



Metabolismo del ferro, infiammazione e malattie croniche

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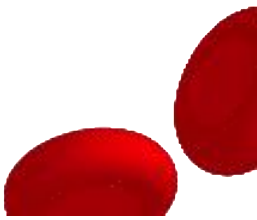


Hematological Diseases
(ERN EuroBloodNet)



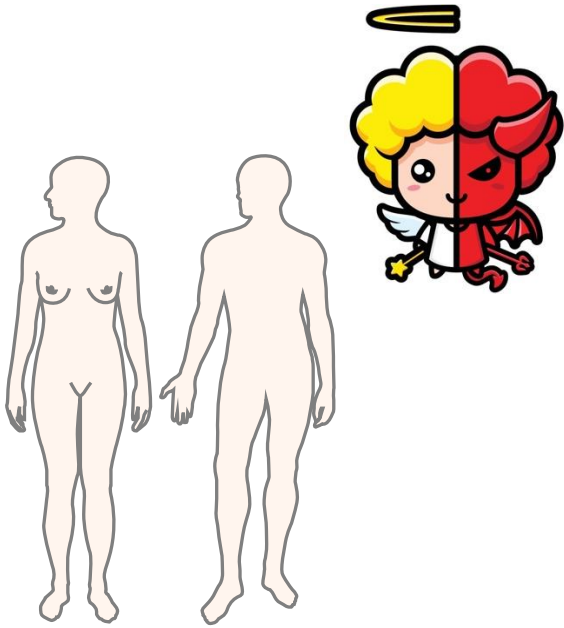
Agenda

- Iron trafficking in health and disease: inflammation rewires iron metabolism
- From iron restriction to anemia of inflammation
- Absolute and functional iron deficiency: different diseases, shared mechanisms
- How do we recognize ID in inflammatory conditions?
- How can we restore iron availability?



Iron homeostasis requires strict regulation

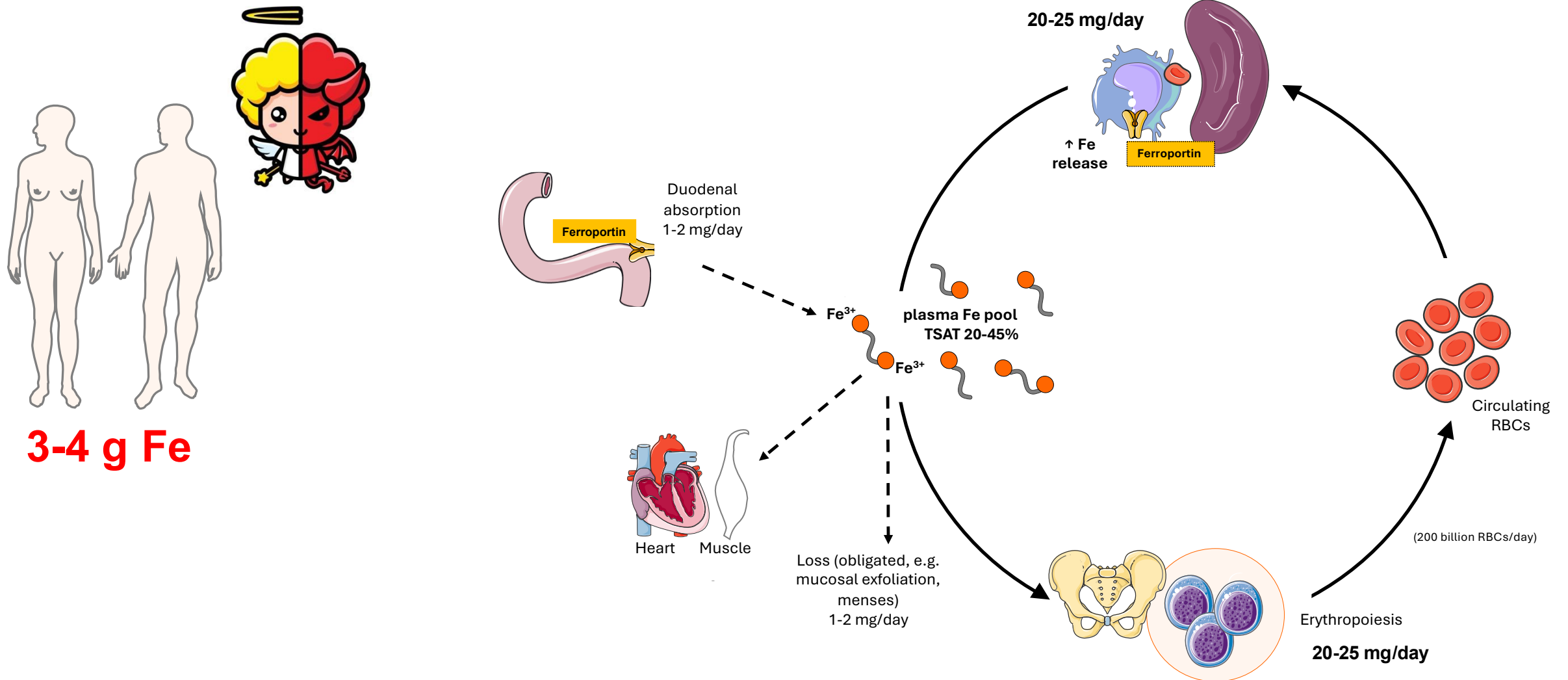
Essential...but potentially toxic!



3-4 g Fe

Iron metabolism is a circular economy

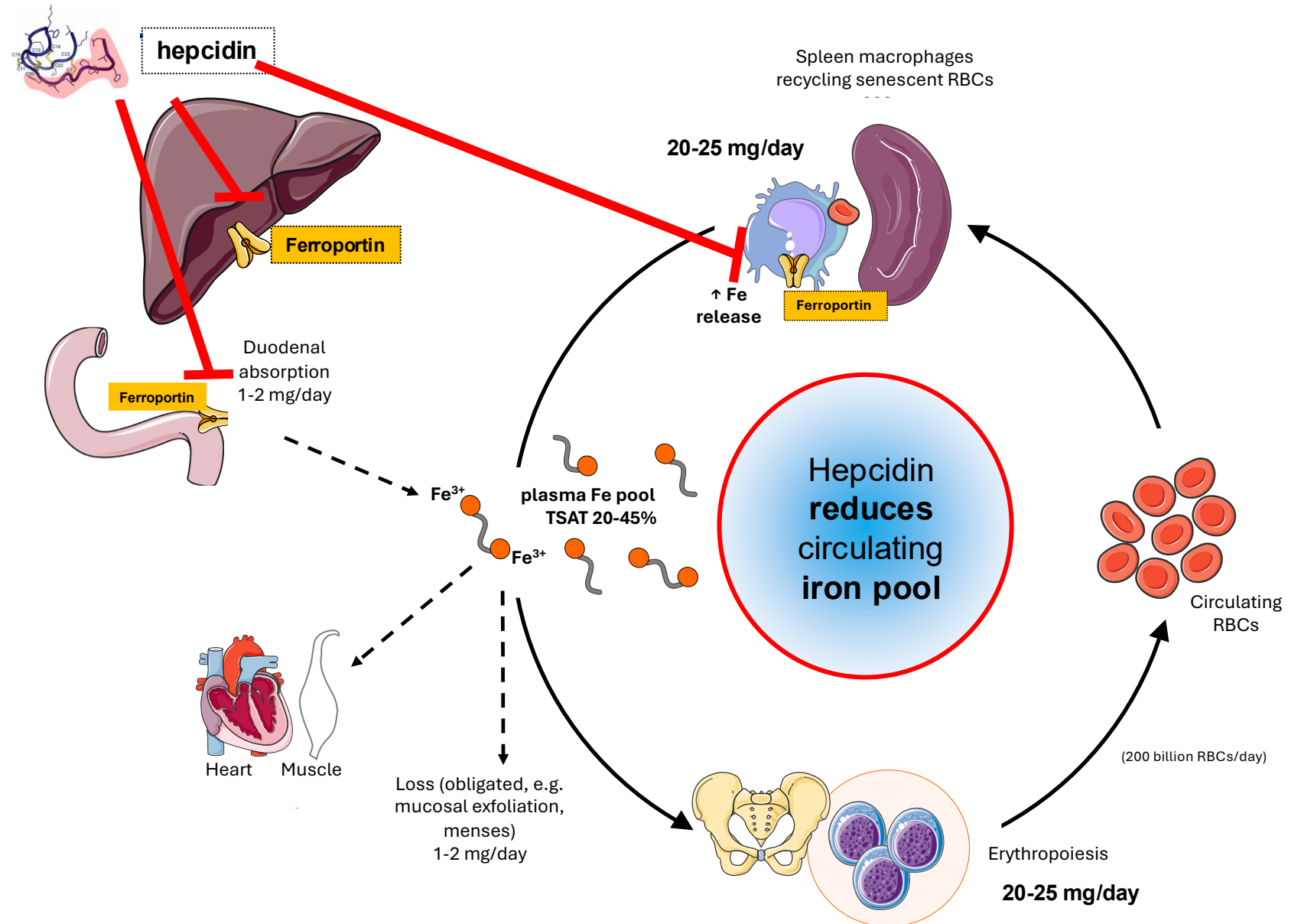
Essential...but potentially toxic!



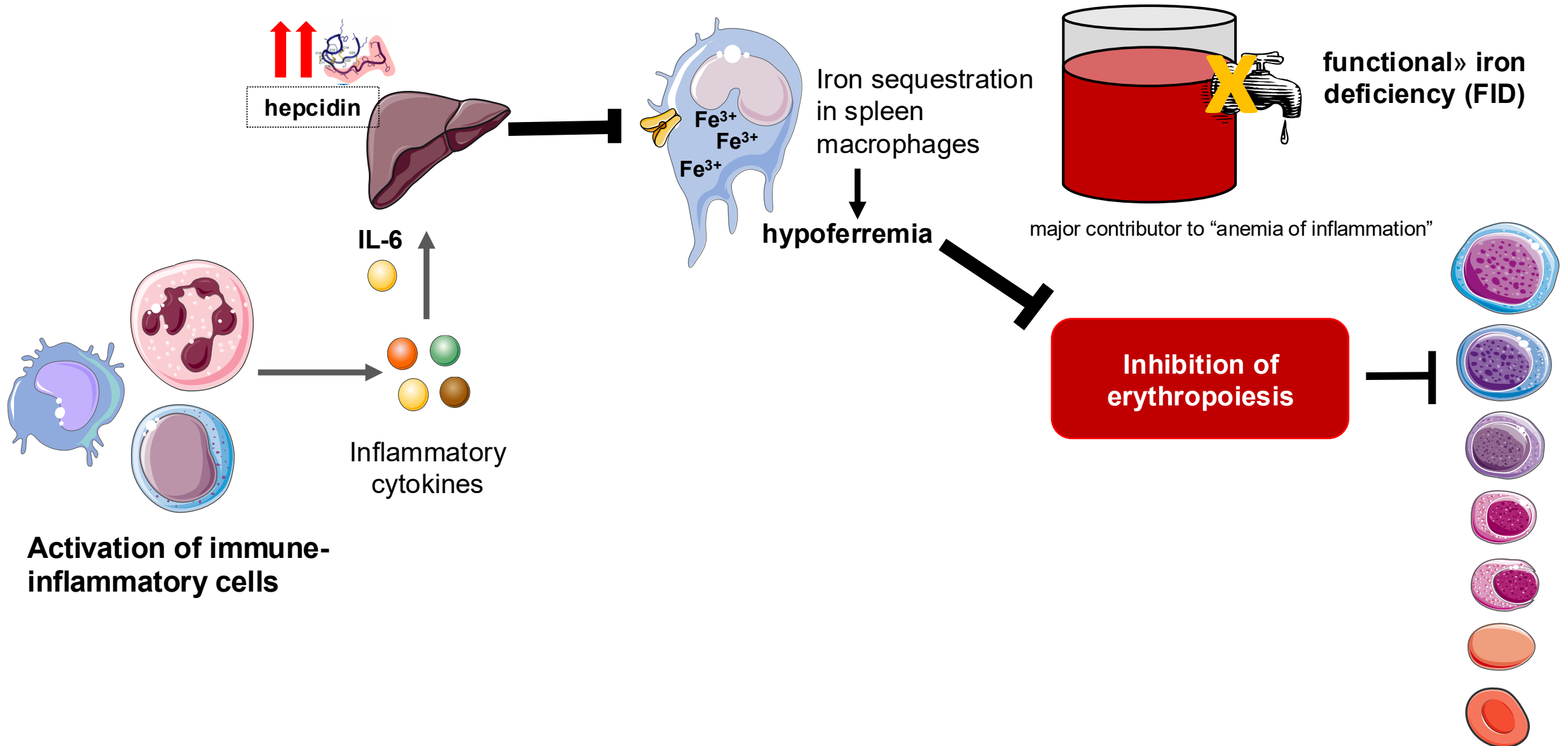
Hepcidin is the key regulator of iron homeostasis

Hepcidin: small peptide hormone mainly produced by the liver

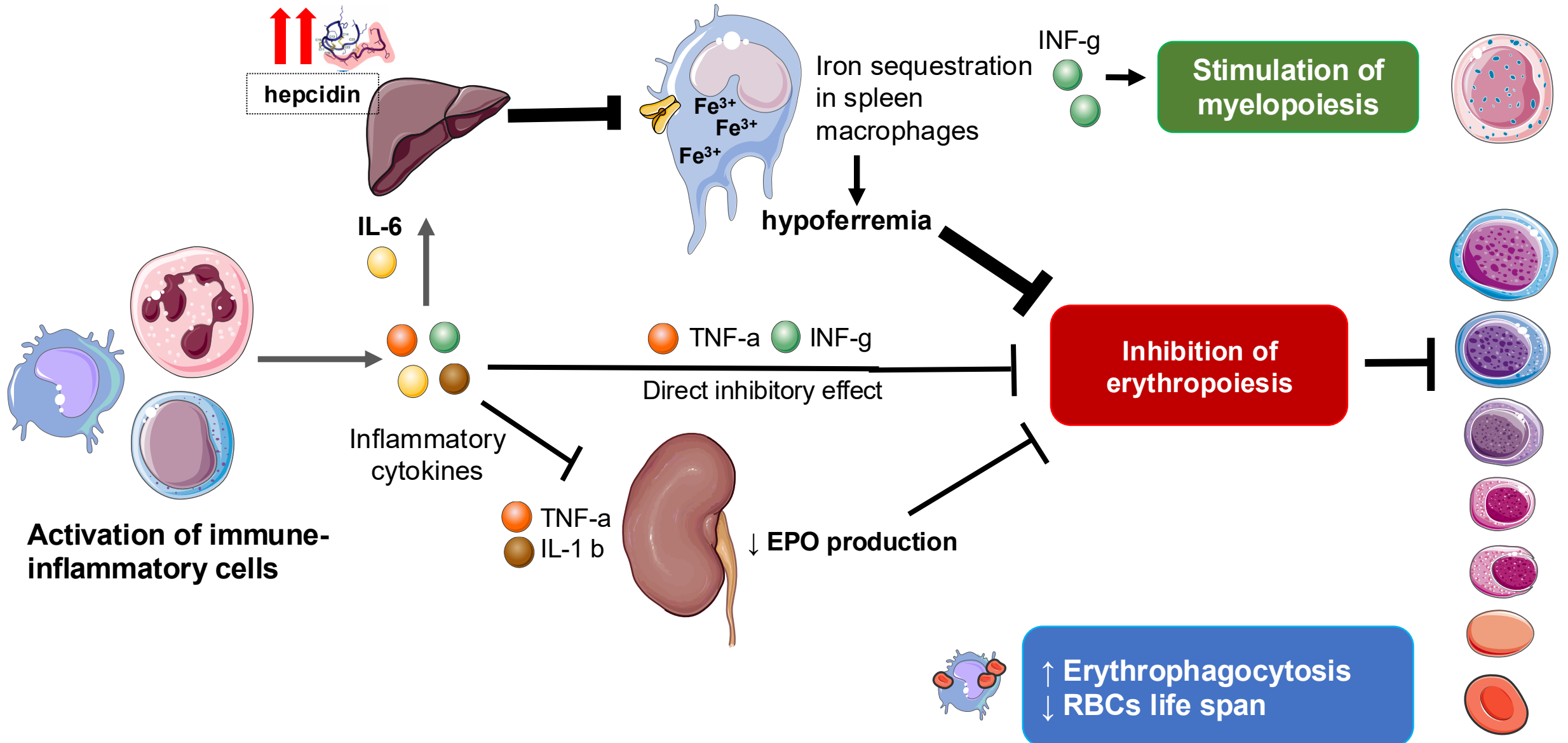
Ferroportin: “hepcidin receptor”; the only known iron exporter from the cells



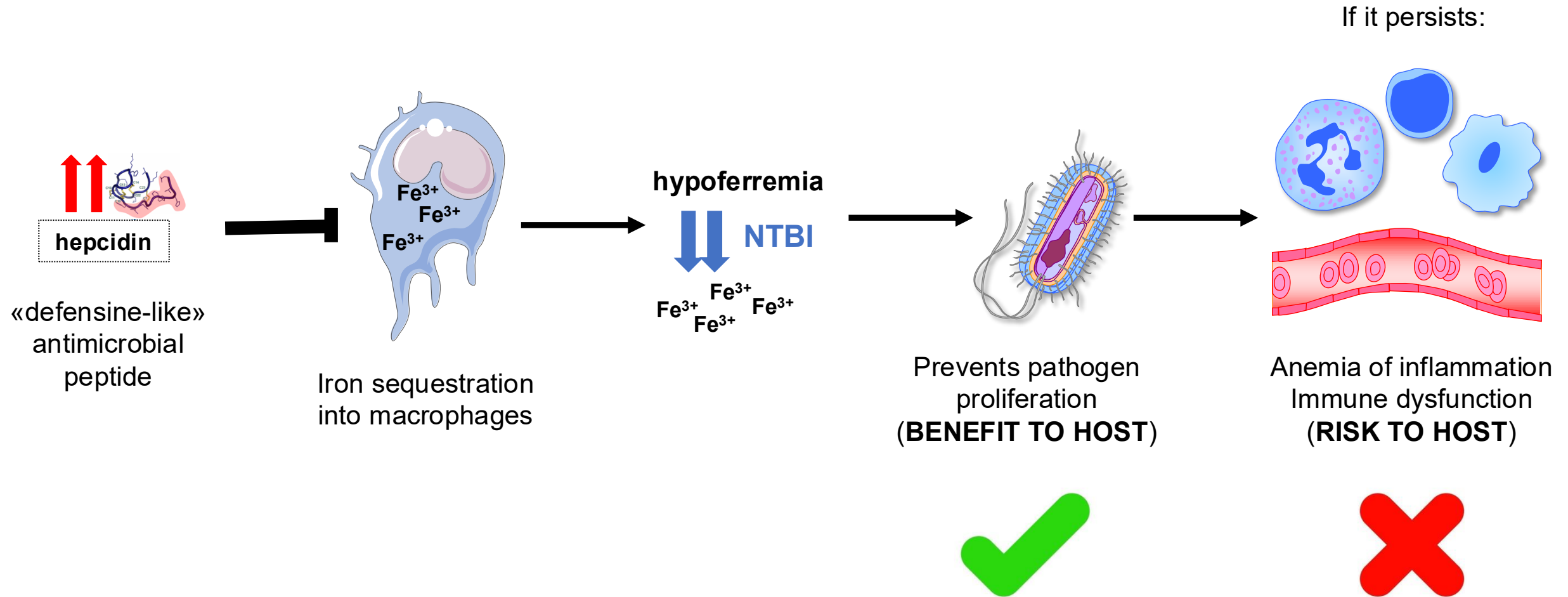
Inflammation induces hepcidin causing iron-restricted erythropoiesis



Several mechanisms contribute to «anemia of inflammation»



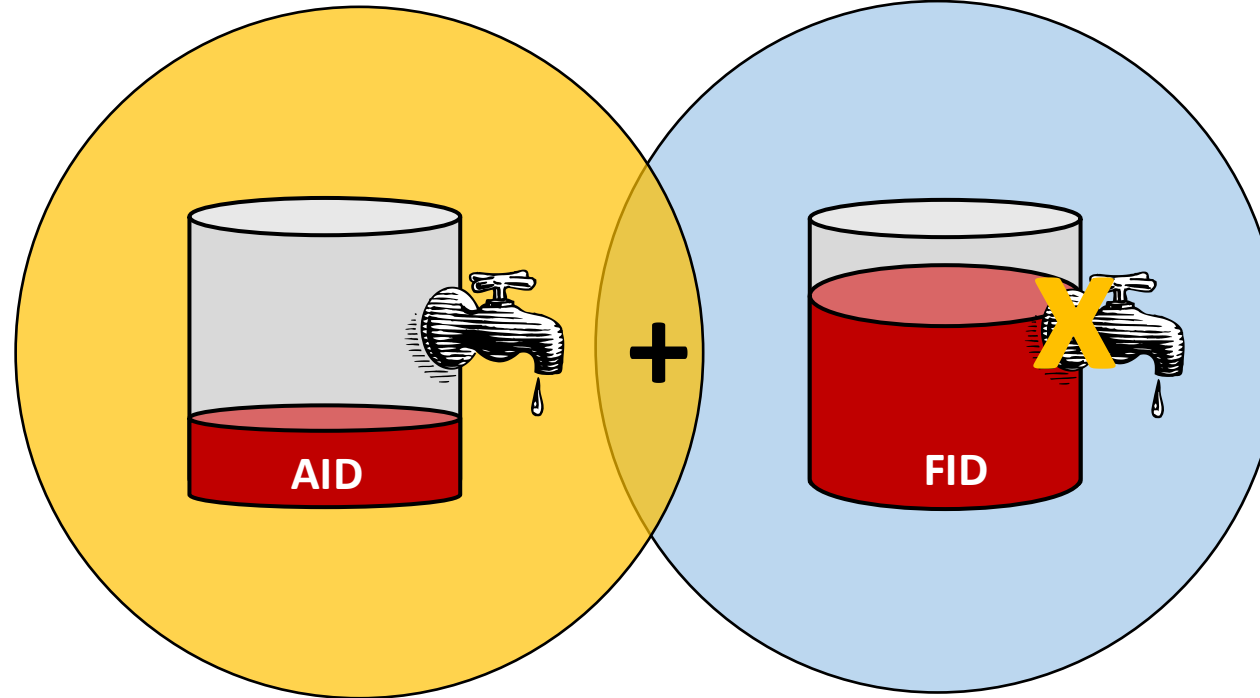
Iron sequestration into macrophages is part of a wider antimicrobial strategy known as «nutritional immunity»



During inflammatory states, functional and absolute ID may coexist

Absolute ID

- Depleted body iron stores
- Total available iron is inadequate
- Hepcidin suppressed



Functional ID

- Normal body iron stores
- Mobilization of iron is inadequate
- Hepcidin increased

Increased iron requirements

Malnutrition (low iron intake)

Malabsorption

Chronic blood loss

Overt or subclinical inflammation (IL-6, IL-1, TNF-a)

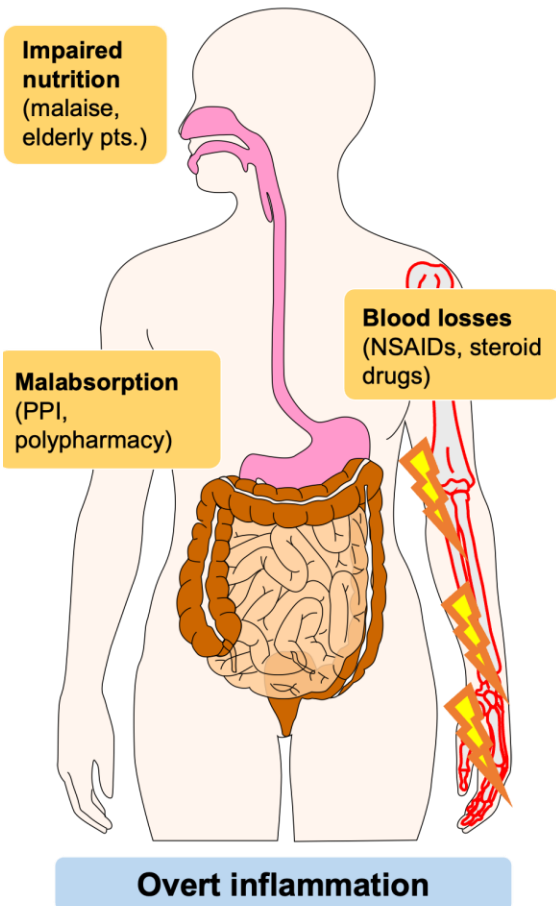
Many inflammatory diseases combine iron restriction and deficiency

RHEUMATOID ARTHRITIS

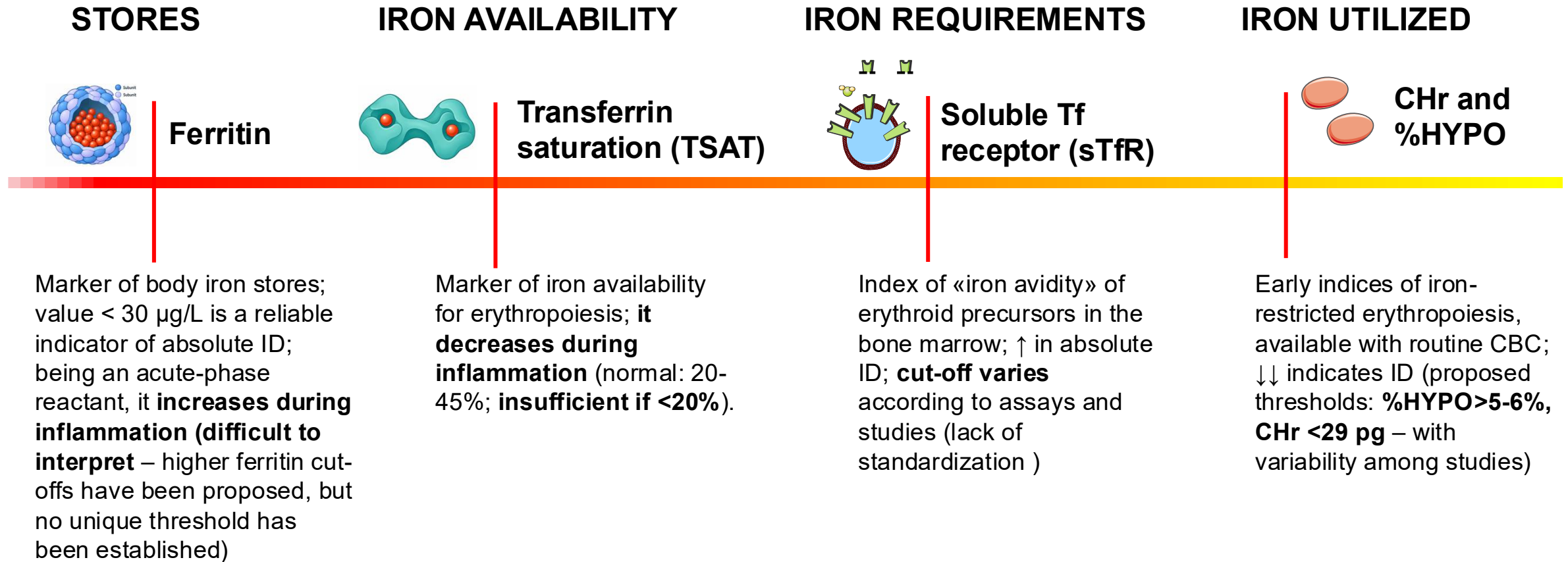
INFLAMMATORY BOWEL DIS.

CHRONIC KIDNEY DISEASE

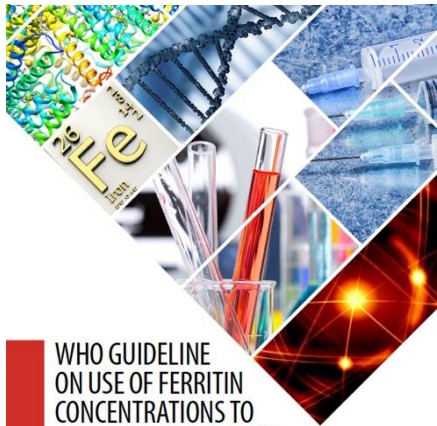
HEART FAILURE



Evaluation of iron status during inflammatory states



Definition of iron deficiency in inflammatory disorders



WHO GUIDELINE
ON USE OF FERRITIN
CONCENTRATIONS TO
ASSESS IRON STATUS IN
INDIVIDUALS AND
POPULATIONS



	Serum ferritin (µg/L)
	Iron deficiency
	Individuals with infection or inflammation
Infants and young children (0–23 months)	<30
Children under 5 years (24–59 months)	<30
Children (5 to less than 10 years)	<70
Adolescents (10 to less than 20 years)	<70
Adults (20–59 years)	<70
Older persons (60+ years)	<70
Pregnant women	—

Ferritin thresholds for defining ID/indication to iron treatment

Society	threshold	Pts. category
Expert consensus (Cappellini et al., 2027)	<100	<20%
European Society of Cardiology American Heart Association (2023)	<100 <300 with TSAT <20%	Heart Failure
KDIGO-National Kidney Foundation (2025)	≤ 500 (TSAT ≤ 30%)	CKD
NCCN (2020)	<500-800 (TSAT <50%)	Cancer
European Society of Medical Oncology (2020)	<100	Cancer
ECCO Guidelines (2024)	<100	Active IBD



ID likely in most patients with
TSAT <20-30%

Treatment depends on what predominates: iron depletion or iron restriction

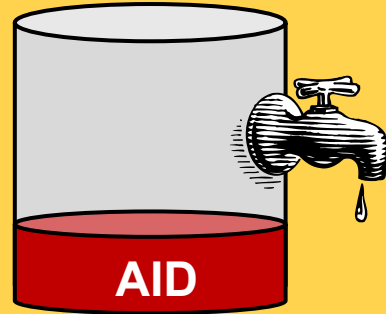
Predominant iron depletion (AID)

RESTORE IRON

Iron
replacement
therapy



Oral or IV?



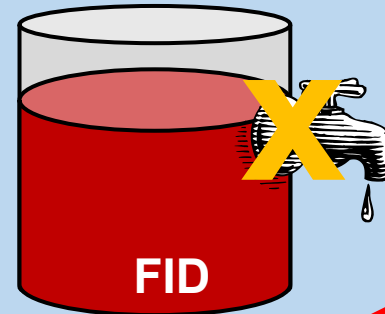
AID

Predominant iron restriction (FID)

RESTORE IRON AVAILABILITY

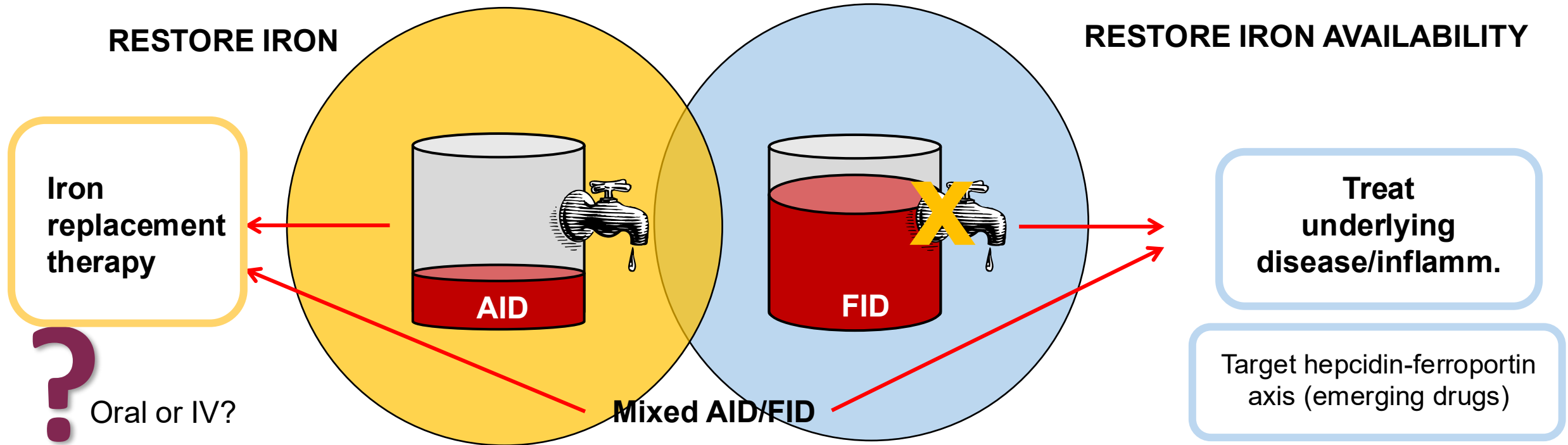
Treat
underlying
disease/inflamm.

Target hepcidin-ferroportin
axis (emerging drugs)

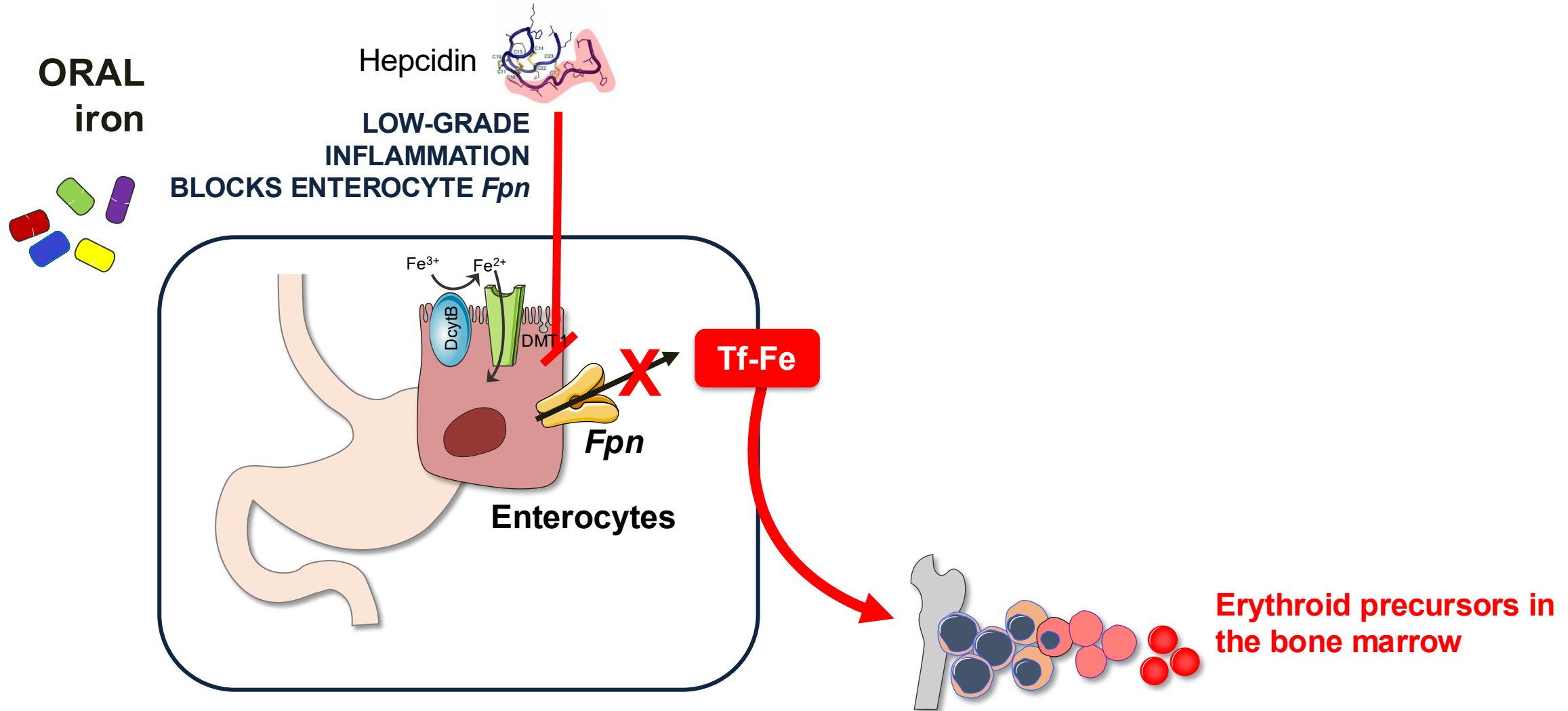


FID

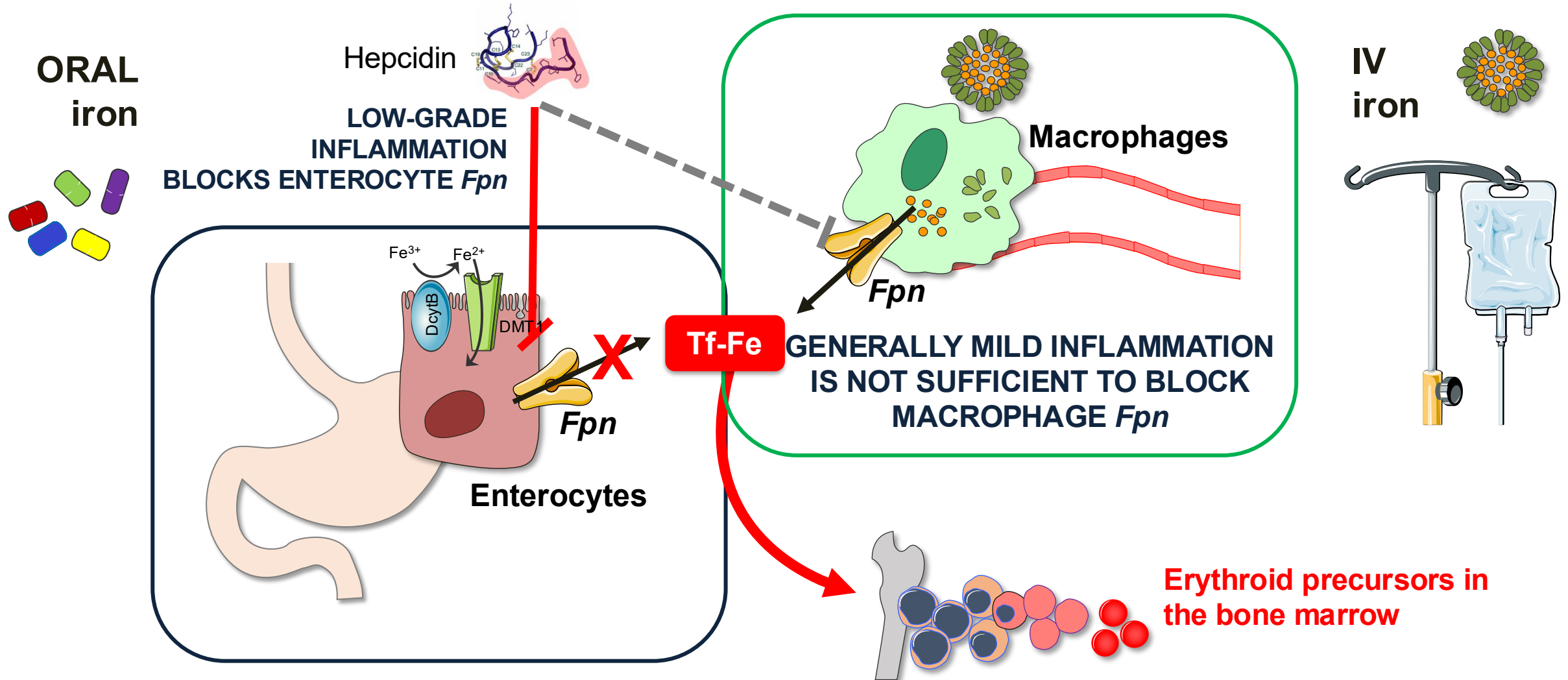
Mixed AID/FID



Inflammation creates a biological barrier to oral iron



IV iron bypasses intestinal iron malabsorption



Concluding remarks

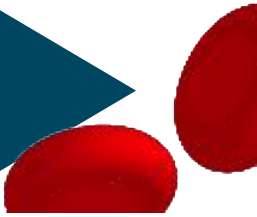
Inflammation induces **hepcidin-mediated iron restriction (functional ID)** and **impairs erythropoiesis**

In many chronic inflammatory diseases, **absolute and functional iron deficiency may coexist.**

Precise **ascertainment of iron status in inflammation may be difficult** (comprehensive evaluation includes both ferritin and transferrin saturation!)

Treatment should **address both absolute ID and the underlying inflammatory disease** causing functional ID

When indicated, **IV Iron should be preferred** (inflammation limits the effectiveness of oral iron).





Interdisciplinary team for iron disorders
(with families and friends)

THANK YOU!



European
Reference
Network



UOC Medicina d'urgenza
Prof. Domenico Girelli
Claudia Bozzini
Giacomo Marchi
Alice Vianello
Fabio Chesini

LURM
Annalisa Castagna
Elisa Antinori
Camila dos Santos Lima



Clinical Case



**78-year-old
woman**

Persistent fatigue and hand-predominant joint pain; **rheumatoid arthritis was suspected after rheumatologic evaluation. She frequently used NSAIDs**

Past medical history: arterial hypertension; previous cholecystectomy.

Physical examination:
BP: 155/80 mmHg
HR: 90 bpm
Mild pallor
Symmetric arthritis involving the small joints of both hands



CBC:

Hb 9.8 g/dl
MCV 86 fl
RBC 3.79 mil/mmc
PTLs 465,000/mmc
WBC: N

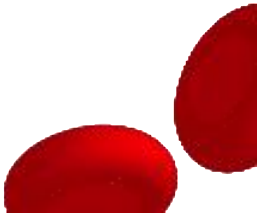
Iron biomarkers:

Ferritin 90 µg/L
Transf. Satur. 12%

CRP ↑↑ (80 mg/L,
n.v.<5)

***Is she iron
deficient?***

***Is sufficient iron
available (for
erythropoiesis)?***



Clinical Case – mixed absolute and functional ID



**78-year-old
woman**

Persistent fatigue and joint pain, predominantly affecting the hands (recently evaluated by a rheumatologist, suspected diagnosis of **rheumatoid arthritis**) – frequent use of NSAIDs

CBC: Hb 9.8 g/dl, MCV 86 fl

Iron biomarkers: Ferritin 90 µg/L, Transf. Satur. 12%

CRP ↑↑ (80 mg/L, n.v.<5)

→ TSAT 12% indicated **iron-restricted erythropoiesis** despite a ferritin level of 90 µg/L.

→ Ferritin <100 µg/L raised suspicion of **concomitant absolute iron deficiency**; upper gastrointestinal endoscopy revealed erosive gastritis

→ Treatment with **intravenous ferric carboxymaltose and anti-inflammatory** therapy restored hemoglobin and iron availability:

After 1 month: CRP 22 mg/L, Hb 12.2 g/dL, ferritin 180 µg/L, TSAT 23%