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Human Apollo deficiency causes IBMFS

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Kermasson L, Churikov D, Awad A, Smoom R, Lainey E, Touzot F, Audebert-Bellanger S, Haro S, Roger L, Costa E, Mouf M, Bottero A, Oleastro M, Abdo C, de Villartay J-P, Géli V, Tzfati Y, Callebaut I, Danielian S, Soares G, Kannengiesser C, Revy P. Inherited human Apollo deficiency causes severe bone marrow failure and developmental defects. *Blood*. 2022;139(16):2427-2440.

1. Your patient is a 6-year-old boy with an inherited bone marrow failure syndrome (IBMFS) in whom a biallelic variant in the gene encoding the 5′-to-3′ DNA exonuclease Apollo/SNM1B (Apollo) is suspected. According to the case series by Kermasson and colleagues, which of the following statements about clinical features of 3 unrelated patients with biallelic *Apollo* variants is correct?

- ☐ The patients all had a dyskeratosis congenita (DC)/Høyeraal-Hreidarsson (HH) phenotype, with features such as early-onset hypocellular bone marrow failure (BMF), immunodeficiency, developmental defects, and premature aging
- ☐ Profound T-cell lymphopenia with normal B cells was the predominant feature on immunologic evaluation
- ☐ Only 1 patient had developmental anomalies or mucocutaneous features
- ☐ All 3 patients had growth retardation

2. According to the case series by Kermasson and colleagues, which of the following statements about genetic features of 3 unrelated patients with biallelic *Apollo* variants is correct?

- ☐ All 3 patients had a homozygous missense variant affecting the same amino acid residue, L142 (L142F or L142S), located in the catalytic domain of Apollo
- ☐ Apollo-deficient cells from patients showed spontaneous chromosome instability and impaired DNA repair that was complemented by CRISPR/Cas9-mediated gene correction
- ☐ Patients' cells and human Apollo KO HT1080-cell lines had shortened telomeres
- ☐ The missense variant increased interaction of Apollo with TRF2

3. According to the case series by Kermasson and colleagues, which of the following statements about clinical and research implications of clinical and genetic features of 3 unrelated patients with biallelic *Apollo* variants is correct?

- ☐ The findings suggest that the L142F and L142S Apollo mutants have no protective function
- ☐ Patients with Apollo deficiency can be distinguished clinically from patients with DC and HH
- ☐ The findings do not warrant any special monitoring for parents of patients with L142F and L142S Apollo mutants
- ☐ The findings suggest that Apollo is a genome caretaker critical for the proper development of the immunohematological system in humans

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