3 – 4g
- Minimal loss: 1 – 2 mg/d
- Erythropoietic iron requirement only 20mg/d
- Excretion of iron: minimum, daily loss: 0,01% (1-2 mg)
 - by intestine, bleeding, skin, hair, pregnancy, menstrual bleeding

Absorbtion of iron:

Factors affecting absorption:

1. Quality of iron in food: heme iron (meat, liver) – 10-30%
non-heme iron (plant origin) – 1-5%
2. Form of iron: heme > Fe²⁺ > Fe³⁺
3. Other components of food:
 - inhibitory: salts of Ca²⁺, phosphate, milk, cheese, tea (tanin), coffee, oxalates
 - stimulatory: ascorbate, citrate, amino acids amino acids

Absorbption of iron:

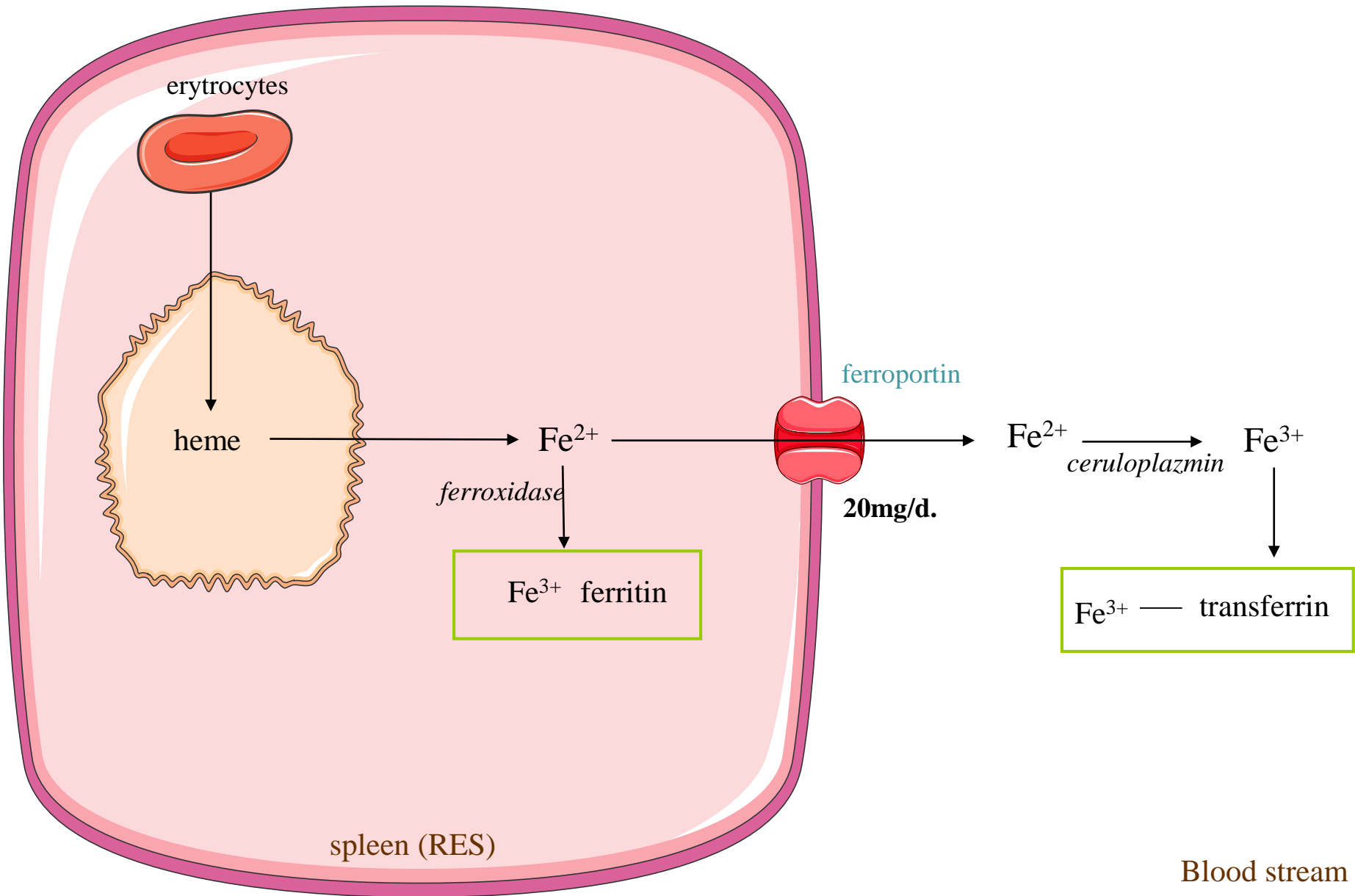


HCP1 – „hem carrier protein“

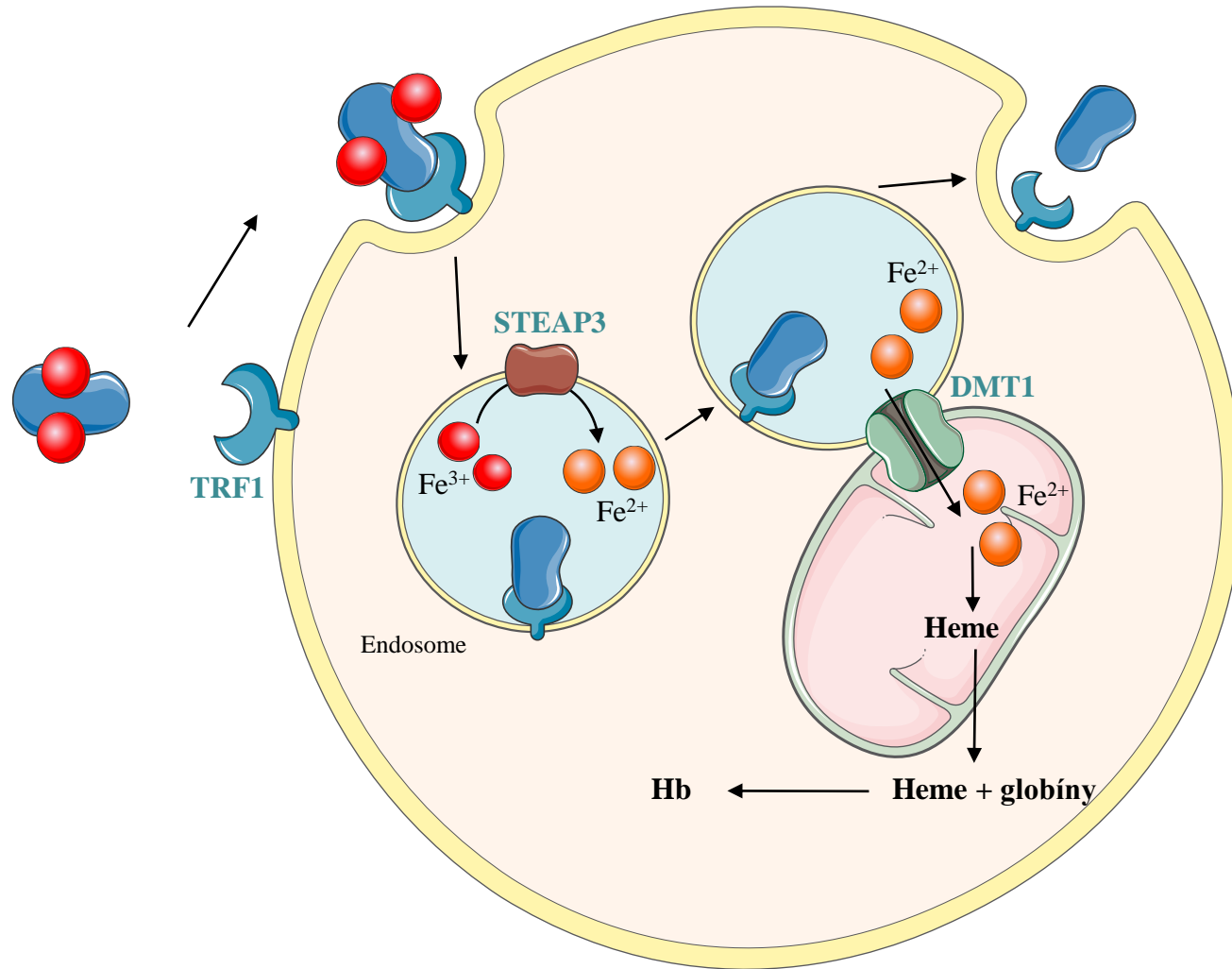
DMT – „divalent metal transporter“

Dcytb – duodenal cytochrome b (ferrireductase)

Recyclation of iron (erythrocyte lifespan)



Transport of iron



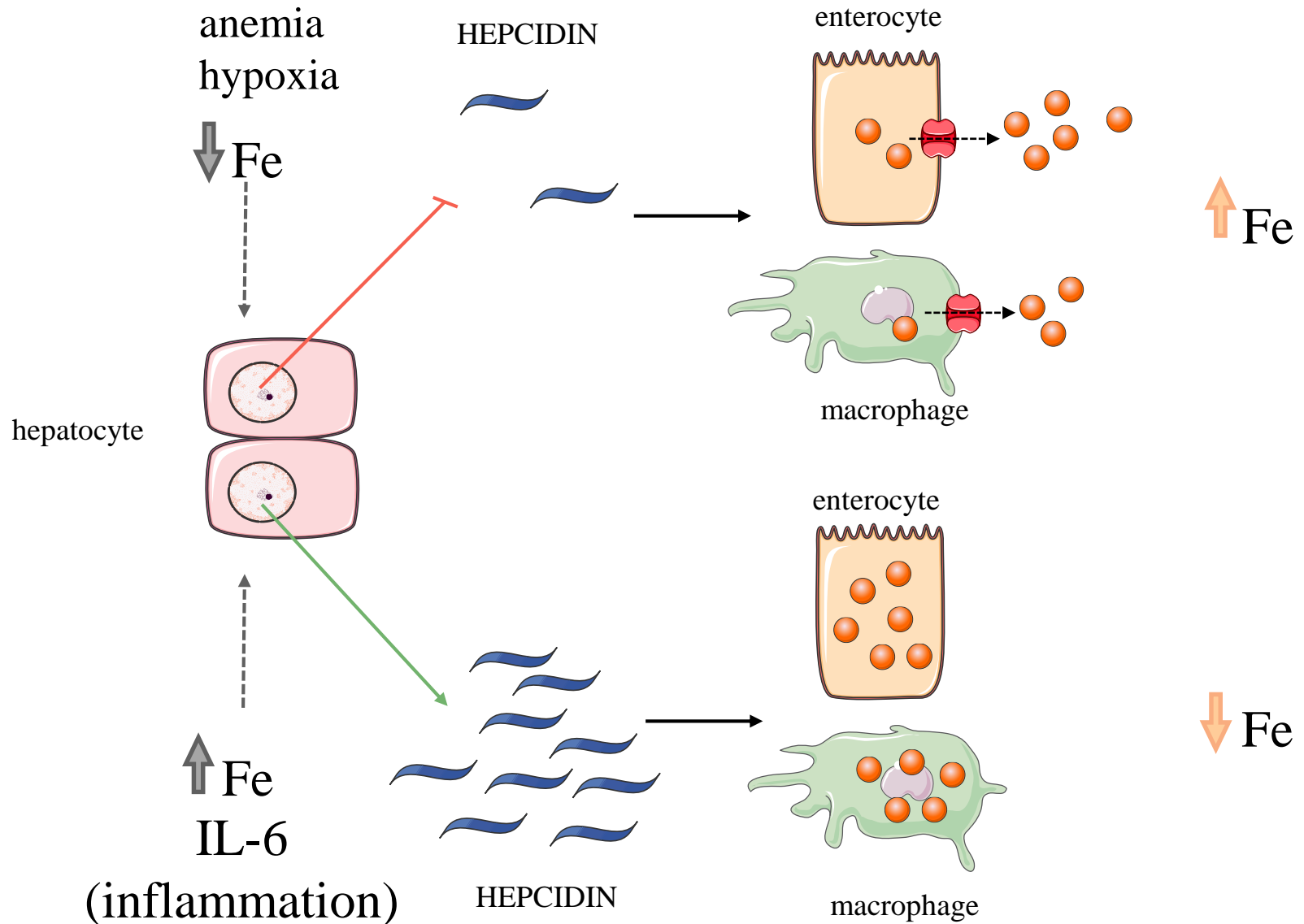
STEAP3 – endosomal ferrireductase

Regulation of iron metabolism in organism

Hepcidin

- key regulator of iron homeostasis
- **antibacterial protection (Hepatic bactericidal protein)**
- produced **in liver** during increasing stores of iron in liver or during inflammation (IL-6)
- main iron regulatory hormone
- target structure = **ferroportin - internalization, degradation**
(**reduces** transport of Fe across the basolateral membrane of enterocytes and releasing of Fe from macrophages)

Regulation of iron metabolism in organism



Regulation of iron metabolism in cell

• **posttranscription modification of mRNA** → system IREs/IRPs

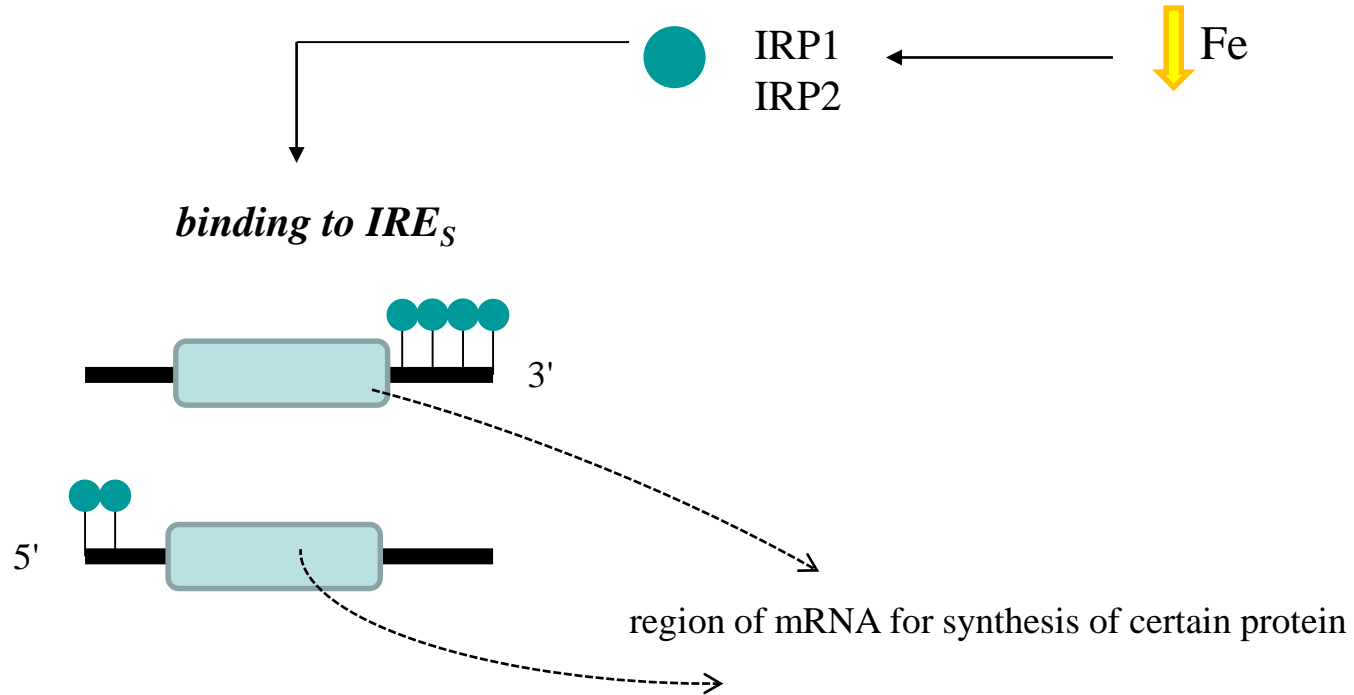
IRE_S – „*iron responsive elements*“ – non coding regions of mRNA at 3' or 5' ends for proteins of iron metabolism



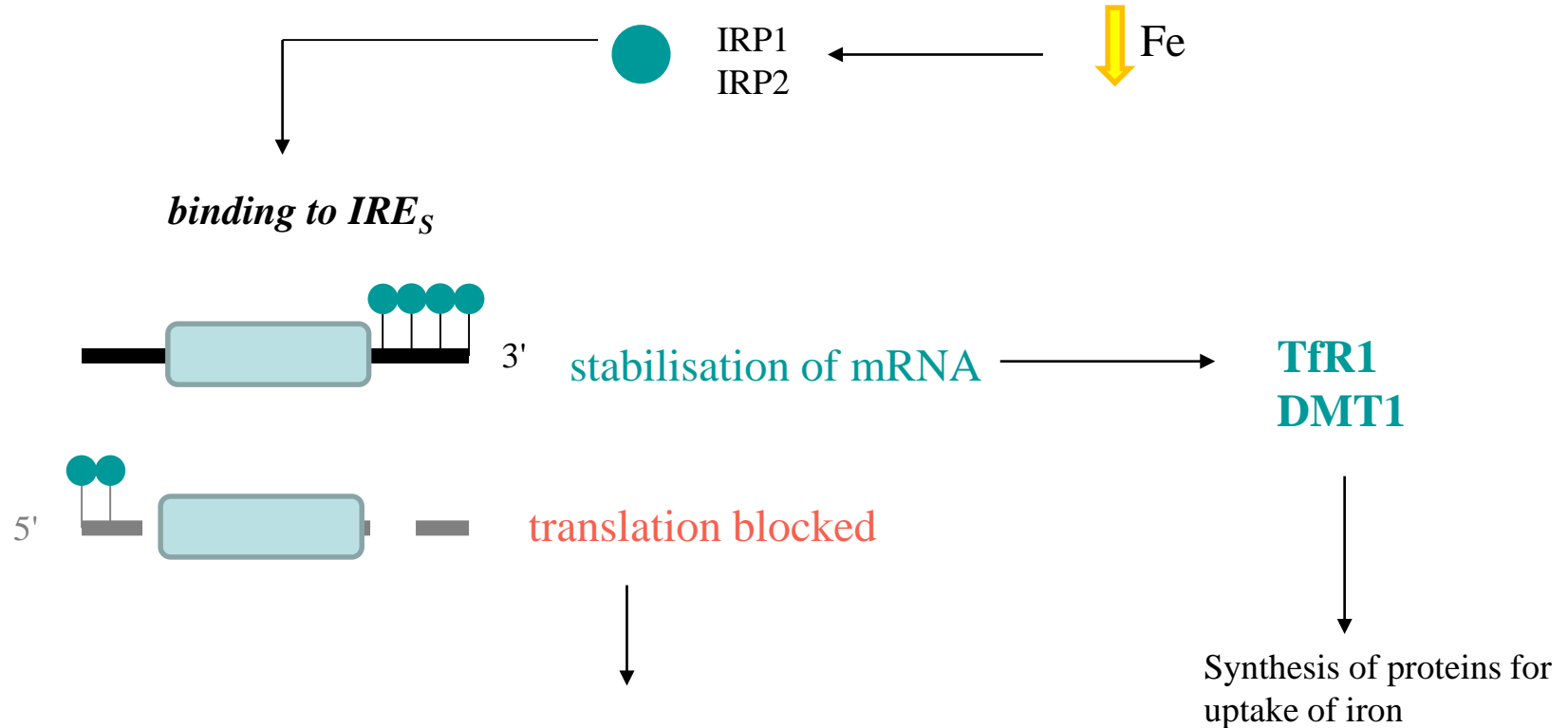
IRP_S – ● „*iron regulatory proteins*“ – proteins able to bind to IREs

- binding of IRP to IRE at **5' end of mRNA** = **block translation**
- binding of IRP to IRE at **3' end of mRNA** = **stabilization of mRNA** (protection from its degradation)

Regulation of iron metabolism in cell



Regulation of iron metabolism

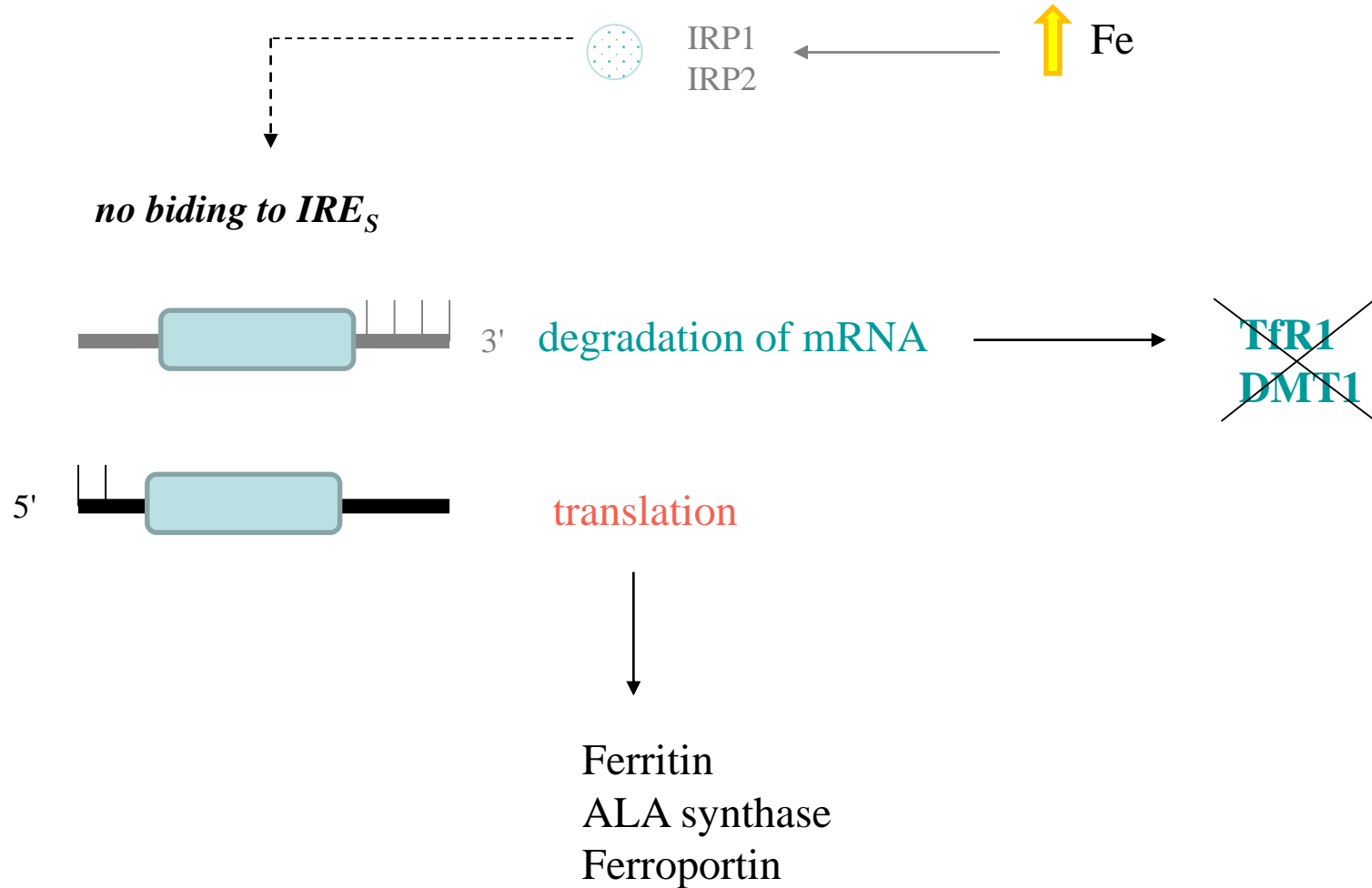


Ferritin - not needed storing of iron

ALA synthase – key enzyme in synthesis of porphyrines

Ferroportin - cell keeps iron inside, blocks export outside

Regulation of iron metabolism

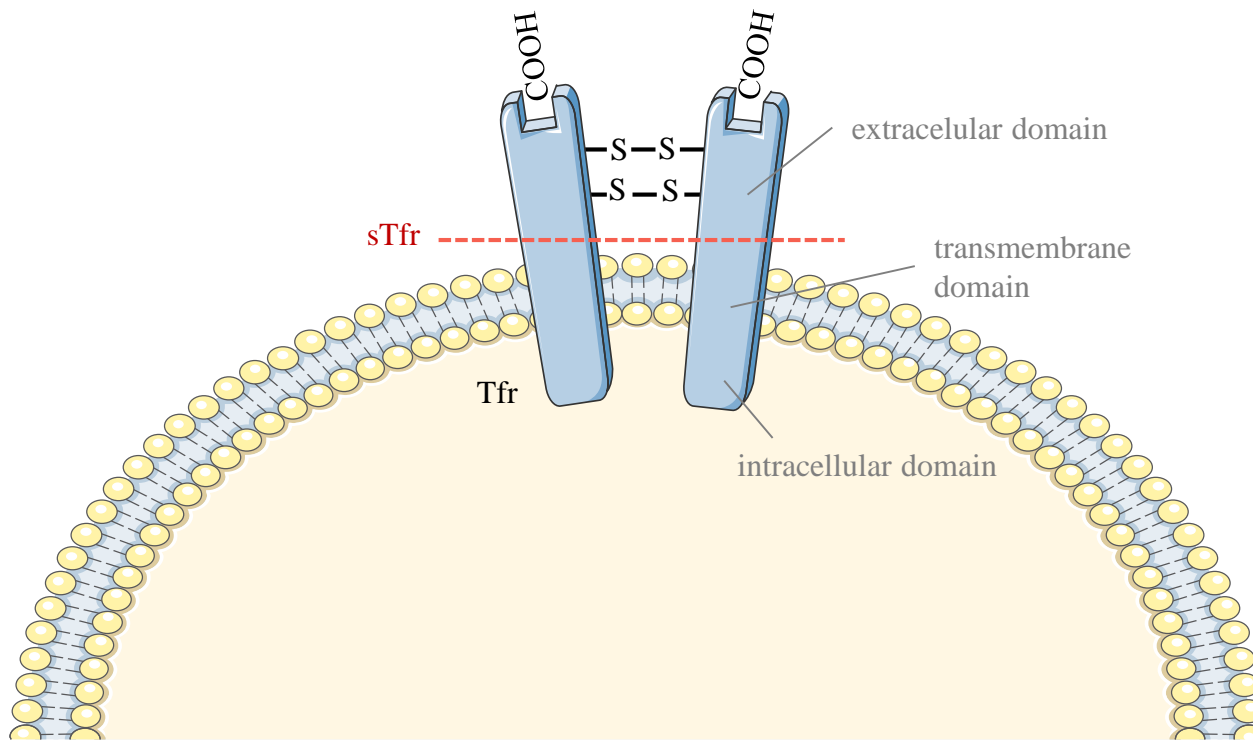


Transferrin

- β_1 -globulin synthesized predominantly in liver
- under physiological conditions transferrin is saturated by iron
approx. to 1/3 – binding capacity
- concentration in organism **increases with iron deficiency**
- **decreased level** occurs with an excess of iron, failure of liver proteosynthesis, as well as during reaction of organism to acute stress
- 80 % of transferrin receptors are on immature erythrocytes

Transferrin receptor

- cells which need iron – expression of high number of **transferrin receptors** on their surface
- soluble serum fraction
- indicator of iron deficiency (rises in serum with Fe deficiency anemia)



Ferritin

- complex of apoferritin and $\text{Fe}(\text{OH})_3$ with phosphate
- represents **storage of Fe^{3+} (ferric ions)**
- subunits H (heavy) and L (light)
- deposits into cells of liver, spleen, intestinal mucosa
- completely saturated ferritin contains several thousand of Fe^{3+} atoms
- binding of iron - after oxidation of Fe^{2+} to Fe^{3+} , H-ferritin is ferroxidase

Hemosiderin

- macromolecular complex of ferritin with lipid structures
- less soluble in water
- deposition in tissues can reach toxic level

Disorders of iron metabolism

Sideropenia

- decreased amount of iron in the body
- decreased absorption of iron from the gut
- chronic blood loss
- can lead to a decrease in hemoglobin and microcytic anemia

decrease in serum ferritin
increase in TrfR
increase in transferrin
decrease in serum iron

Hemochromatosis

- increased absorption of iron from the gut

increase in serum iron
increase in ferritin
increase transferrin
saturation

Anemia

1. defect of red blood cells synthesis:

- **iron deficiency**
 - increased iron loss (menstruation, pregnancy, blood loss from GIT)
 - increased need for iron utilization (body growth, puberty)
 - decreased iron absorption (gastrectomy, achlorhydria)
- **megaloblastic**
 - folate deficiency
 - B₁₂ deficiency
- **sideroblastic**
 - heme synthesis defects
- **aplastic**
 - bone marrow doesn't make enough red blood cells

Anemia

2. increased degradation/loss of red blood cells: :

- **hemolytic**
 - increased degradation of red blood cells
 - sickle cell anaemia, talassemia, enzyme deficiency, immune haemolytic anaemia, mechanical haemolytic anaemia)
- **posthemorrhagic**
 - blood loss

Hemochromatosis/hemosiderosis

- iron accumulates in the liver, heart and pancreas
- symptoms:
 - ↓ skin pigmentation
 - connective tissue damage
 - heart disease
 - diabetes mellitus
 - liver cirrhosis
- causes:
 - primary: genetic abnormalities, impaired regulation of iron absorption (↓ expression of hepcidin)
 - secondary: blood transfusion, increased intake of iron-containing preparations