

ICD-10-CM Virtual Meeting
September 14, 2021

WHIM Syndrome

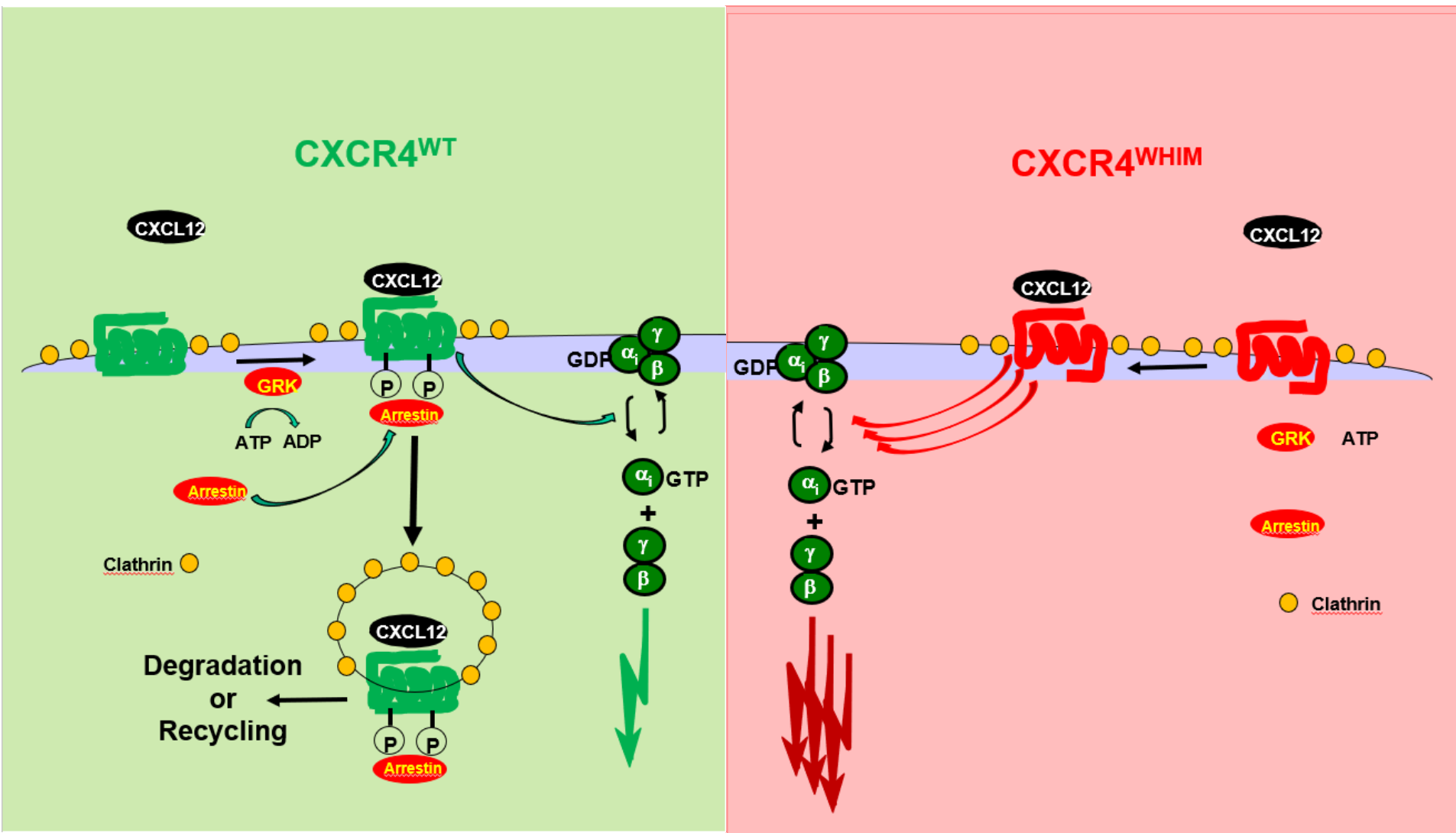
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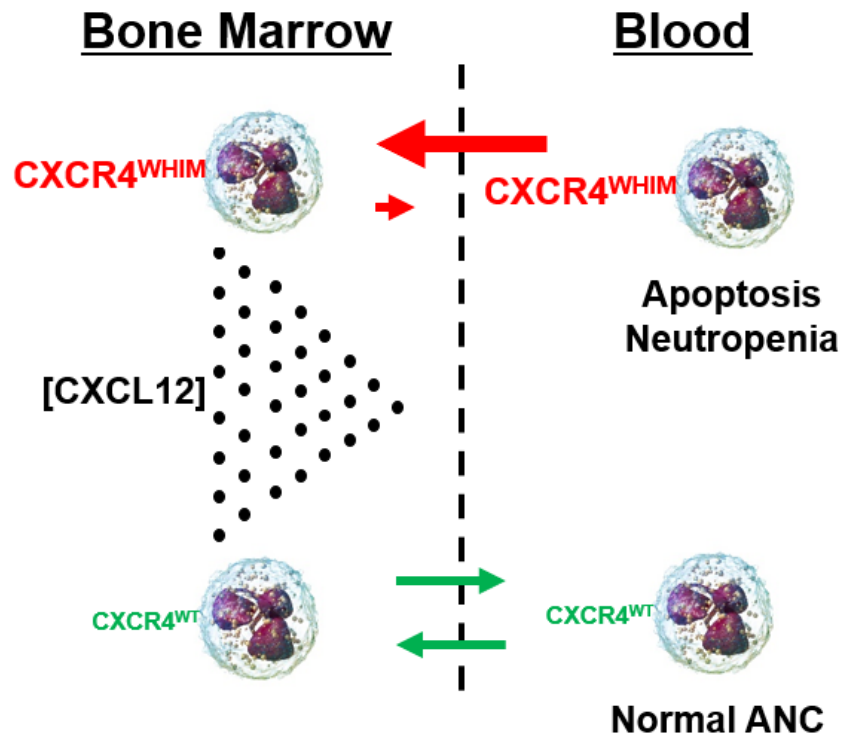
WHIM Syndrome at a Glance

- Rare (n~105, mostly Europe and the US)
- Autosomal dominant Mendelian inheritance
- Combined primary immunodeficiency disorder
 - ❑ Panleukopenia
 - lymphopenia
 - monocytopenia
 - neutropenia (retention in BM=Myelokathexis)
 - ❑ Hypogammaglobulinemia
- Infections
 - HPV (Warts, SCC)
 - otosinopulmonary
 - skin
- Developmental defects (heart, urogenital, brain)
- Cancer

WHIM Syndrome is caused by GoF mutations in CXCR4



Myelokathexis: abnormal leukocyte distribution



WHIM Syndrome: Keys to Diagnosis

- **Positive family history**
 - **Recurrent non-invasive bacterial infection**
 - **Neutropenia**
 - **Myelokathexis**
 - **CXCR4 mutation**
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- **Delay in diagnosis and ‘doctor-hopping’ is common because of:**
 - incomplete penetrance of phenotypes
 - mobilization of neutrophils during infection
 - **Underdiagnosis is likely**

WHIM Syndrome: Prognosis

- **Infections may be, but are usually not, life-threatening**
- **Cardiovascular defects may dominate the clinical course early**
- **Chronic complications of recurrent infection include hearing loss, bronchiectasis, disfiguring warts and splenectomy**
- **Pediatric mortality is rare**
- **Premature death may occur in adults, usually due to virus-associated cancer (HPV, EBV)**
- **Impaired quality of life: Disruption of education, ambitions and emotions**

WHIM Syndrome: Treatment

- **Consensus not yet established**
- **Best medical management:**
 - **G-CSF (low dose)**
 - **Immunoglobulin supplementation**
 - **Prophylactic antibiotics**
 - **Vaccination**
 - **Wart ablation, HPV disease surveillance**
 - **HSC transplantation**
- **Experimental mechanism-based therapy:**
 - **Plerixafor (Sanofi-Genzyme)**
 - **Mavorixafor (X4-Pharma)**