

Fig. S1. Subpopulation of phenotypically normal LLPCs in CVID exhibit normal functions. Supernatant was collected from the bottom Transwell chambers of plasma cell cultures between Day 6 to Day 41, every 3.5 days. Sandwiched ELISA was used to measure the total amounts of $\operatorname{IgM}, \operatorname{IgA}$, and $\operatorname{IgG}$ in the cultures. $\operatorname{IgM}$, $\operatorname{IgA}$, and $\operatorname{IgG}$ were corrected to the total plasma cell counts (SLPC + LLPC) on Day 13, Day 27, and Day 41 (HC, n=10-6; CVID, n=14-8). Statistical differences were calculated by two-way ANOVA. Median and interquartile ranges are shown (A-B). Plasma cell cultures were harvested on Day 13 and washed with PBS before total mRNA was extracted for qPCR. Gene expression ratios $\left(2^{\triangle A C T}\right)$ of BLIMP-1, XBP1, IRF4, PAX5, and BCL6 were calculated using endogenous (average of beta-actin and GAPDH) and undifferentiated controls (Day 0 naïve B-cells). Statistical differences between HC ( $\mathrm{n}=5$ ) and CVID ( $\mathrm{n}=5$ ) were calculated by Mann-Whitney U test. Median and interquartile ranges are shown (D). Statistical significances are indicated as *p<0.05, **p<0.01, and ***p<0.001.

## Supplementary Table:

Supplementary Table 1. Clinical presentation of patients demonstrating clonal hematopoiesis.

| $\begin{gathered} \hline \text { Pati } \\ \text { ent } \\ \text { no. } \end{gathered}$ | Age of presenta tion | $\begin{gathered} \mathrm{IgM} \\ \mathrm{~g} / \mathrm{L} \end{gathered}$ | $\begin{aligned} & \hline \mathbf{I g A} \\ & \mathrm{g} / \mathrm{L} \end{aligned}$ | $\begin{gathered} \mathrm{IgG} \\ \mathrm{~g} / \mathrm{L} \end{gathered}$ | Bronchie ctasis | Splenomega ly, lymphadeno pathy | Autoimm une, inflamm atory complica tions | $\begin{aligned} & \hline \mathbf{H b} \\ & \mathrm{g} / \mathrm{L} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| C1 | 43 | 0.59 | $\begin{gathered} \hline<0.0 \\ 5 \end{gathered}$ | Histor cal | Mild | N | N | 132 |
| C2 | 59 | <0.10 | $\begin{gathered} \hline<0.0 \\ 5 \end{gathered}$ | 1.06 | Mild | N | N | 165 |
| C3 | 37 | 0.25 | $\begin{gathered} <0.0 \\ 5 \end{gathered}$ | 3.28 | Mild | N | N | 128 |
| C4 | 29 | 0.69 | 0.08 | 2.48 | Mild | N | N (Coeliac) | 128 |
| C5 | 13 | 0.31 | $\begin{gathered} \hline<0.0 \\ 5 \end{gathered}$ | 5.13 | Mild | N | N | 123 |
|  | $\begin{aligned} & \hline \text { WBC } \\ & 10^{9} / \mathrm{L} \end{aligned}$ | Neutro phils $10^{9} / \mathrm{L}$ | $\begin{array}{\|c} \hline \text { Plate } \\ \text { let } \\ 10^{9} / \mathrm{L} \\ \hline \end{array}$ | CD3 cells/ $\mathrm{mm}^{3}$ | $\begin{gathered} \mathrm{CD} 4 \\ \text { cells } / \mathrm{mm}^{3} \end{gathered}$ | $\begin{gathered} \text { CD8 } \\ \text { cells } / \mathrm{mm}^{3} \end{gathered}$ | $\begin{gathered} \hline \text { CD19 } \\ \text { cells/mm } \\ 3 \\ \hline \end{gathered}$ | $\begin{gathered} \hline \mathrm{NK} \\ \text { cells/ } \\ \mathrm{mm}^{3} \\ \hline \end{gathered}$ |
| C1 | 4.47 | 3.15 | 217 | 596 | 452 | 108 | 123 | 241 |
| C2 | 9.41 | 6.89 | 524 | 1000 | 607 | 321 | 317 | 317 |
| C3 | 5.13 | 3.38 | 381 | 658 | 446 | 193 | 147 | 301 |
| C4 | 8.43 | 5.16 | 359 | 1008 | 577 | 453 | 377 | 19 |
| C5 | 6.75 | 3.64 | 318 | 1517 | 598 | 848 | 245 | 337 |

