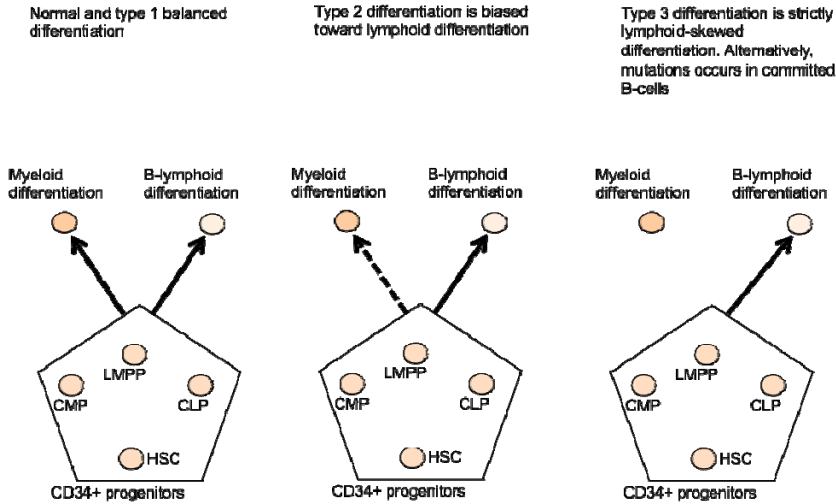


### Supplementary Figure S3.

**S3A:** Proposed variations in the balance between myeloid and B-cell lineages in mutated progenitor differentiation. Type 1 and 3 patients are likely to represent the extremes of a continuous between normal and lymphoid-skewed differentiation. lymphoid-primed multipotential progenitor (LMPP), Common myeloid progenitor (CMP), Common lymphoid progenitor (CLP), Hematopoietic stem cells (HSC)



**S3B:** We analyzed a bone marrow sample from a CLL patient relapsing 10 years after allograft. We identified acquired mutations in CLL cells from limited molecular analyses and sorted progenitor sub-fractions according to Goardon et al, Cancer Cell, 2011. We obtained 2950 hematopoietic stem cells (HSC; CD34+/38-/CD45RA-/CD90+); 4280 multipotential progenitors (MPP; CD34+/38-/CD45RA-/CD90-); 1880 lymphoid-primed multipotential progenitor(LMPP;CD34+/38-/CD45RA+/CD90-); 11670 common myeloid progenitors (CMP; CD34+/CD38+/CD45RA-/CD123+); 55120 granulocyte-macrophage progenitors (GMP; CD34+/CD38+/CD45RA+/CD123+).

In addition to the CD14+ and CD34+ fractions, the SF3B1 mutation was detected in LMPP, and also in colonies from CD34+ single cells. The results are shown below. (the numbers of analyzed reads are in brackets)

These results establish the presence of the SF3B1 mutations in very immature progenitors. The chimeric status of the analyzed sample precludes any accurate quantification of the mutation burden in the current setting.

Mutations	CD3+	CD14+	CD5+C D19+	CD34+CD 19-	HSC	MPP	LMPP	CMP	GMP	CFU
<b>SF3B1</b> , NM_012433:c.A2098G:p.K700E	1% (3526)	14% (2904)	47% (9402)	25% (2620)	0% (3142)	0% (7659)	14% (1061)	0% (30996)	1% (2368)	5/29 = 18%
<b>TP53</b> , NM_001126118:c.254_255insA:p.C 85_T86delinsX	0% (7329)	2% (10238)	99% (7720)	7% (8305)	0% (8901)	0% (5524)	4% (6231)	0% (7004)	0% (8284)	0/93
<b>DIS3</b> , NM_001128226:c.G1372A:p.D458N	0% (4507)	1% (6127)	46% (5296)	2% (5001)	0% (3300)	0% (4917)	0% (2385)	0% (3328)	0% (4026)	ND
<b>ASB12</b> , NM_130388:c.A901G:p.I301V	1% (12817)	3% (19718)	99% (26674)	11% (22309)	0% (17169)	0% (20143)	0% (16444)	1% (18598)	0% (14469)	0/89