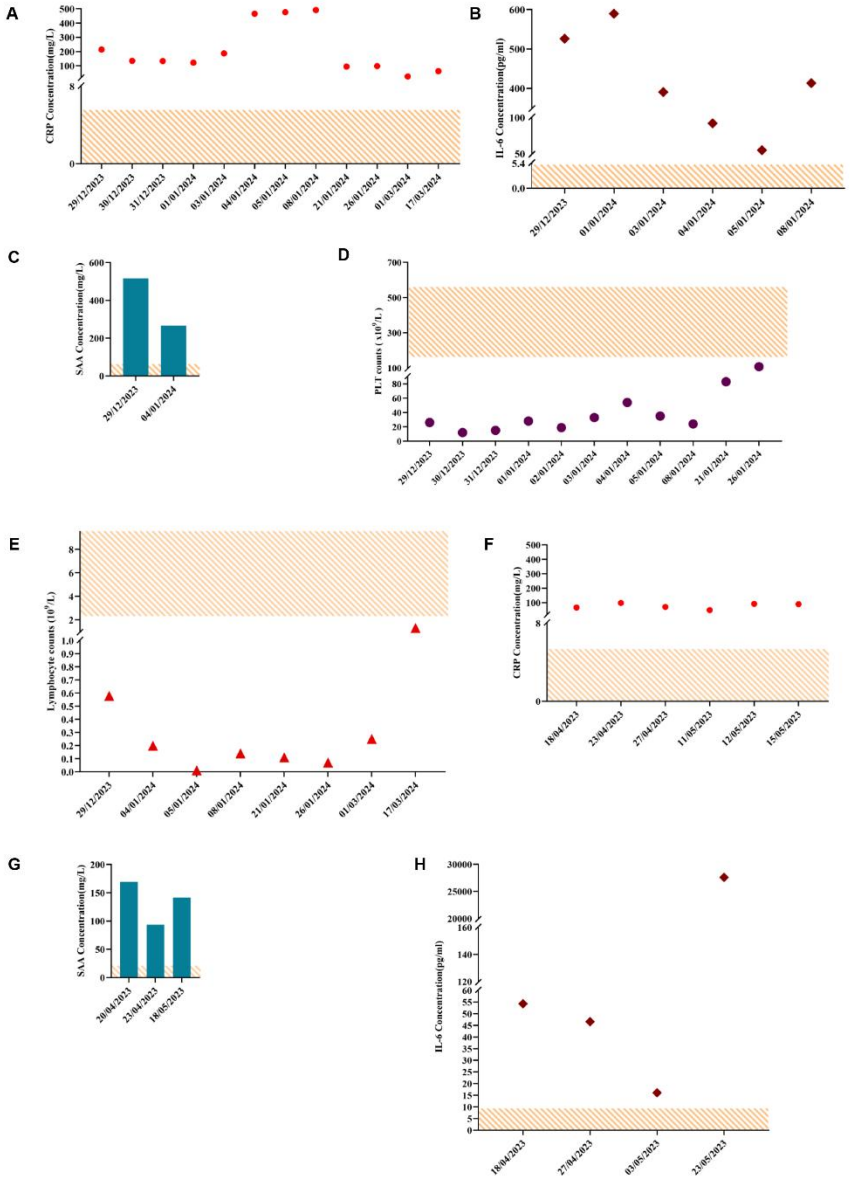

Figure S1 Results of inflammatory markers in Ⅱ-1 of Family Ⅰ and Ⅱ-1 of Family Ⅱ

(A-E) Blood tests of the patient (Ⅱ-1) from Family Ⅰ, showing significantly elevated inflammatory markers (CRP, SAA, and IL-6) and persistently low platelet and lymphocyte counts. (F-H) Blood tests of the patient (Ⅱ-1) from Family Ⅱ, showing reduced levels of inflammatory markers (CRP, SAA, and IL-6). The X-axis indicates the date when the patient underwent testing for the relevant indicator, while the Y-axis represents the corresponding values of each indicator.

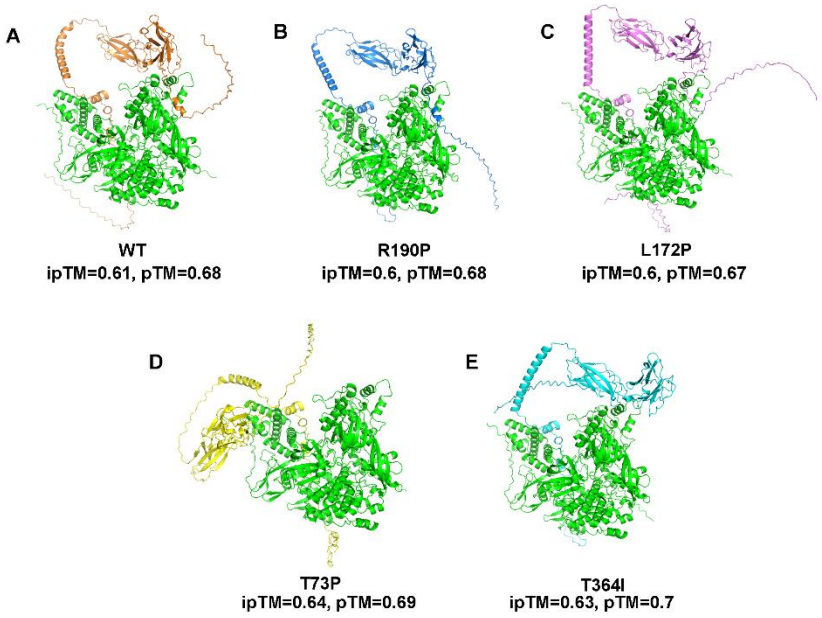

Figure S2 The predicted results of AlphaFold

The results showed that both the WT and the four mutant proteins interact with JAK3. In panels A-E, the green protein represents protein JAK3, while the other colors correspond to the WT and the four mutant IL2RG proteins, respectively. The ipTM score measures the accuracy of predictions of one component of the complex relative to the other components (0-1). The values higher than 0.8 represent confident high-quality predictions, while values below 0.6 suggest likely a failed prediction. ipTM values between 0.6 and 0.8 are a gray zone where predictions could be correct or incorrect. The predicted TM (pTM) score is a single-value metric reflecting the accuracy of the overall predicted structure (0-1), with higher scores indicating greater reliability. A pTM score above 0.5 means the overall predicted fold for the complex might be similar to the true structure.

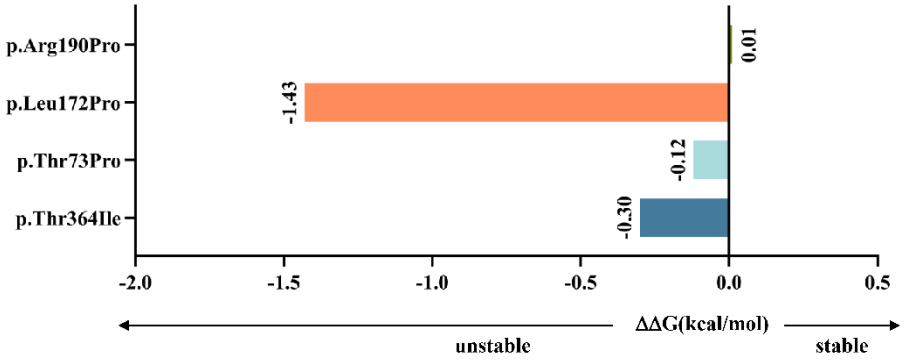

Figure S3 Stability predictions of IL2RG mutants (p.R190P, p.L172P, p.T73P and p.T364I) by DynaMut2 tool

Three variants (p.L172P, p.T73P, and p.T364I) were predicted to be instable, with p.L172P being the most unstable.

Table S1 Prediction of pathogenicity by bioinformatics

Family	Individuals	Gene	Variant	Exon	Prediction of pathogenicity by bioinformatics		
					Polyphen2	CADD	Mutation Taster
Ⅰ	Ⅱ-1	*IL2RG*	p.R190P	4	PD	24.8	DC
Ⅱ	Ⅱ-1	*IL2RG*	p.L172P	4	PD	26.2	DC
Ⅲ	Ⅱ-1	*IL2RG*	p.T73P	2	PD	26	DC
Ⅳ	Ⅲ-1	*IL2RG*	p.T364I	8	B	14.13	Poly

Table S2 X-SCID molecular case reports or series in China

Patient number	Exons	Nucleotide change	Amino acid change	Mutation type	References
1	1	UTR5 exon1 del	/	Splicing	21
2	1	c.52delG	L18Cfs*	Nonsense	22
3	2	c.202G>A	E68K	Missense	23
4	2	g.IVS2-2 A>C	/	Splicing	24
5	2	c.147_150 ins ACTA	44Tfs*49	Frame shift	24
6	2	c.269+1G > T	/	Splicing	21
7	2	c.172C>A	P58T	Missense	21
8	2	c.202G>A	E68K	Missense	21
9	2	c.209T>C	M70T	Missense	21
10	2	c.260T>C	L87P	Missense	25
11	3	c.445C>T	Q149*	Nonsense	23
12	3	c.316_318delinsGTGAT	L106Vfs*42	Frame shift	2
13	3	c.295C>A	S94*	Nonsense	24
14	3	c.304T>C	C102R	Missense	24
15	3	c.312C>T	Q100*	Nonsense	24
16	3	c.324-325CA>G	H104fs*146	Frame shift	24

17	3	c.385T>C	L124P	Missense	24
18	3	c.391C>T	Q131*	Nonsense	26
19	3	c.270-1G>C	/	Splicing	21
20	3	c.420A>T	R140S	Missense	27
21	3	c.324-325CA>G	H104fs*146	Frame shift	28
22	3	c.385T>C	L124P	Missense	28
23	3	c.390C>T	Q126*	Nonsense	28
24	3	c.435delC	Q141fs*146	Frame shift	28
25	3	c.373-374insA	K120fs*167	Frame shift	28
26	4	c.548T>A	L183*	Nonsense	23
27	4	c.483C>T	P157S	Missense	24
28	4	c.529T>C	L172P	Missense	24
29	4	c.580ins T	Y189fs*201	Frame shift	24
30	4	c.557dupT	/	Splicing	25
31	4	c.576C>T	Q188*	Nonsense	28
32	4	c.521delG	Q169fs*170	Frame shift	28
33	5	c.722G>T	S241I	Missense	23
34	5	c.670C>T	R224W	Missense	23

35	5	c.677G>A	R226H	Missense	23
36	5	c.595-430_757+140del723	E199Rfs*218	Frame shift	23
37	5	c.711G>A	W237*	Nonsense	23
38	5	c.684C>T	R224W	Missense	24
39	5	c.732T>C	W240R	Missense	24
40	5	c.738G>A	W246*	Nonsense	24
41	5	c.670C>G	R224W	Missense	21
42	5	c.664C>T	R222C	Missense	21
43	5	c.677C>T	R226H	Missense	29
44	5	718T>C	W240R	Missense	30
45	5	c.676C>T	R226C	Missense	25
46	5	c.691G>A	R226H	Missense	28
47	5	c.684C>T	R224W	Missense	28
48	5	c.736G>T	S241I	Missense	28
49	5	c.725G>A	W237*	Nonsense	28
50	6	c.854G>C	/	Splicing	23
51	6	c.849G>A	V279M	Missense	24

52	6	c.868G>A	R285Q/Change of exon6/intron6 splice junction from CG/GT to CA/GT, predicted aberrant splicing	Missense/Splicing	24
53	6	g.IVS6+5G>A	/	Splicing	24
54	6	c.854G>A	R285Q	Missense	31
55	6	c.794T>A	I265N	Missense	32
56	6	c.849delG	V279fs*293	Frame shift	28
57	6	g.IVS6+5G>A	/	Splicing	28
58	6	g.IVS6+5G>A	/	Splicing	28
59	7	g.IVS7-72 to IVS8-11del487	Exon 7 del	Frame shift	24
60	7	c.879C>T	R289*	Nonsense	24
61	7	c.924+5G>C	/	Splicing	5
62	7	g.IVS6-72 to g.IVS7-11del487	Exon7del	Frame shift	28
63	7	c.868G>A	/	Splicing	28
64	8	c.925-13 T > G	/	Splicing	33