

Introduction

Spondyloenchondrodysplasia (SPENCD) is a rare inborn error of immunity causing:

1. Immune overactivity
2. Abnormal bone development
3. Neurological dysfunction

SPENCD is linked to damaging ACP5 variants

- ACP5 produces **tartaric-acid-resistant acid phosphatase (TRAP)**

Case Summary

2-Year-Old Male Patient

- Autoimmune hemolytic anemia
- Splenomegaly

- Skeletal dysplasia
- Short stature

- Autism spectrum disorder
- Intracranial calcification

Compound heterozygous ACP5 variants

- c.550C>T (p.Q184*)
- c.740T>G (p.L247R)

Figure 1: Patient imaging demonstrating phenotypic markers of SPENCD. (A) Skeletal dysplasia on radiography (B) Intracranial calcification on CT.

Objective

Elucidate the functional impact of **two ACP5 variants** and expand **SPENCD's disease mechanism**.

Methods

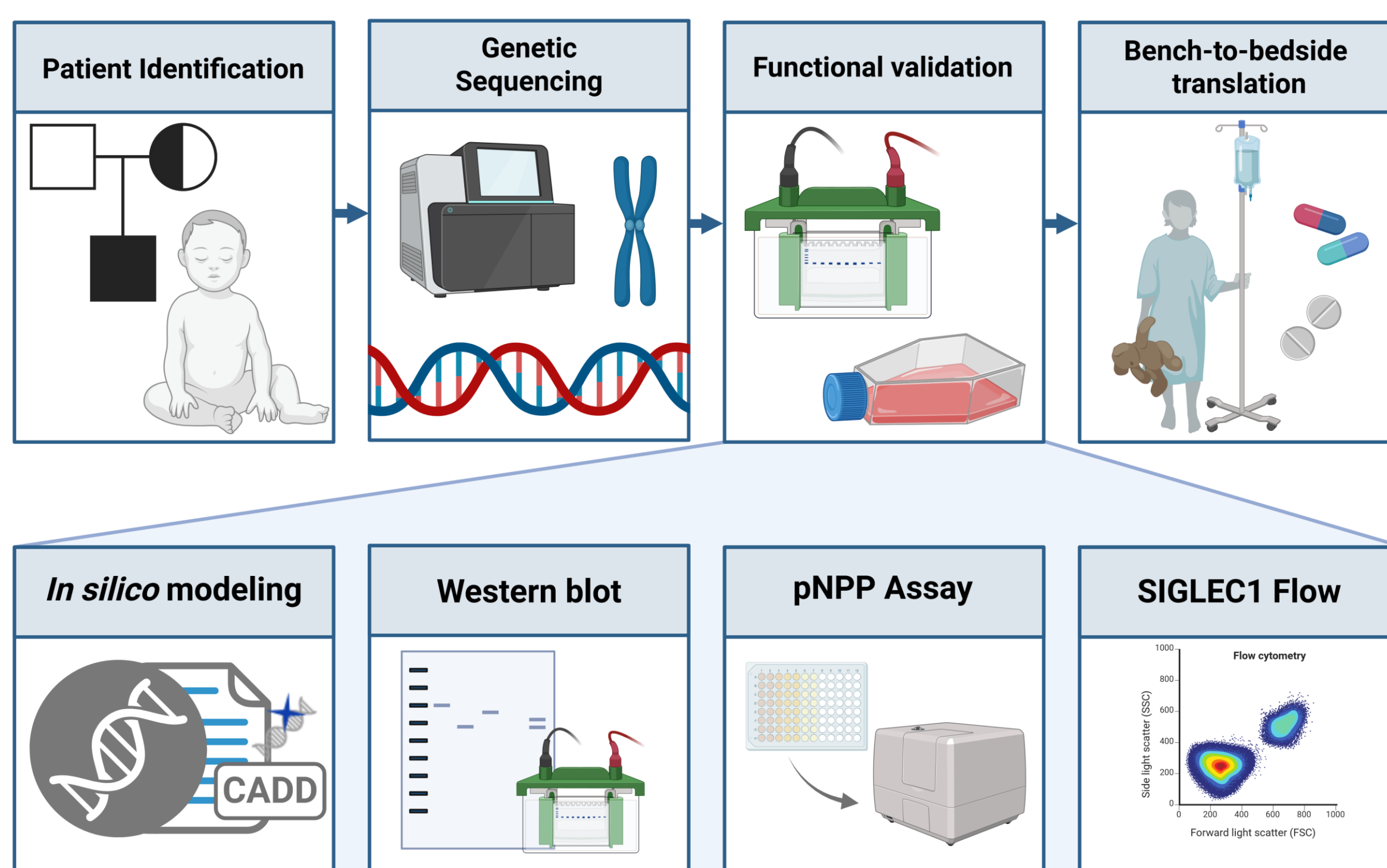


Figure 2: Methods.

Results

Patient variants are pathogenic *in silico* and segregate with disease

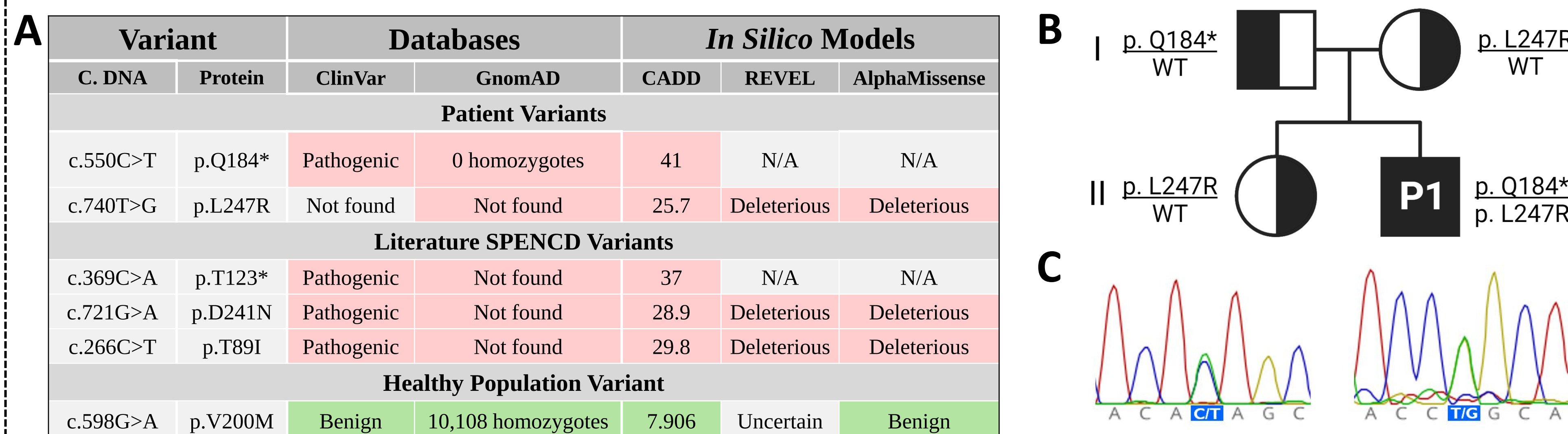


Figure 3: Identification of compound heterozygous ACP5 variants. (A) *In silico* modeling. (B) Segregation. (C) Sanger sequencing.

SPENCD variant protein is produced but has impaired phosphatase activity

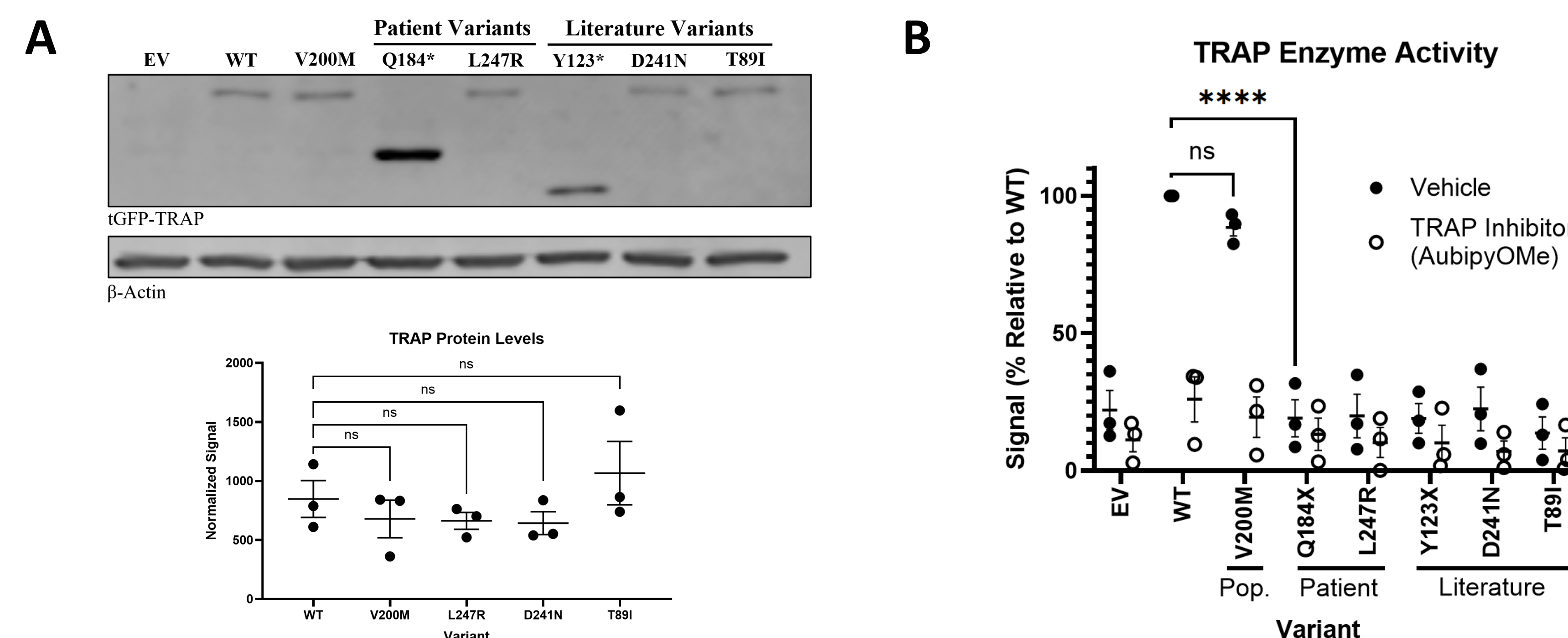


Figure 4: Functional assessment. (A) Western blotting. (B) p-Nitrophenyl phosphate (pNPP) phosphatase activity assay.

Patient samples show evidence of elevated type I interferon signaling

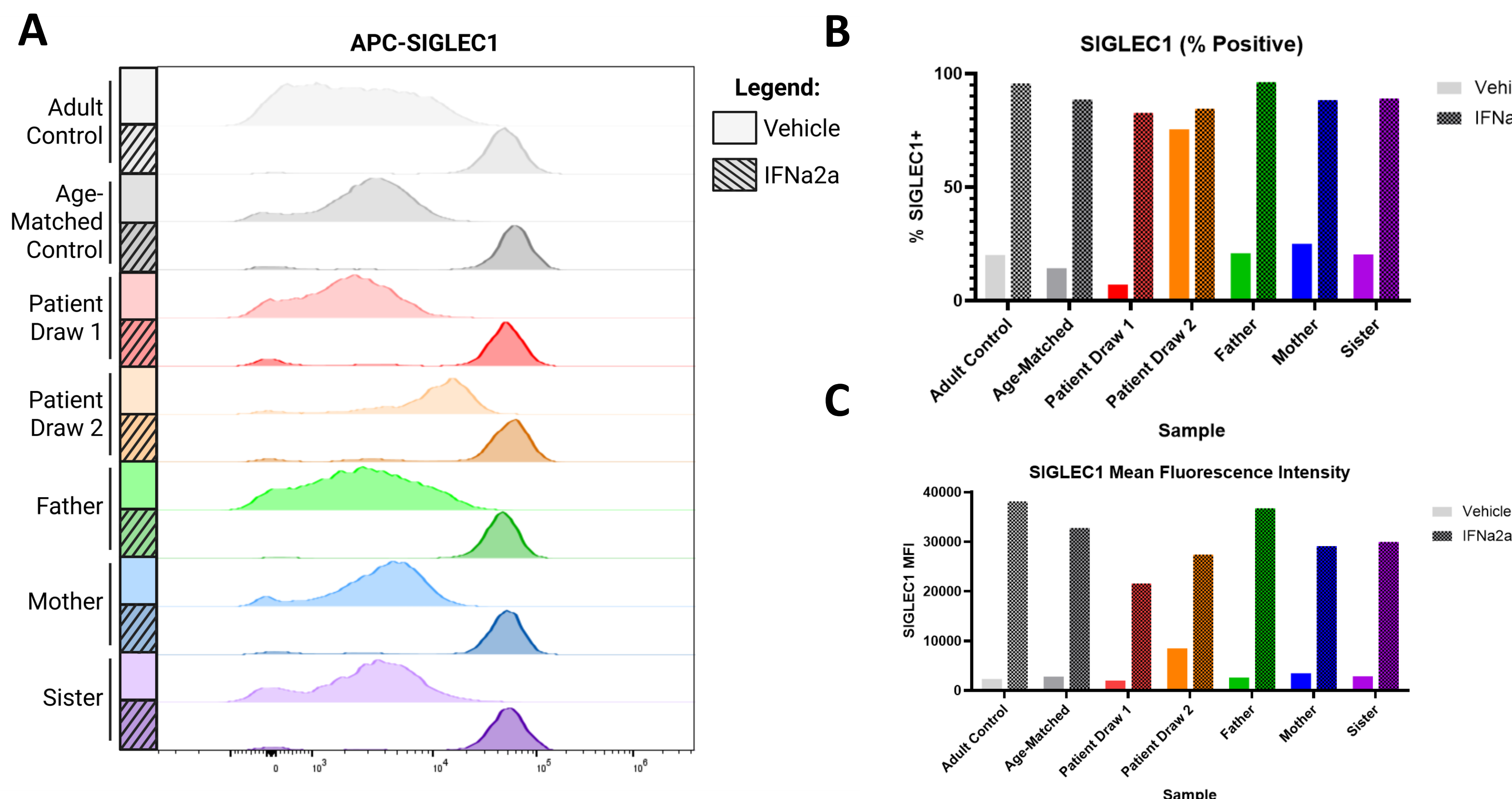


Figure 5: Flow cytometry assessment. (A) APC-SIGLEC1 histograms. (B) SIGLEC1 percent positive. (C) SIGLEC1 MFI.

Discussion

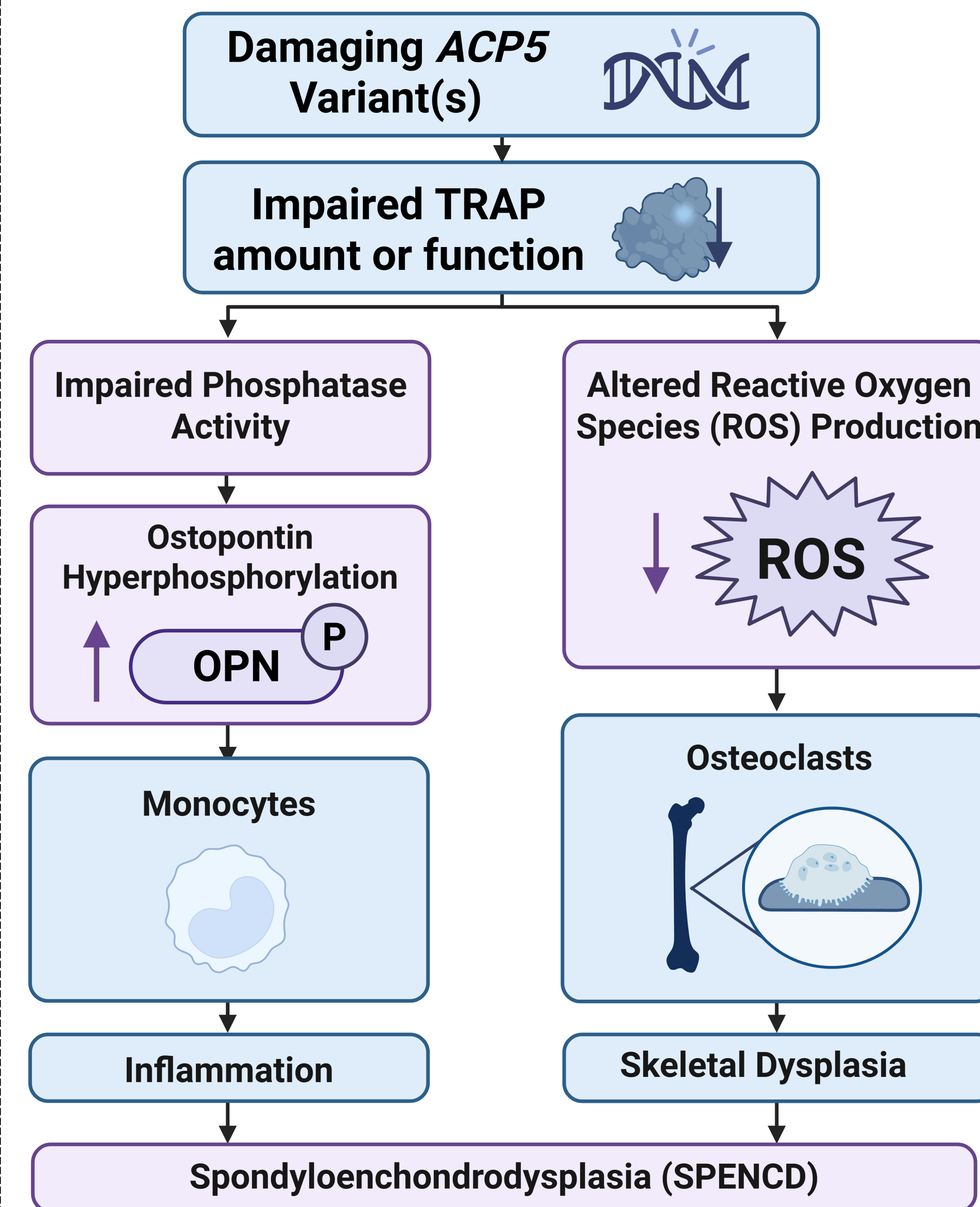


Figure 6: The proposed impact of ACP5 variants in SPENCD.

Ongoing & Future Steps

- Link phosphatase impairment to **osteopontin (OPN)**
- **Quantify inflammation** in response to a JAK inhibitor
- Assess variant TRAP's ability to generate **reactive oxygen species (ROS)**

Conclusion

This study presents a **novel SPENCD case** and provides insight into **SPENCD's mechanism of disease**.

Acknowledgments

Thank you to the **patient and their family**.

