Supplementary Table 1. Antibodies for markers used for FACS analysis.

ANTIGEN	CLONE	SUPPLIER	CATALOGUE #	FLUOROCHROME
CD56	B159	BD Bioscience	560360	V450
CD19	SJ25C1	BD Bioscience	562947	BV510
CD45	HI30	Biolegend	304042	BV605
KI-67	Ki-67	Biolegend	350516	BV711
TCRγ/δ	11F2	BD Bioscience	347903	FITC
CD4	SK3	BD Bioscience	347327	PE
CD45RO	UCHL1	Beckman Coulter	IM2712U	ECD
CD3	SK7	BD Bioscience	341101	PE-Cy7
CD8	SK1	BD Bioscience	340584	APC
CD27	O323	Biolegend	302814	Alex700
CD19	HIB19	eBioscience	48019942	eFluor450
CD10	HI10a	BD Bioscience	563032	BV510
CD34	581	Biolegend	343530	BV605
CD45	HI30	BD Bioscience	564357	BV711
TCR$\alpha\beta$	T10B9.1A-31	BD Bioscience	555547	FITC
CD45RA	HI100	Biolegend	304122	PerCP-Cy5.5
CD7	M-T701	BD Bioscience	555361	PE
CD1a	HI149	BD Bioscience	563938	BV421
CD4	OKT4	Biolegend	317440	BV711
CD5	UCHT2	Biolegend	300620	PerCp-Cy5.5
Mouse CD45	30F11	BD Bioscience	557659	APC-Cy7

Supplemental Figures

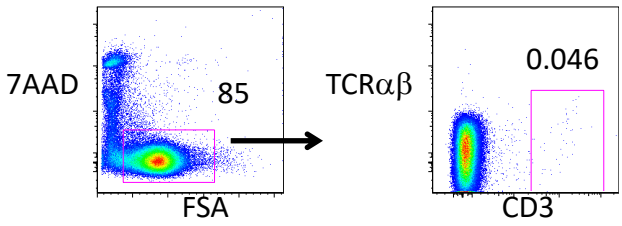

Figure S1. **Minimal CD3+ T cell contamination in the purified hCD34+ preparations.** Representative flow cytometry of hCD34. Left panel shows the forward scatter versus 7-Aminoactinomycin D (7AAD) within the live gate. Right panel shows the CD3 versus TCRαβ within the live gate. Numbers represent the percentage of events on each gate. In this particular transfer each mouse would have received around 460 CD3+ T cells.

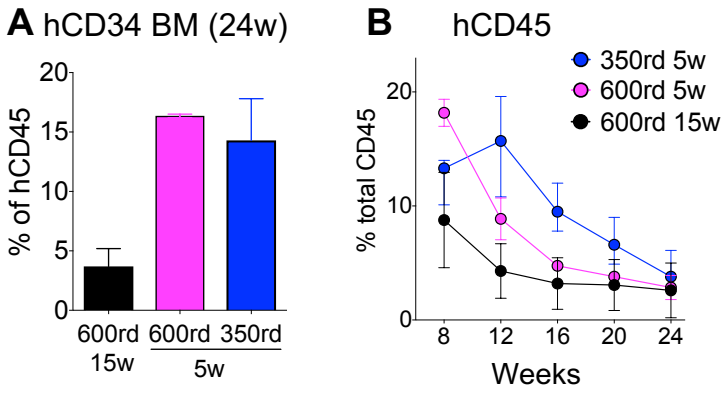

Figure S2. **Effect of radiation dose and mice age on long term human bone marrow (BM) engraftment and hematopoietic cells development. (A)** Long-term h-CD34 engraftment in the bone marrow. **(B)** Percentages of hCD45 cells in the blood of NRG mice at different time points after hCD34 transfer. Median values of two to three mice per time point and condition with the interquartile range are shown.

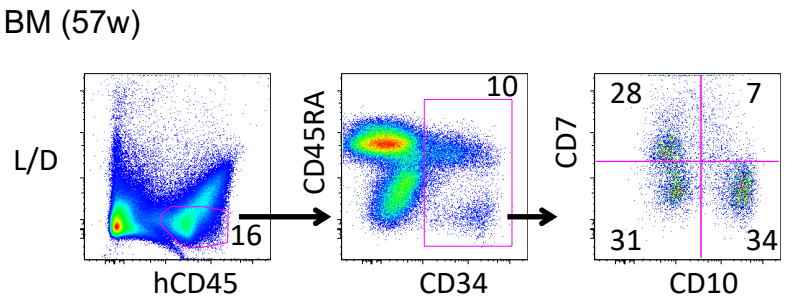

Figure S3. **Stable hCD34 Hematopoietic Stem Cell (HSC) engraftment 57 weeks after hCD34 transfer.** Representative flow cytometry of the bone marrow harvested from the femurs of mice transplanted 57 weeks earlier with hCD34 cells as described in Methods. Numbers represent the percentage of events on each gate or quadrant.

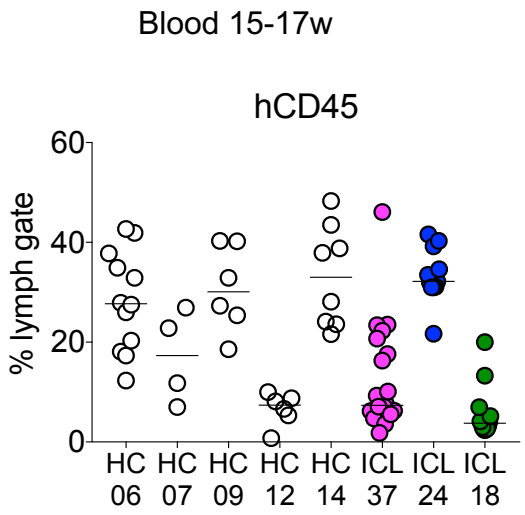

Figure S4. **The percentages of hCD45+ cells found in blood of mice 15 to 17 weeks after hCD34 transfer of Healthy Control (HC) or Idiopathic CD4 Lymphopenia (ICL) patients were similar.** Percentages of hCD45 within the lymphocyte gate found in blood of mice that 15 to 17 weeks earlier received either HC (open circles) or ICL (colored circles) CD34+ cells. Data shown correspond to four independent experiments. ICL 37 was tested in three independent experiments and ICL 24 and 18 were tested in two. Each circle represents an individual mouse and the horizontal line the median value for that donor.

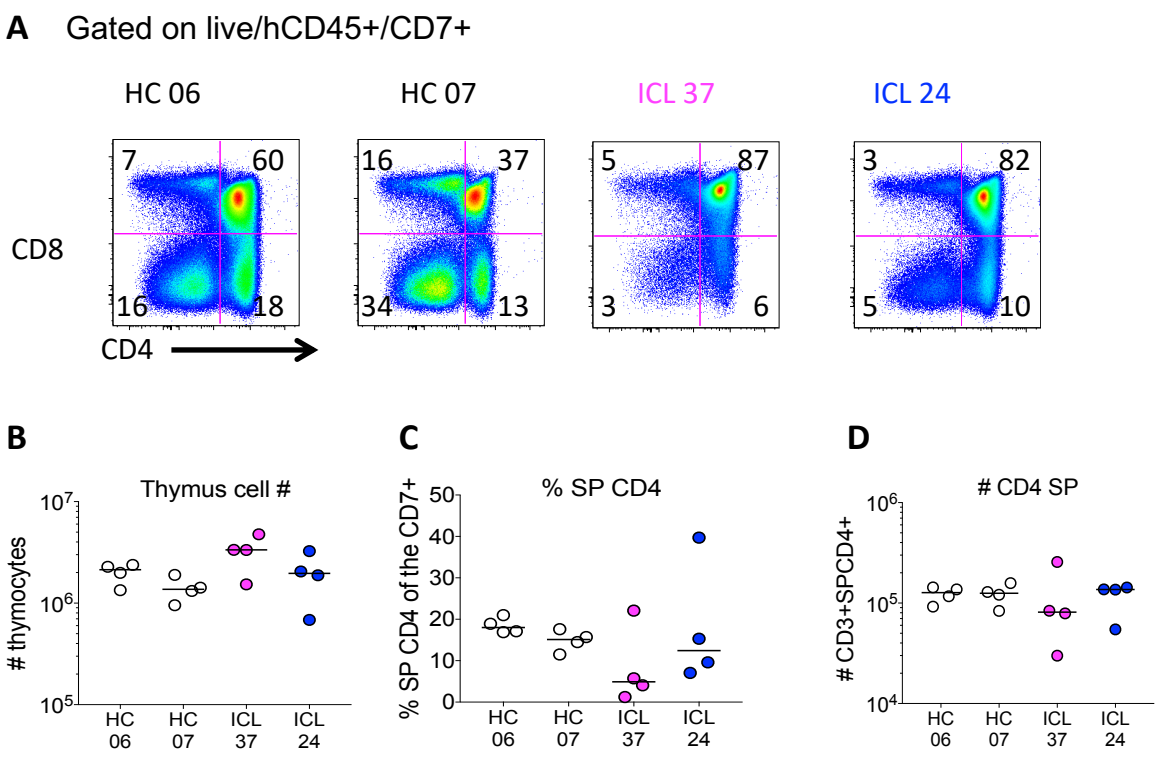

Figure S5. **No differences in thymi cellularity or numbers of CD4 Single Positive (SP) in hCD34-mice that received either Healthy Control (HC) or Idiopathic CD4 Lymphopenia (ICL) CD34+ cells.** Thymi of individual mice were analyzed 17 weeks after transfer of either HC (open circles) or ICL (colored circles) CD34+ cells. (**A)** Representative dot plots of the thymus of one mouse per experimental group, gating on live/hCD45+/CD7+ cells. **(B)** Number of thymocytes. **(C)** Percentages of CD4 SP cells of the same gate as in (A). **(D)** Number of CD3+CD4 SP cells in each individual thymus. Each circle represents an individual mouse and the horizontal line the median value for that group. Similar results were found at week 13. Data shown are representative of four independent experiments.

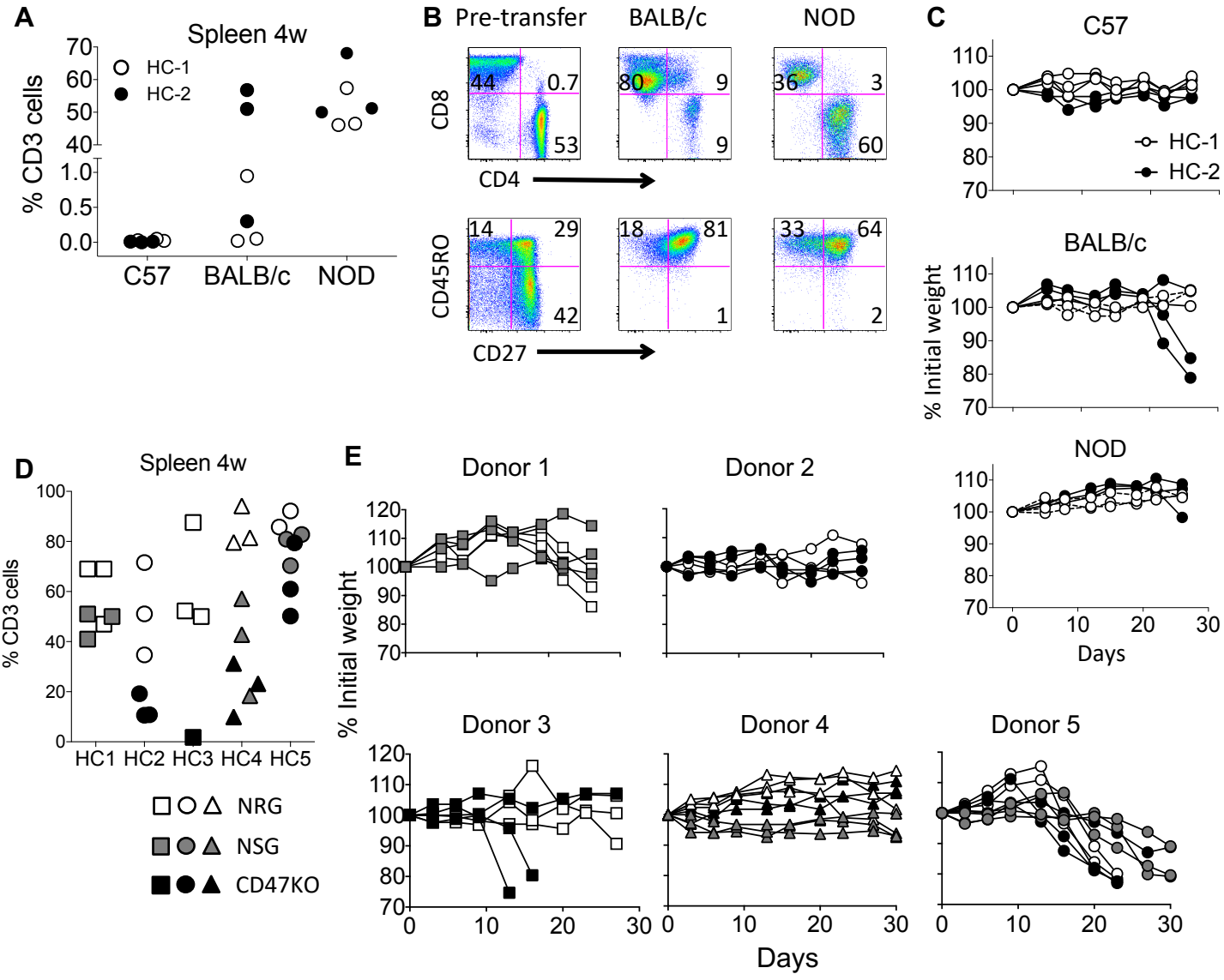

Figure S6. **RAGKOγcKO mice in the NOD background are the optimal hosts for human PBMC out of five different strains tested. (A)** Percentage of hCD45+CD3+ cells in spleen four weeks after transfer of two different HC PBMC into C57Bl/6RAGKOγcKO (C57), BALB/cRAGKOγcKO (BALB/c) or NODRAGKOγcKO (NOD) mice. Data from same experiment as in Figure 3A and B. **(B)** Dot plot of HC-2 PBMC just before the transfer (left column), and of the spleens from either BALB/c or NOD mice four weeks after receiving HC-2 PBMC cells, gating on hCD45+CD3+ cells. Numbers represent the percentage of the population in each quadrant. **(C)** Percentage of initial body weight of three mice per donor and strain of mice after receiving HC PBMC from two different donors. Open and closed symbols in A and C, correspond to individual mice that received either HC-1 or HC-2 donor PBMC, respectively. (**D)** Percentage of hCD45+CD3+ cells in spleen four weeks after transfer of five different HC PBMC into either NODRAGKOγcKO (NRG), NODSCIDγcKO (NSG) or C57Bl/6RAGKOγcKO (CD47KO) mice. **(E)** Percentage of initial body weight of three mice per donor and strain of mice after receiving HC PBMC from five different donors. D and E, data pooled from same five experiments shown in Figure 3D. Open, grey and black symbols are NRG, NSG and CD47KO hosts, respectively.

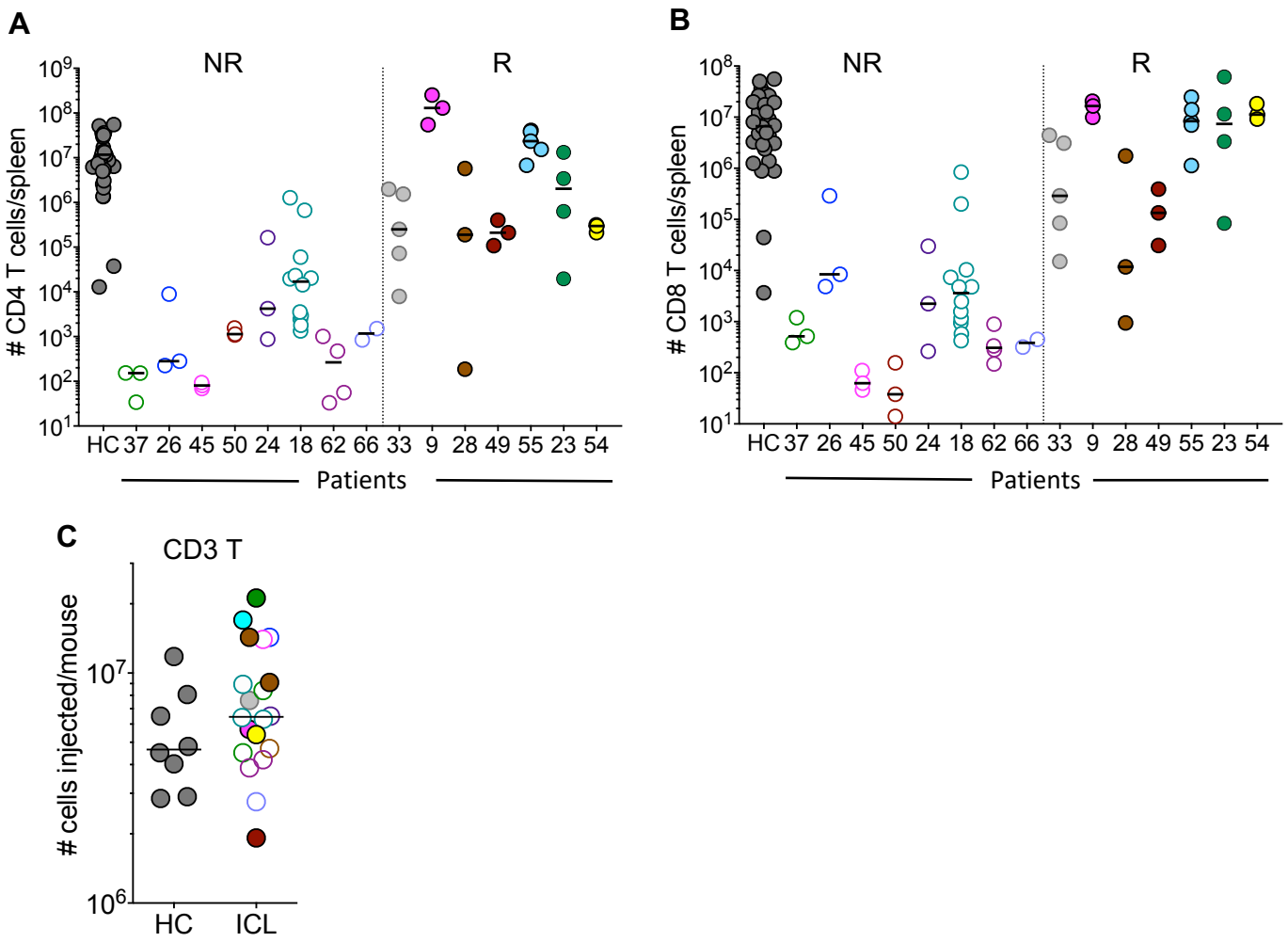

Figure S7. **Both CD4 and CD8 T cells behave similarly regarding their reconstitution capability in NOD-RAGKO-γcKO (NRG) mice, and independently from the number of CD3 T cells transferred.** Number of CD4 **(A)** or CD8 **(B)** T cells found in the spleen of h-PBMC mice 4 weeks after transfer of either Healthy Controls (HC) or Idiopathic CD4 Lymphopenic (ICL) PBMC. Each symbol represents an individual mouse. **C)** Number of CD3 T cells injected per mouse for each of the donors shown in A and B. Each symbol represents one donor. In **A, B,** and **C**, same symbol color represents same donor. Pooled data from the same experiments shown in Figure 5.

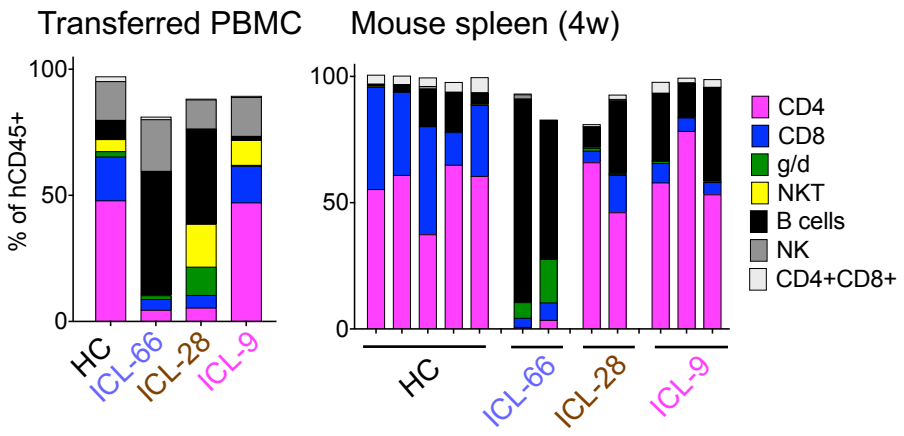

Figure S8. **PBMC from Reconstituting (R) Idiopathic CD4 Lymphopenia (ICL) patients revert to HC proportions in the hPBMC model.** Percentages of the different populations found within the live hCD45+ gate in either the original PBMC inoculum (left) or in the spleen of individual mice four weeks after PBCM transfer (right). In cases where the total percentage does not add up to 100, there was a subset of events that were hCD45+ but negative for any of the markers used.

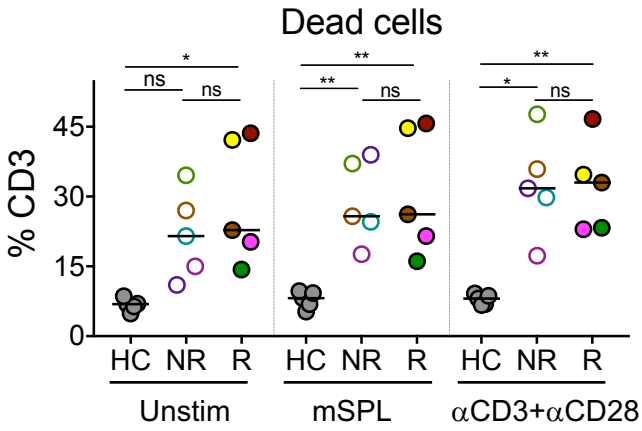

Figure S9. **CD3 T cells from both Non-Reconstituting (NR) or Reconstituting (R) Idiopathic CD4 Lymphopenic (ICL) patients show similar high levels of cell death during different in vitro culture conditions.** Percentage of total cell dead (Annexin V+/7AAD+or neg) on CD3 T cells from Healthy Controls (HC) (grey symbols) or ICL patients belonging to the (NR) or (R) groups, open or closed colored circles, respectively, 24h after in vitro culture with just complete media (Unstim) or with either NOD-RAGKO-γcKO **(**NRG) mouse splenocytes (mSPL), or with anti-CD3 and anti-CD28 antibodies (αCD3+αCD28). Each symbol represents two pooled duplicate wells from each donor and condition. Colors of open and closed circles represent same individual ICL patient as in Figure 5. The horizontal line represents the median of the group. *, $p<0.05$; **, $p<0.01$; ns, not significant.