



# Mecanismes moleculars implicats en la formació de sideroblasts en anell

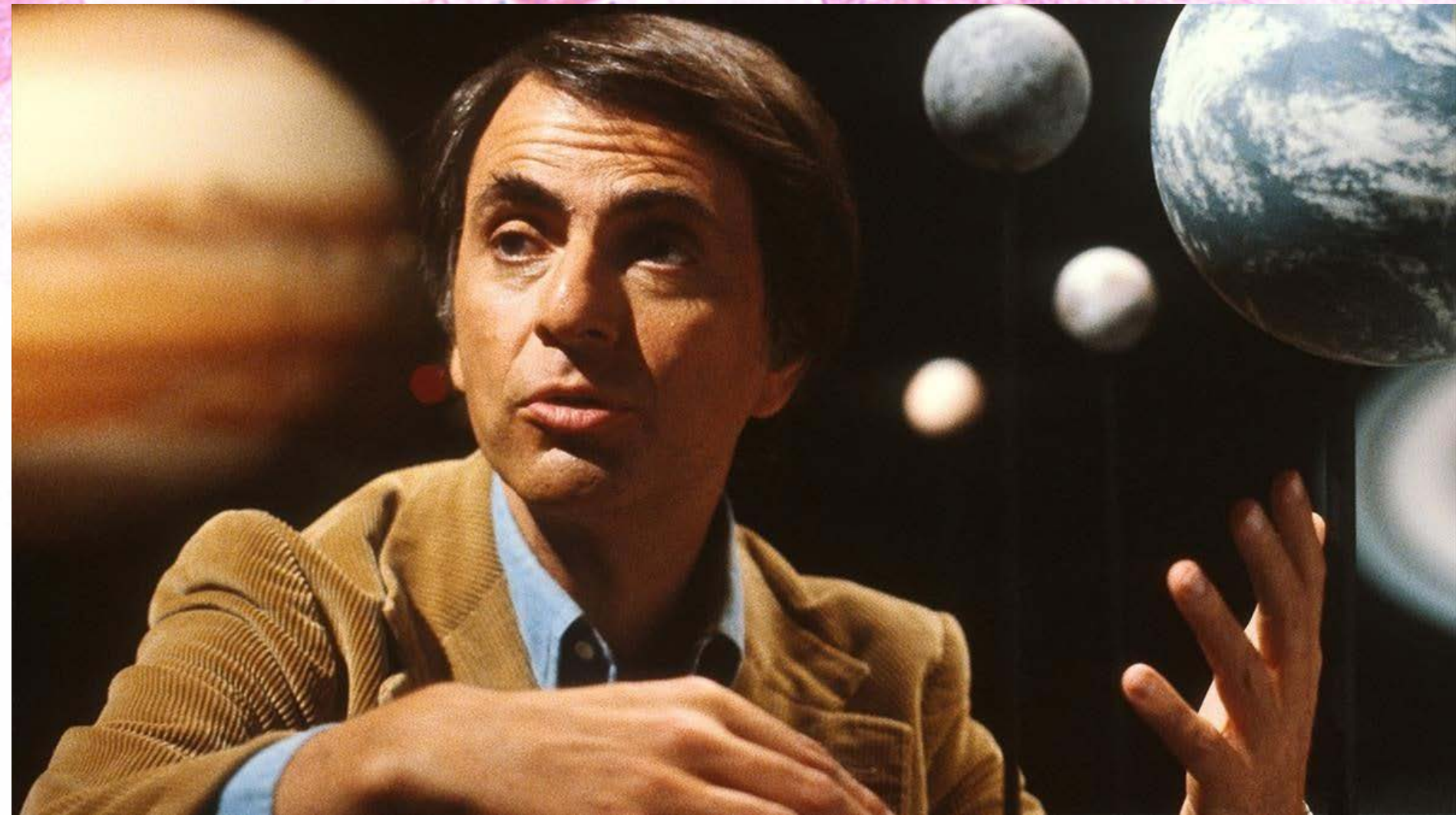
Albert Altés

Cap de servei hematologia Althaia

Professor hematologia Uvic-UCC







**Carl Sagan, 1934 - 1996**

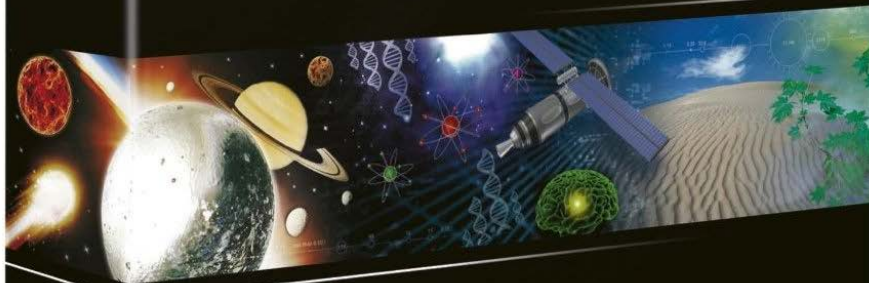
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CARL SAGAN'S

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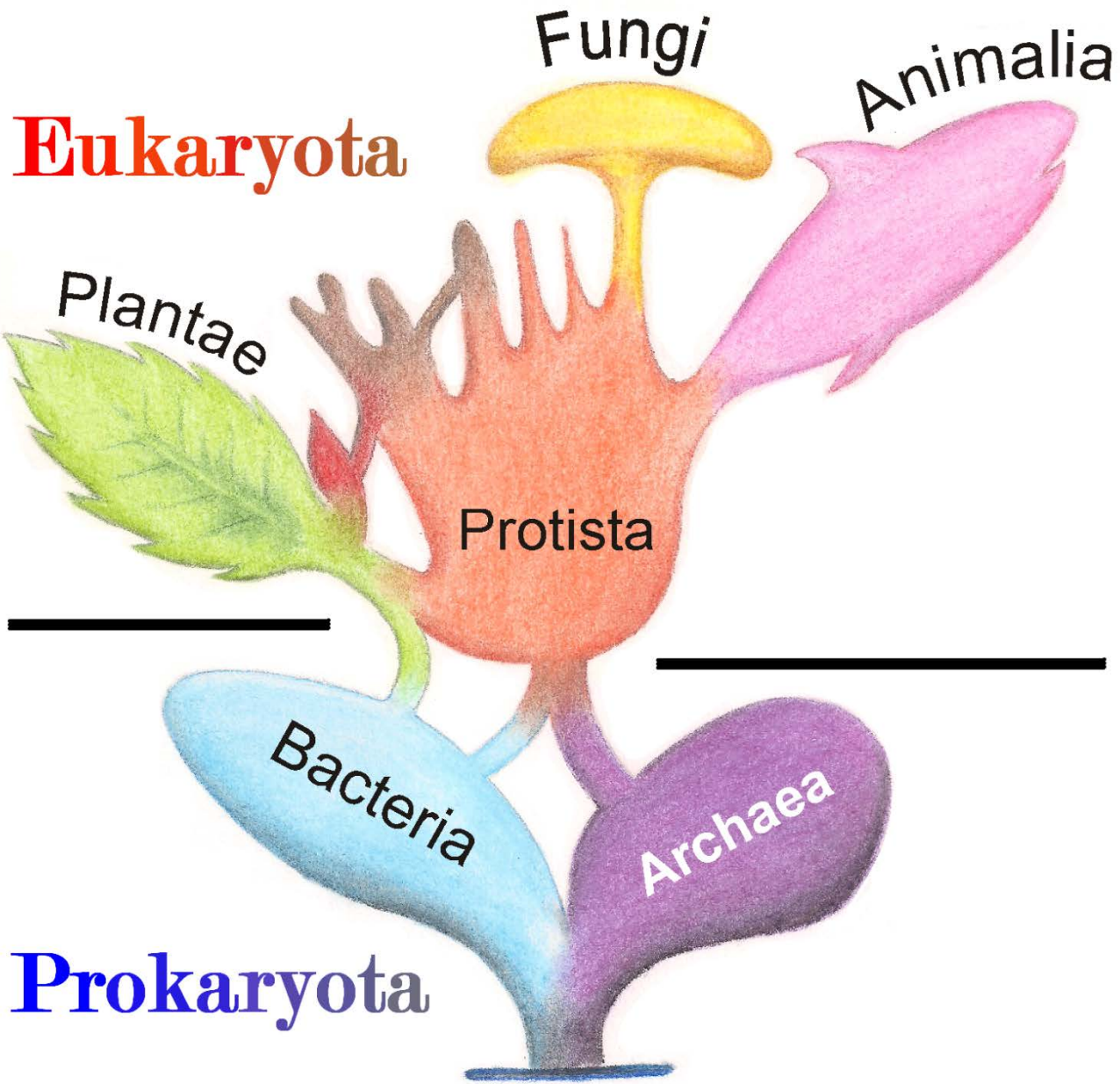


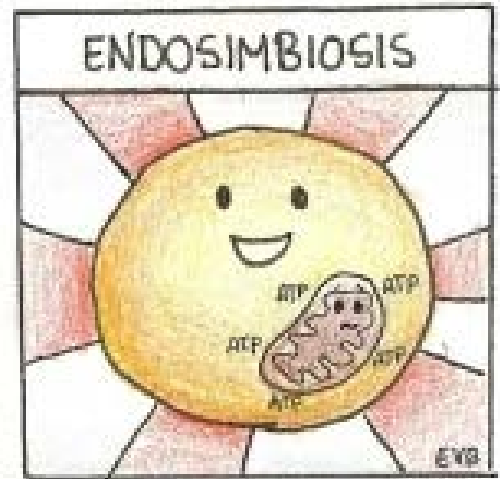
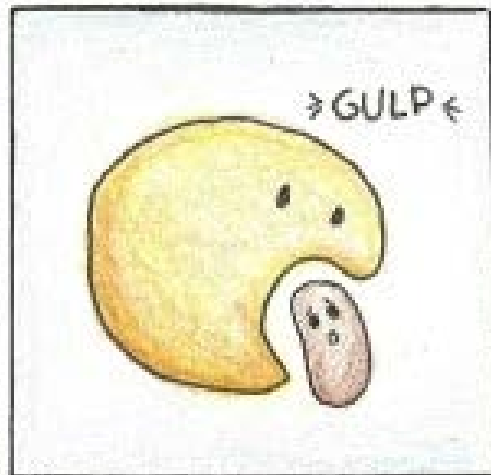
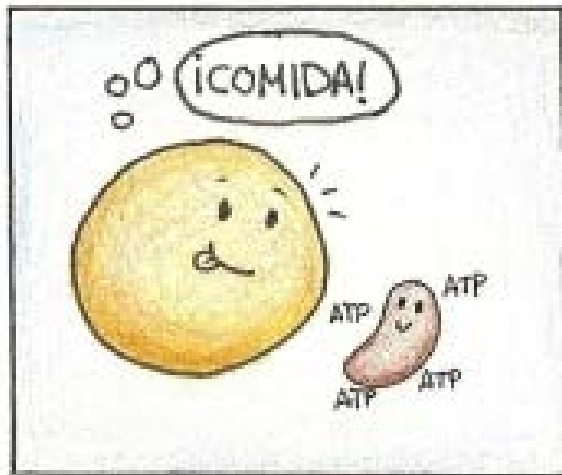




Lynn Margulys 1938 - 2011









## EVIDÈNCIES TEORIA ENDOSIMBIÒTICA MITOCONDRIA

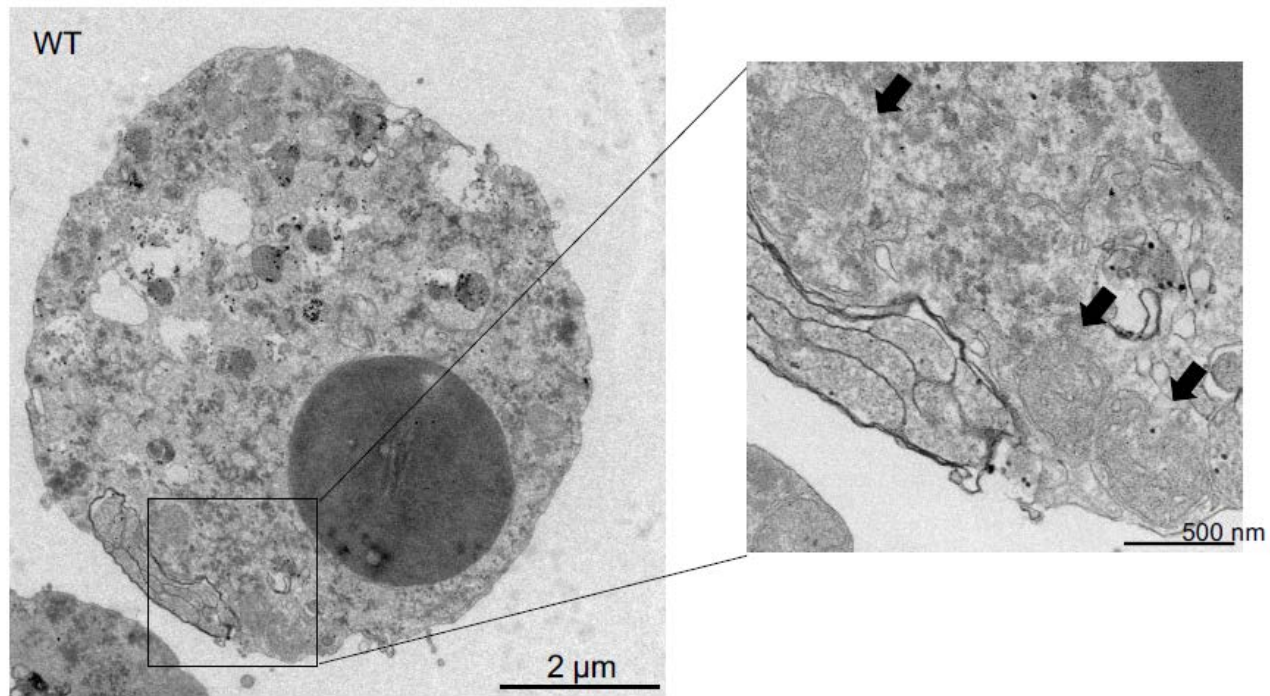
- Tamany mitocondria similar a arquea
- ADN bicatenari circular sense introns
- Divisió per fisió binaria, no mitosi
- Centres energetics en membranes
- Ribosomes 70S i no 80S
- RNAr 16s identic a arquea
- Codi genètic diferent

A light micrograph showing a field of cells, likely from a tissue section. The cells are stained with hematoxylin and eosin (H&E). The nuclei are stained dark purple, and the cytoplasm and extracellular matrix are stained pink. Numerous mitochondria are visible within the cells, appearing as small, dark, oval structures with internal cristae. The overall appearance is that of a highly cellular tissue, possibly muscle or a glandular tissue.

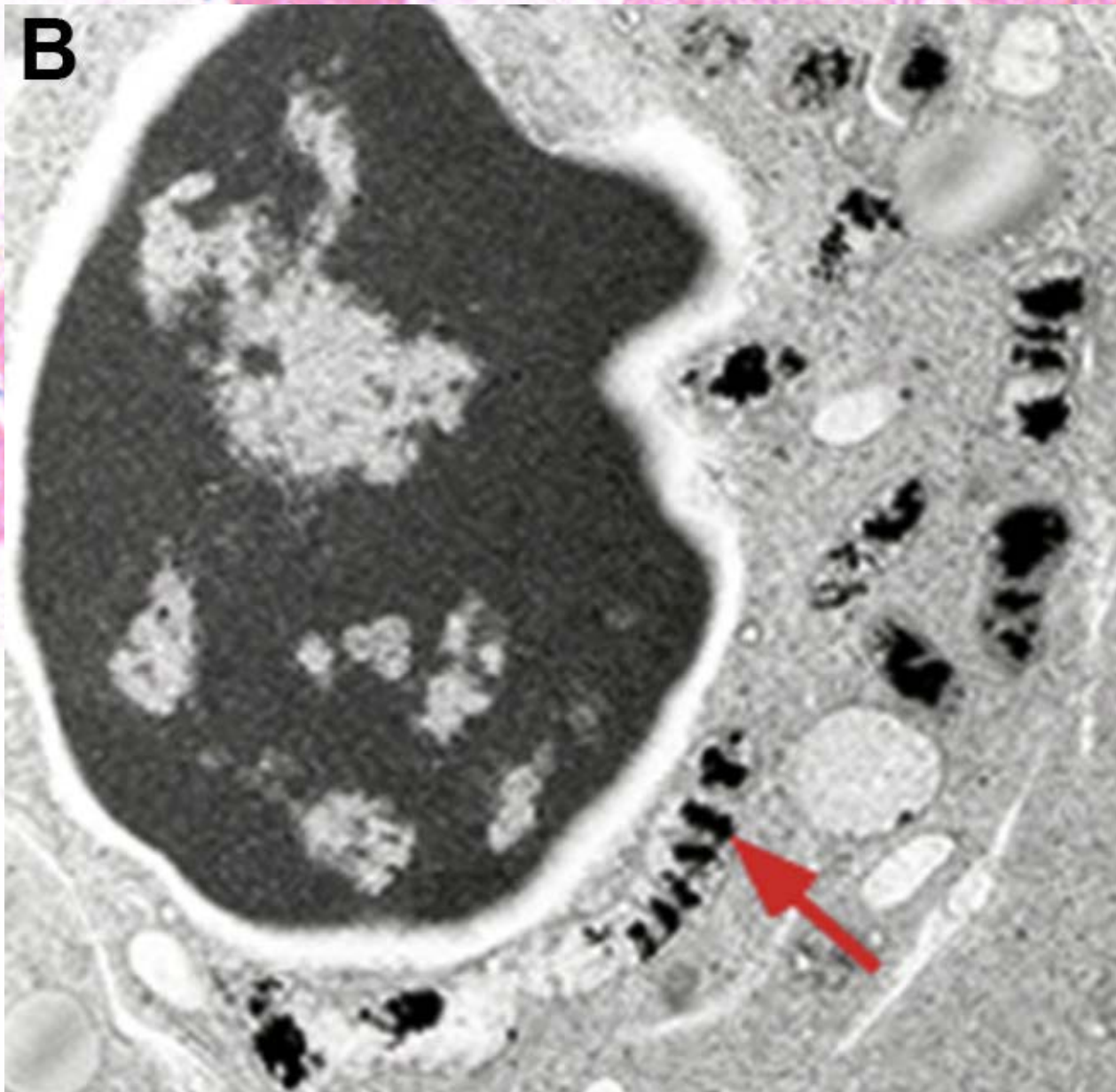
## **FUNCIONS MITOCONDRIA**

- Producció ATP per F.O.
- Vies metabòliques. Síntesi hemo
- Producció Fe-S clusters
- Alliberament caspases
- Vies de diferenciació a través de caspases



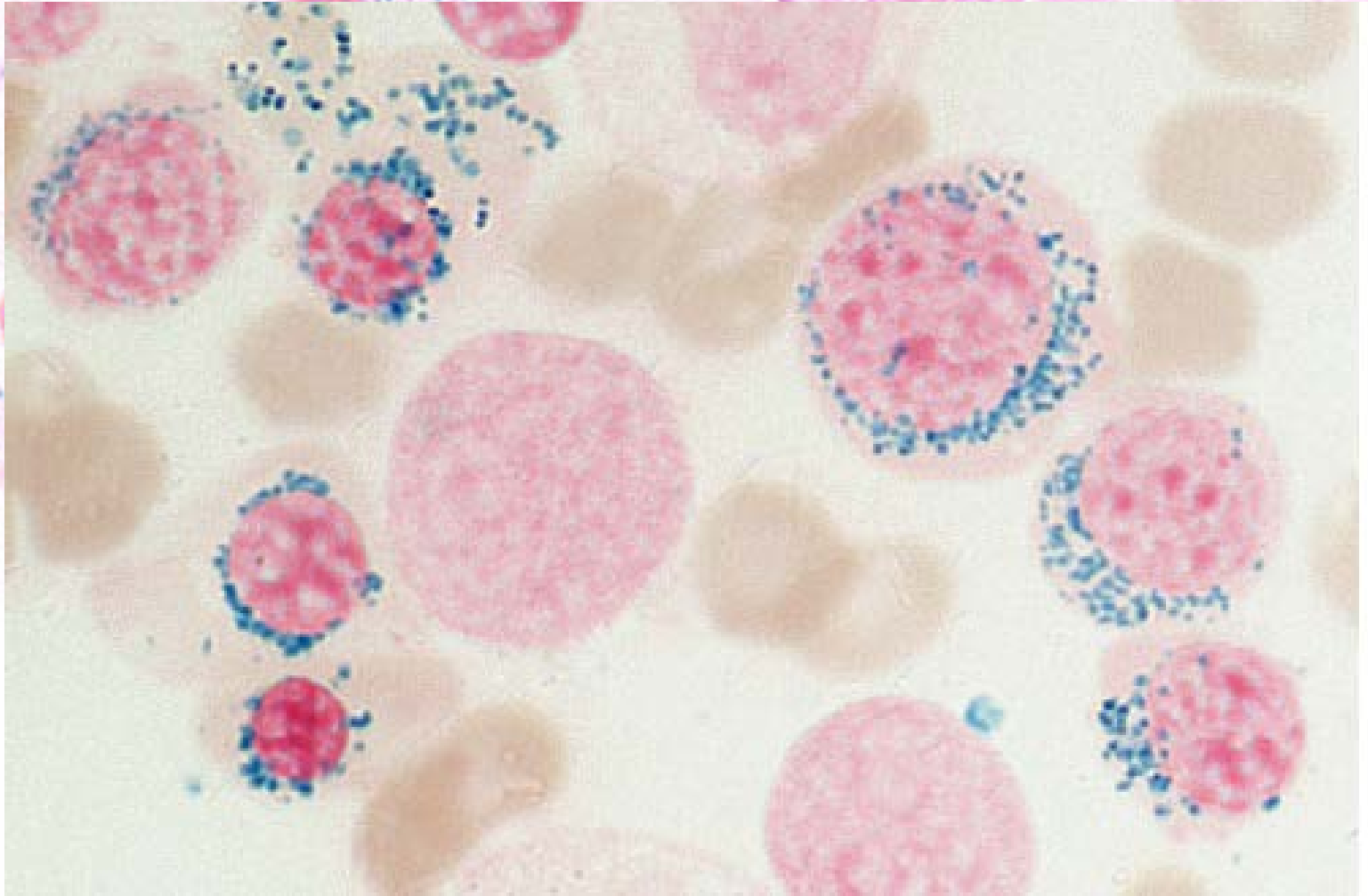


- 200 mitocòndries per eritroblaste
- 5-10 copies ADN 16.569 pb. Codifica 13 mRNA, 22 RNAt, 2 RNAr
- Més de 1000 genes mitoconcrials situats en el nucli celular



Bottomley SS, Fleming MD, Hematol Oncol Clin N Am 2014



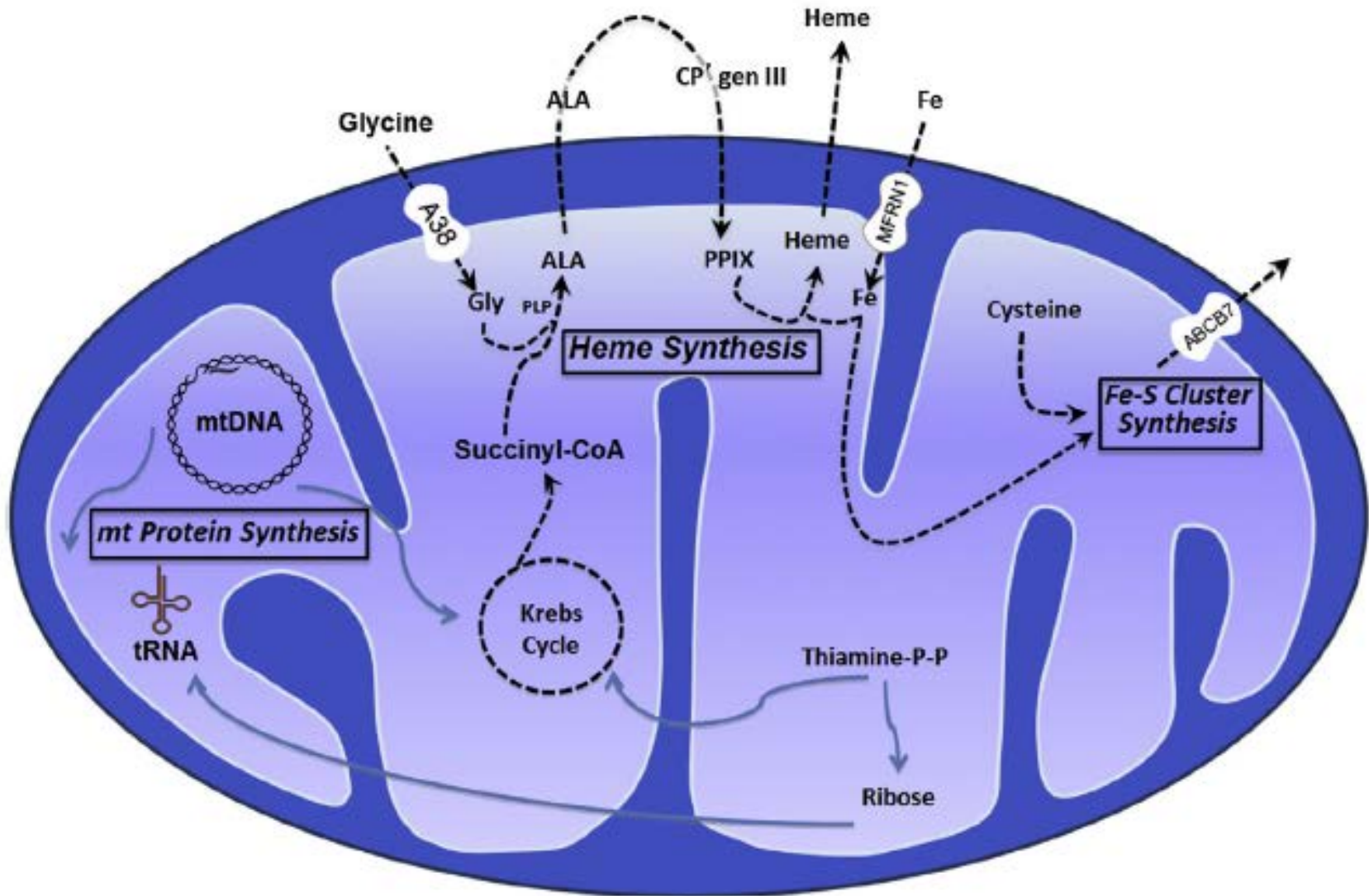


Cazzola M, Malcovati L, BJH 2016

**TABLE 1** Differential diagnosis of bone marrow ring sideroblasts

Clonal - Myeloid Neoplasms	Non Clonal Causes
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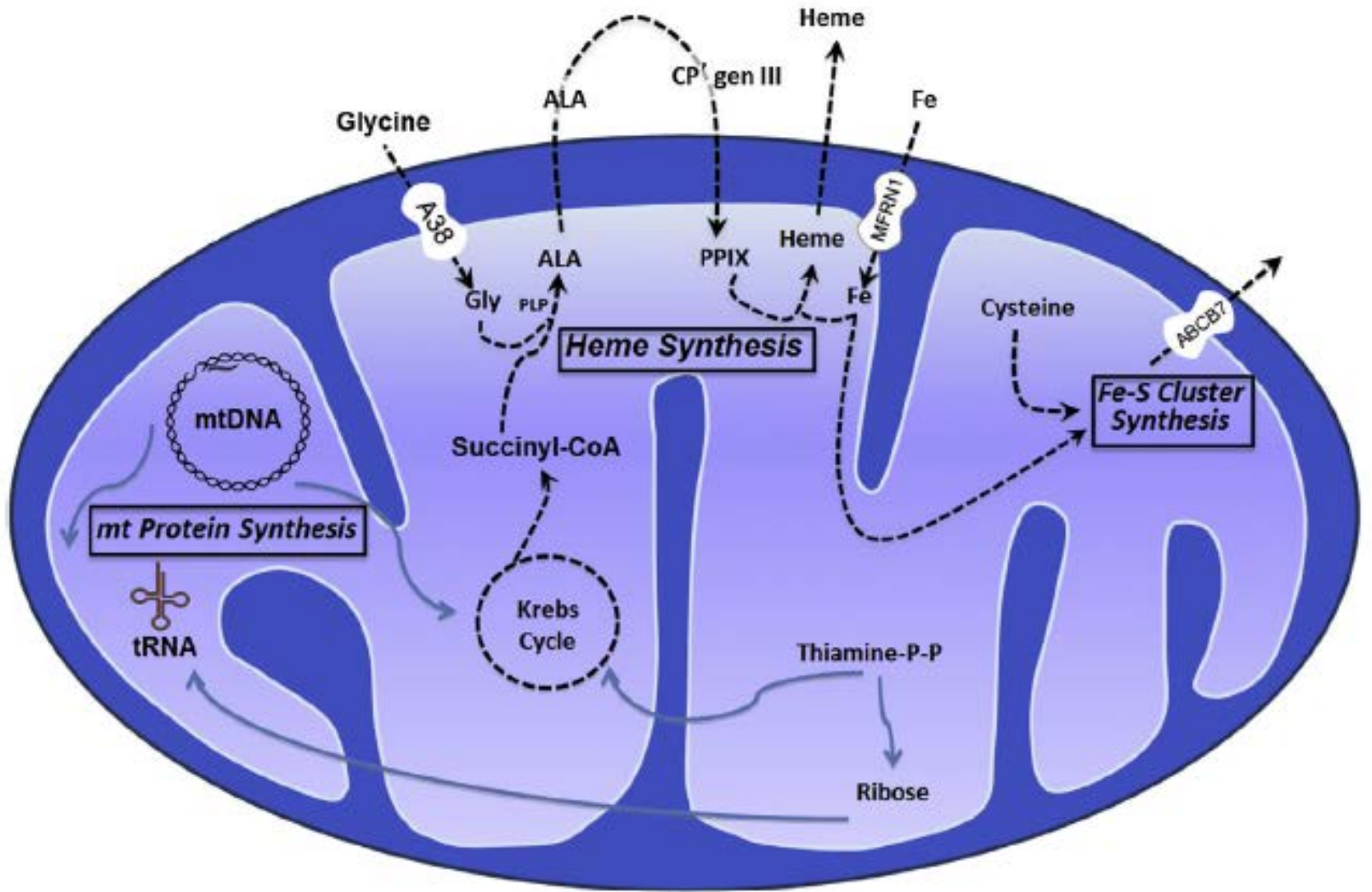


Bottomley SS, Fleming MD, Hematol Oncol Clin N Am 2014

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Bottomley SS, Fleming MD, Hematol Oncol Clin N Am 2014

# ASC lligada al sexe per mut ALAS2

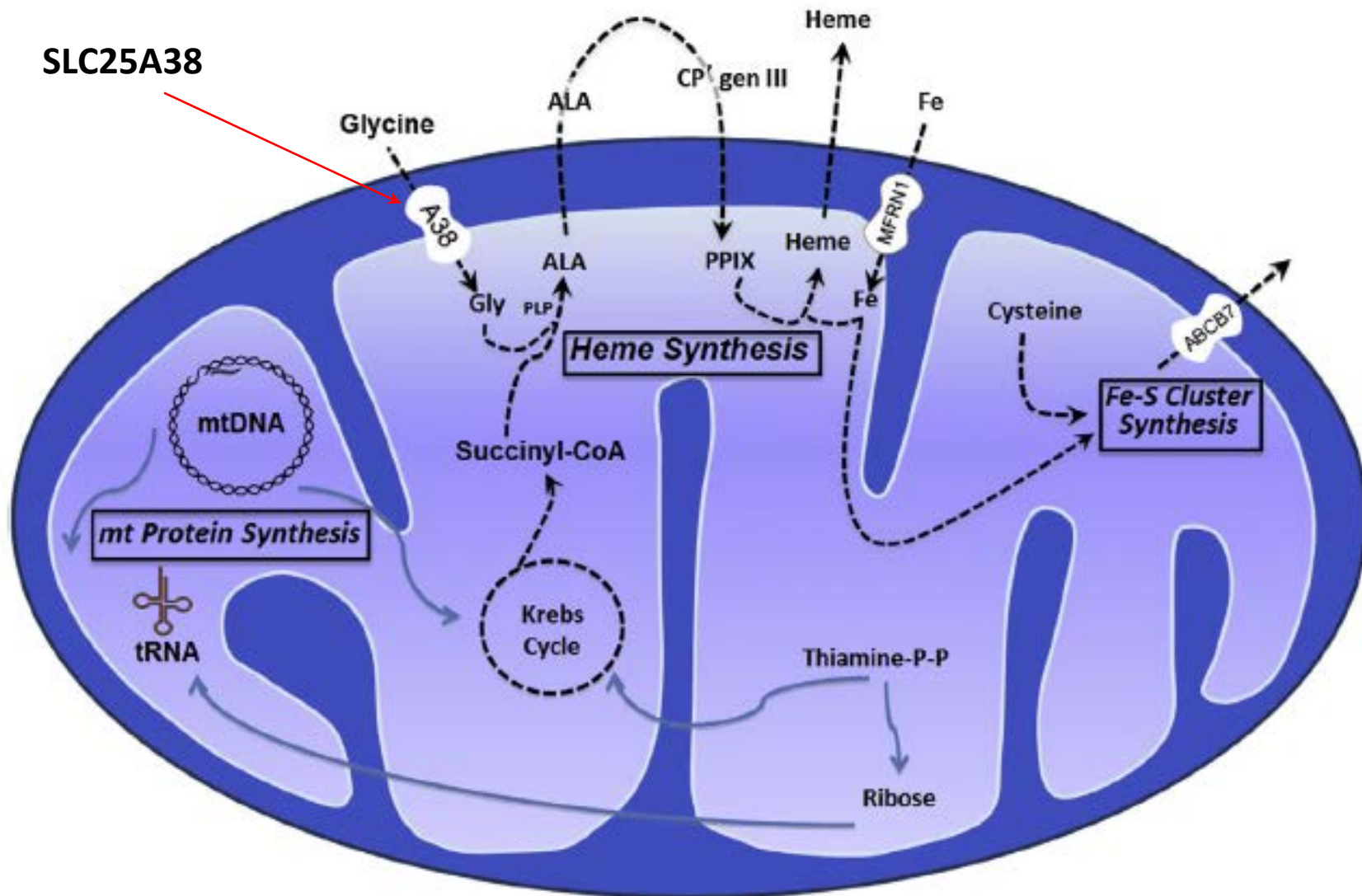
- Tipus més freqüent de ASC (40%)
- Gravetat clínica molt variable. Sol ser lleu
- Afectació homes mitjana edat.
- Anèmia VCM 60-70
- Sense necessitat transfusional
- Hemocromatosi
- DD Anèmia refractària, HH i Talassemia intermitja
- Ocasionalment dèficit afinitat piridoxina



**TABLE 1** Differential diagnosis of bone marrow ring sideroblasts

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SLC25A38





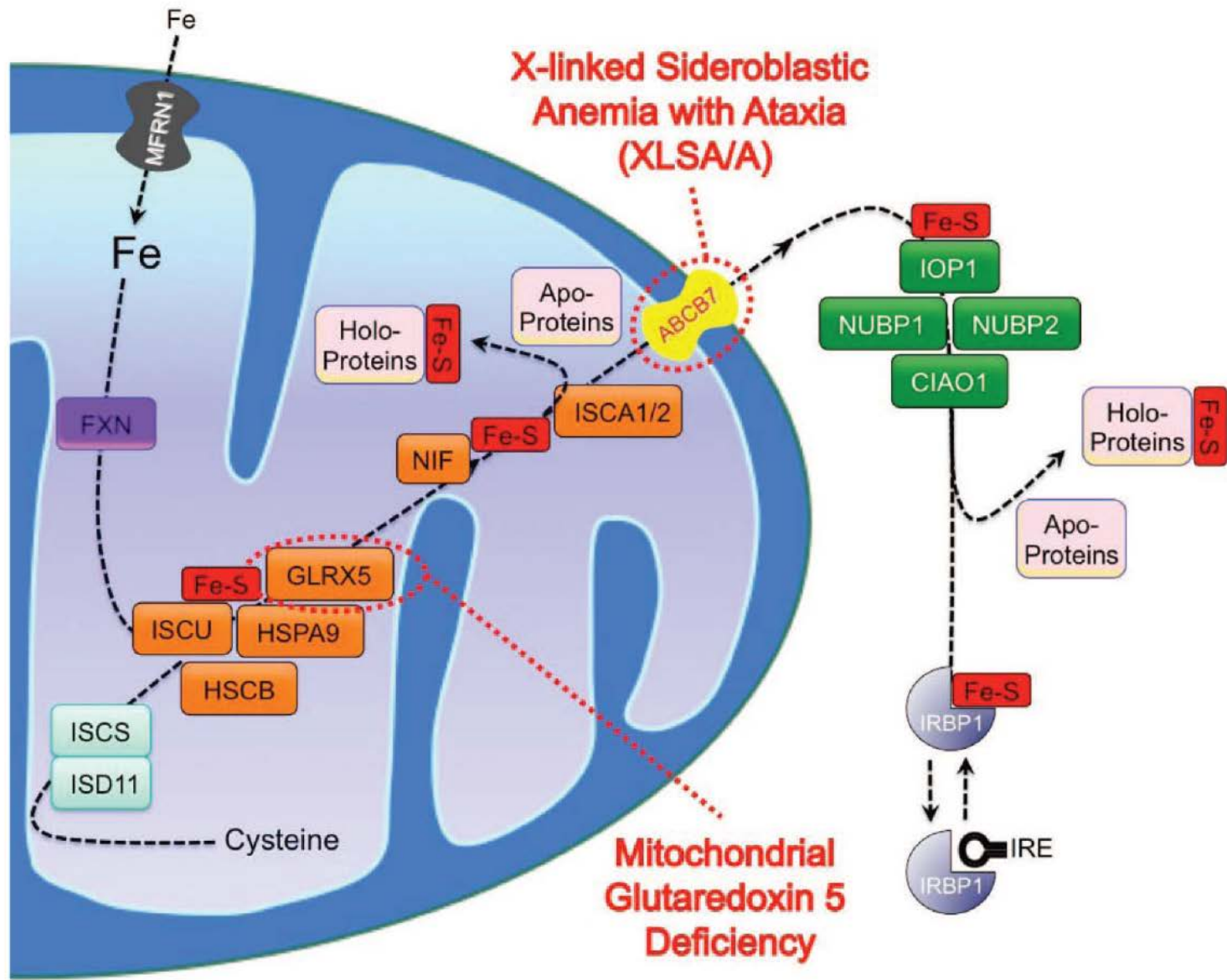
# ACS rel. amb mutacions SLC25A38

- 15% ASC
- Autossòmica recessiva
- Anèmia microcítica hipocroma severa
- Necessitats transfusionals infància
- Curs similar a la talassèmia major

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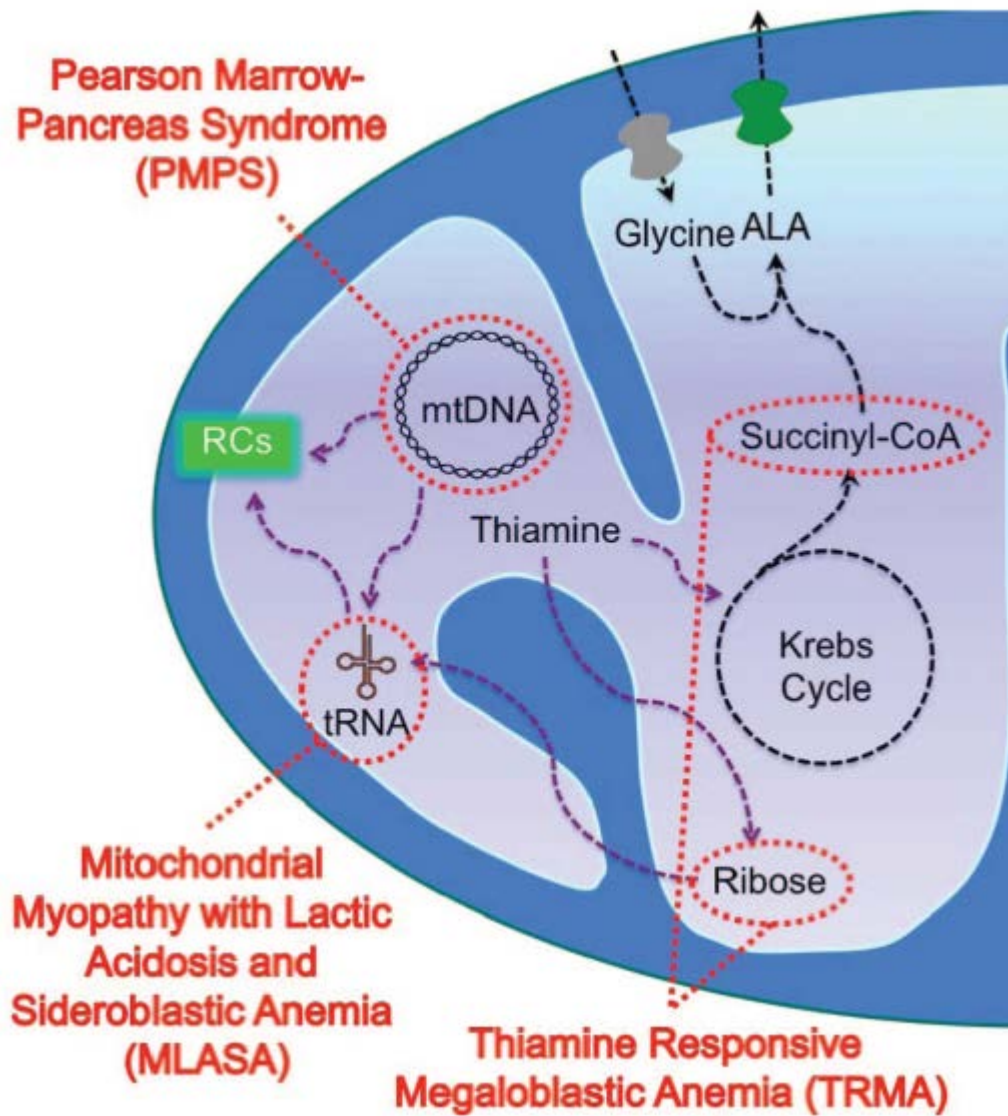
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**Clonal - Myeloid Neoplasms**

1. Myelodysplastic syndrome (MDS)

- i. MDS with ring sideroblasts and single lineage dysplasia (MDS-RS SLD)
- ii. MDS with ring sideroblasts and multilineage dysplasia (MDS-RS-MLD)
- iii. MDS with excess blasts and ring sideroblasts
- iv. MDS-U with ring sideroblasts

2. Myeloproliferative neoplasms (MPN)

- i. Essential thrombocythemia with ring sideroblasts
- ii. Primary myelofibrosis with ring sideroblasts

3. MDS/MPN overlap syndromes

- i. MDS/MPN with ringed sideroblasts and thrombocytosis (MDS/MPN-RS-T)
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- iii. Unclassified MDS/MPN with ring sideroblasts

**Non Clonal Causes**

1. Hereditary sideroblastic anemia

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  - VII. Congenital sideroblastic anemia due to NDUFB11 mutations.

2. Alcoholism

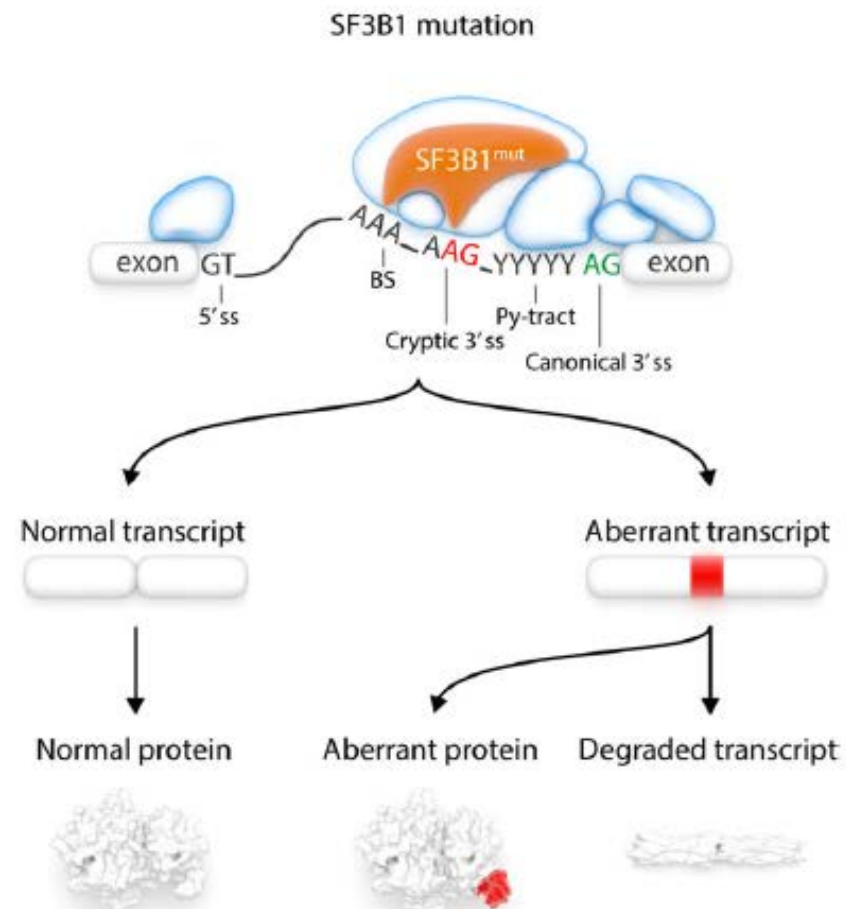
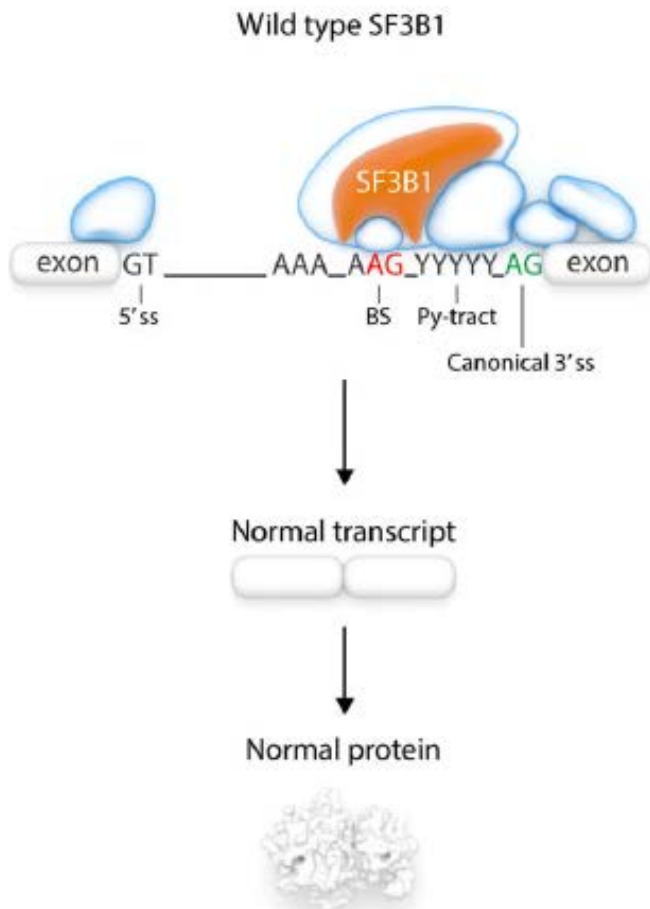
4. Drug-induced sideroblastic anemia

- i. INH
- ii. Chloramphenicol
- iii. Linezolid
- iv. Penicillamine

5. Copper deficiency

6. Lead poisoning

7. Zinc toxicity





```
graph TD; A[> 70ª Mutacions SF3B1 – SRSF2] --> B[Amplificació - Proliferació]; B --> C[RARS]; B --> D[RCMD-RS]; B --> E[RARS-T]; D --- F[• DNMT3A  
• TET2]; E --- G[• JAK II  
• ASXL1  
• MPL, CALR];
```

> 70ª Mutacions SF3B1 – SRSF2

Amplificació - Proliferació

- DNMT3A
- TET2

- JAK II
- ASXL1
- MPL, CALR

RARS

RCMD-RS

RARS-T



Alteració SF3B1, entitat independent?  
Hauria de ser entitat de la WHO?



**TABLE 1** Differential diagnosis of bone marrow ring sideroblasts

Clonal - Myeloid Neoplasms	Non Clonal Causes
<ol style="list-style-type: none"><li>1. Myelodysplastic syndrome (MDS)<ol style="list-style-type: none"><li>i. MDS with ring sideroblasts and single lineage dysplasia (MDS-RS SLD)</li><li>ii. MDS with ring sideroblasts and multilineage dysplasia (MDS-RS-MLD)</li><li>iii. MDS with excess blasts and ring sideroblasts</li><li>iv. MDS-U with ring sideroblasts</li></ol></li></ol>	<ol style="list-style-type: none"><li>1. Hereditary sideroblastic anemia<ol style="list-style-type: none"><li>i. X- linked sideroblastic anemia- ALAS2 mutations</li><li>ii. SLC25A38 related sideroblastic anemia</li><li>iii. Glutaredoxin 5 (GLRX5) related sideroblastic anemia</li><li>iv. Congenital sideroblastic anemia without identified molecular defects</li><li>v. Sideroblastic anemia as a component of genetic syndromes<ol style="list-style-type: none"><li>I. X-linked sideroblastic anemia with ataxia- ABCB7 mutations</li><li>II. Kearns Sayre syndrome</li><li>III. Myopathy, lactic acidosis, and sideroblastic anemia</li><li>IV. Sideroblastic anemia, B cell immunodeficiency, periodic fevers, and developmental delay</li><li>V. Pearson marrow-pancreas syndrome</li><li>VI. Thiamine-responsive megaloblastic anemia syndrome</li><li>VII. Congenital sideroblastic anemia due to NDUFB11 mutations.</li></ol></li></ol></li></ol>
<ol style="list-style-type: none"><li>2. Myeloproliferative neoplasms (MPN)<ol style="list-style-type: none"><li>i. Essential thrombocythemia with ring sideroblasts</li><li>ii. Primary myelofibrosis with ring sideroblasts</li></ol></li></ol>	<ol style="list-style-type: none"><li>2. Alcoholism</li></ol>
<ol style="list-style-type: none"><li>3. MDS/MPN overlap syndromes<ol style="list-style-type: none"><li>i. MDS/MPN with ringed sideroblasts and thrombocytosis (MDS/MPN-RS-T)</li><li>ii. Chronic myelomonocytic anemia with ring sideroblasts</li><li>iii. Unclassified MDS/MPN with ring sideroblasts</li></ol></li></ol>	<ol style="list-style-type: none"><li>4. Drug-induced sideroblastic anemia<ol style="list-style-type: none"><li>i. INH</li><li>ii. Chloramphenicol</li><li>iii. Linezolid</li><li>iv. Penicillamine</li></ol></li></ol>
	<ol style="list-style-type: none"><li>5. Copper deficiency</li></ol>
	<ol style="list-style-type: none"><li>6. Lead poisoning</li></ol>
	<ol style="list-style-type: none"><li>7. Zinc toxicity</li></ol>

# Futursex<sup>18+</sup>

## Placeres del Siglo XXI

VII SALÓN ERÓTICO DE MURCIA

WEBCAMSHOW | ESTRELLAS INTERNACIONALES  
ADULT FUTURE TOYS | CHARLAS EDUCATIVAS