## Supplementary Tables 1 and 2

**Supplementary Table 1. Laboratory values for patients with missense mutations in *BACH2.***

All laboratory readings are reported from the date of initial presentation as adults to medical services except for immunoglobulin levels, which were measured at the ages shown. Parameters are given with respect to the normal ranges of the reporting laboratories. Note that values in **Fig. 1** are those from the research laboratory and measured at a later time from those here. L, low; Ab, antibody; N/A, not assessed; ND, not detected; * patient is on intravenous immunoglobulin so these parameters could not reliably be assessed. † A tetanus antitoxoid IgG concentration of 0.47 iU/mL would be considered in the lowest 25$^{th}$ centile for healthy controls (Median tetanus antibody levels aged 20-60 years = 2.7iU/mL IQR 0.6-4.0iU/mL: [69]).

| | | **N-terminus (L24P)** | **C-terminus (E788K)** | | |
|---|---|---|---|---|---|
| **Patient** | | **A.II.1** | **B.II.1** | **B.III.2** | |
| RBC | x $10^{12}$/L | 4.7 (**L**) | 4.8 | 3.9 | |
| WBC | x $10^{9}$/L | 3.4 (**L**) | 7.64 | 9.7 | |
| Neutrophils | x $10^{9}$/L | 2.8 (**L**) | 5.6 | 6.9 | |
| Monocytes | x $10^{9}$/L | 0.3 (**L**) | 0.6 | 1.1 | |
| Eosinophils | x $10^{9}$/L | 0 (**L**) | 0.23 | 0.3 | |
| Basophils | x $10^{9}$/L | 0 (**L**) | 0.03 (**L**) | 0 (**L**) | |
| Lymphocytes | x $10^{9}$/L | 0.3 (**L**) | 1.1 (**L**) | 1.5 | |
| CD3 | cells/mL | 279 (**L**) | 844 | 1226 | |
| CD4 | cells/mL | 183 (**L**) | 622 | 643 | |
| CD8 | cells/mL | 89 (**L**) | 162 (**L**) | 571 | |
| CD4/CD8 ratio | ratio | 2.1 | 3.8 | 1.1 | |
| NK cells | cells/mL | 24 (**L**) | 31 | 56 | |
| B cells ($CD19^{+}$) | cells/mL | 87 (**L**) | 143 | 92 | |
| $CD27^{+}$ B cells | % of B cells | 0.8 (**L**) | 0.6 (**L**) | 8.7 (**L**) | |
| $IgG^{+}$ B cells | % of B cells | 0.2 (**L**) | 0.2 (**L**) | 3.7 | |
| $IgA^{+}$ B cells | % of B cells | 0.1 (**L**) | 0 (**L**) | N/A | |
| $IgM^{+}$ B cells | % of B cells | 4.0 | 12.6 | 4.2 | |
| $IgD^{+}$ B cells | % of B cells | 81.2 (**H**) | 12.6 | N/A | |
| **Immunoglobulins** | | | | | |
| *Age at examination* | | **21yrs** | **63yrs** | **19yrs** | **40yrs** |
| IgG | mg/dL | 400 (**L**) | 560 (**L**) | 2182 | 1946 |
| IgM | mg/dL | 24 (**L**) | 10 (**L**) | 292 | 383 |
| IgA | mg/dL | 20 (**L**) | **ND** | **ND** | **ND** |
| IgE | iU/mL | **ND** | **ND** | 9.7 | 11 |
| Tetanus antitoxoid IgG | iU/mL | 0.1 (**L**) | * | 0.47$^{\dagger}$ | |
| Diphtheria antitoxoid | iU/mL | 0.05 (**L**) | * | 0.16 | |

**Supplementary Table 2. Bioinformatic evaluation of missense mutations in *BACH2*.**

Conservation scores (GERP, PhastCons and PhyloP) were obtained from the UCSC genome browser. Global minor allele frequencies (gMAF) were derived from the 1000 genomes and ExAc databases, respectively. Multiple sources (PolyPhen2, SIFT, LRT, MutationAssesor Functional Impact, MutationTaster and Combined Annotation-Dependent Depletion (CADD)) were queried to predict the functional impact of each missense mutation using dbNSFP, as described [56,57]. CADD scores of 17 and 19 places the mutation within the top 2% and 1.3%, respectively, of likely deleterious mutations across the genome [70]. The CADD-based mutation significance cutoff (MSC) at 99% confidence interval (CI) was calculated as described [58].

| **Family** | **A** | **B** |
|---|---|---|
| GRCh37/Hg19 physical position (Chr6) | 90,718,493 | 90,642,291 |
| PhyloP (100wayall) | 8.83 | 5.28 |
| PhastCons | 1 | 0.99 |
| GERP | 5.33 | 5.51 |
| cDNA change | c.T71>C | c.G2362>A |
| Amino acid substitution | p.Leu24Pro | p.Glu788Lys |
| gMAF in 1000 genomes | 0 | 0 |
| gMAF in ExAc | 0 | 0.00002478 |
| PolyPhen2 | Probably damaging | Benign |
| SIFT | Damaging | Tolerated |
| LRT | Damaging | Damaging |
| Mutation Assessor Functional Impact | High | Low |
| MutationTaster | Disease causing | Disease causing |
| CADD scaled score | 17 | 19 |
| MSC-CADD score (99% CI) Impact Prediction | High | High |