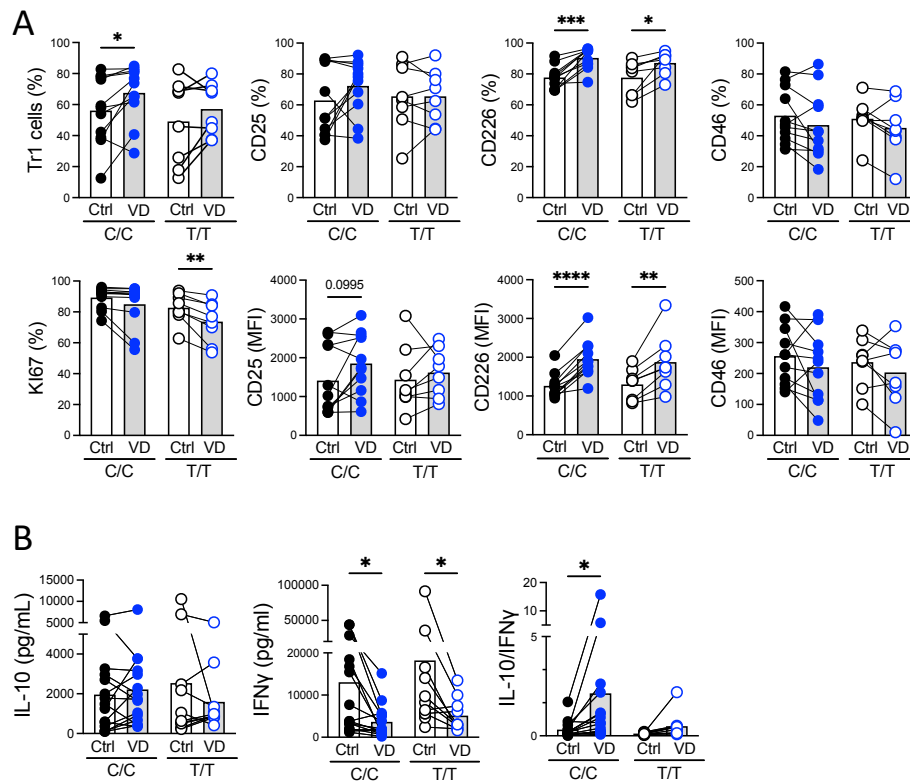
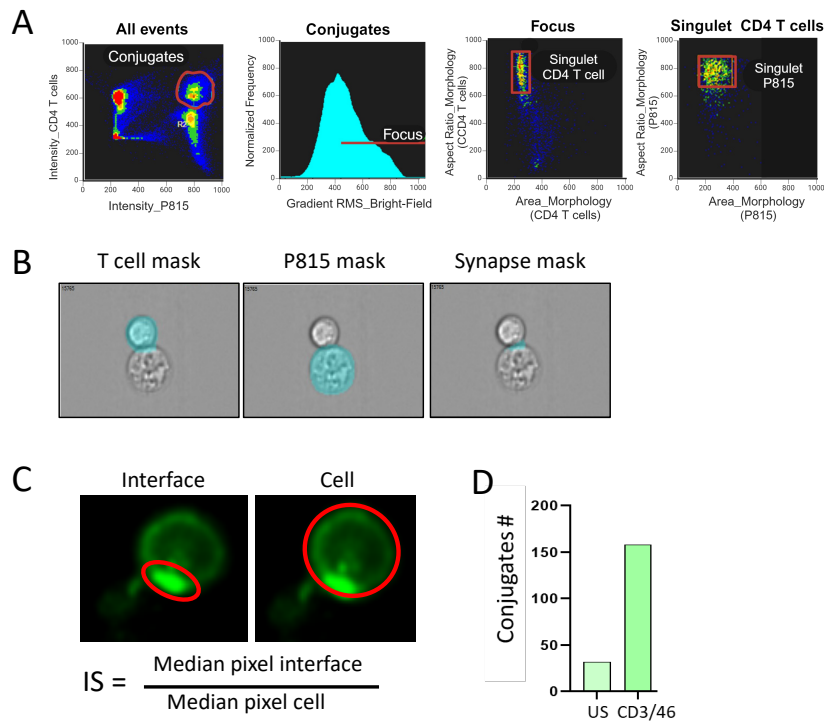


Supp Fig. S1



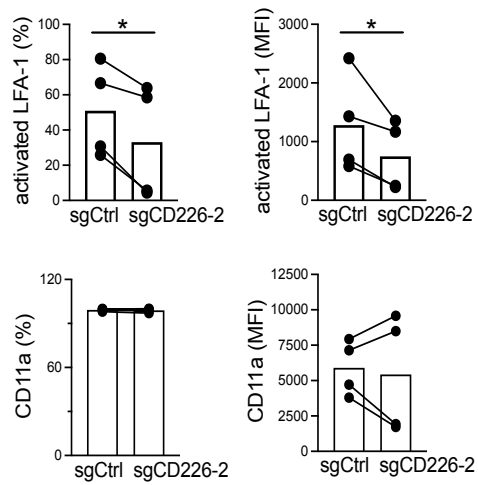
**Supp Fig. S1. The *CD226* risk allele does not have a major impact on T cell phenotype in response to VD.** CD4<sup>+</sup> T cells from HD homozygous for the *CD226* rs763361 variant, C/C, non-risk or T/T, risk, were activated with anti-CD3/CD46 with or without 1,25OH for 5 days. (A) Percentage of Tr1 cells and expression of Ki67, CD25, CD226 and CD46 was assessed by flow cytometry. (B) Secretion of IL-10 and IFN $\gamma$  in the culture supernatants was measured by CBA. (C/C, n=10, T/T, n=8). one-way ANOVA with Sidak's post-test.

## Supp Fig. S2



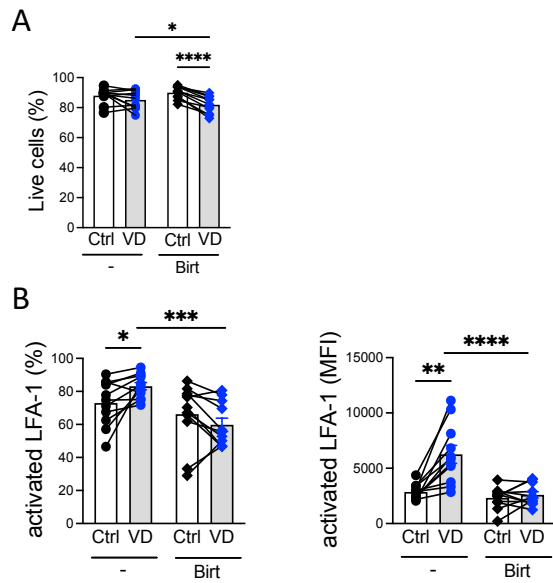
**Supp Fig. S2. Analysis of the recruitment of proteins at the immune synapse.** (A)  $CD4^+$  T cells were co-cultured with anti-CD3/CD46-pre-coated CTV-labelled P815 cells, used as a model APC, for 15 min. Cells were labeled as indicated and acquired by imaging flow cytometer. The strategy to select conjugates in focus with 1 CD4/1 P815 is indicated. (B) Masks on the T cells, on the P815, and at the IS required to quantify recruitment at the IS. (C) Recruitment is determined by calculating the ratio median pixel intensity interface / whole T cell. (D) Numbers of conjugates obtained between T cells and uncoated P815 (US) or CD3/CD46-coated P815.

### Supp Fig. S3



**Supp Fig. S3 Deletion of CD226 reduces activation of LFA-1.** Expression of activated LFA-1 and CD11a in CD3/CD46-costimulated CD4 T cells deleted in CD226 by CRISPR/Cas 9 (sgCD226-2) was determined by flow cytometry. N=4 donors, paired t-test.

## Supp Fig. S4



**Supp Fig. S4. Phenotype of CD4<sup>+</sup> T cells activated in the presence of an LFA-1 allosteric antagonist.** CD4<sup>+</sup> T cells from HD homozygous for the *CD226* rs763361 C/C allele were activated with anti-CD3/CD46 for 5 days with (VD) or without (Ctrl) 1,25OH, and with (Birt) or without (-) BIRT377, an antagonist of LFA-1 activation. **(A)** Percentage of live cells and **(B)** expression of activated LFA-1. N=11 each, one way ANOVA with Sidak's post-test.