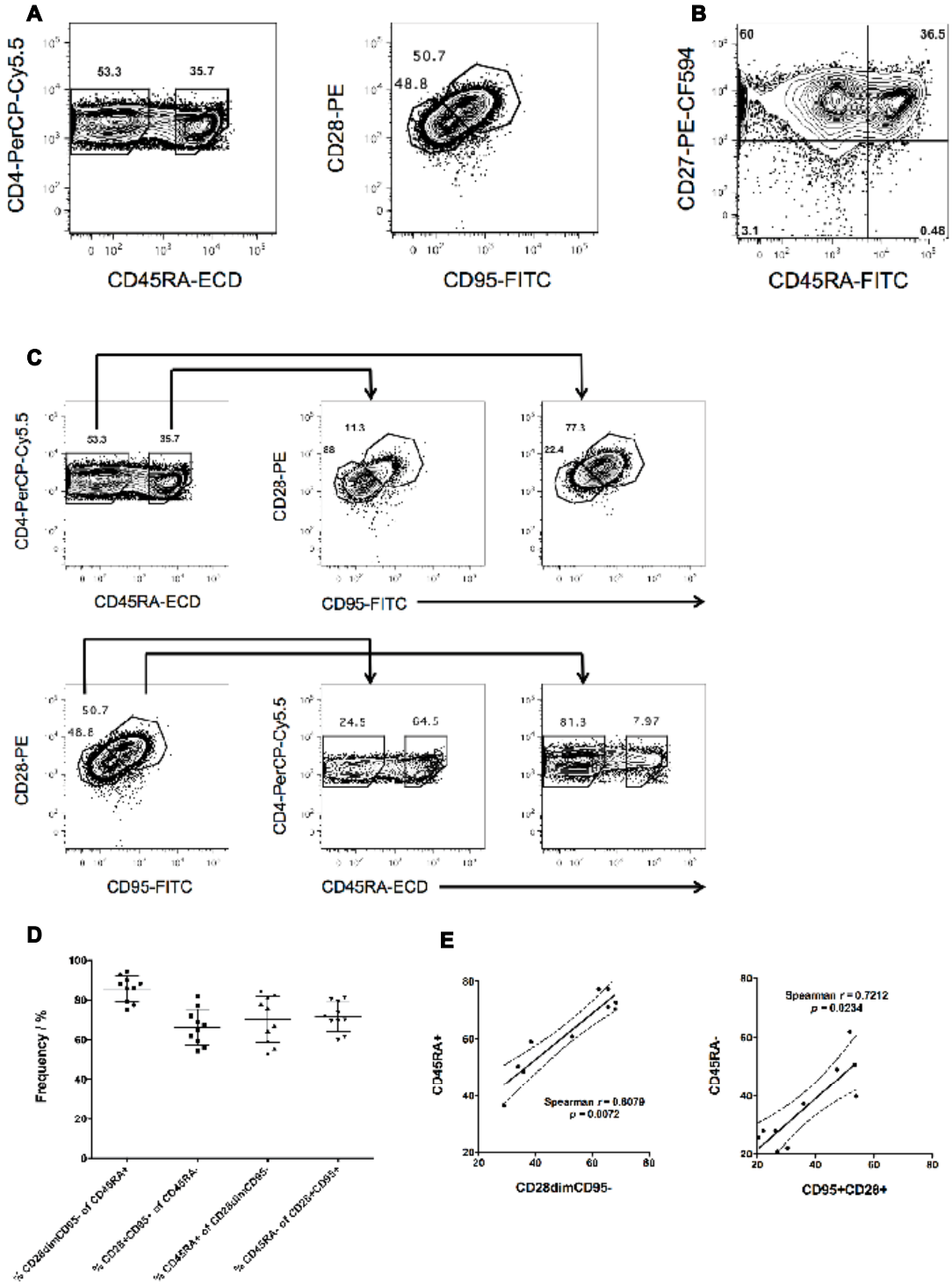
Fig S1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35.7
CD45RA-ECD
CD28-PE
50.7
48.8
CD95-FITC
B
CD27-PE-CF594
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36.5
3.1
0.48
CD45RA-FITC
C
CD4-PerCP-Cy5.5
53.3
35.7
CD45RA-ECD
CD28-PE
11.3
88
CD95-FITC
77.3
22.4
CD28-PE
50.7
48.8
CD95-FITC
CD4-PerCP-Cy5.5
24.5
64.5
CD45RA-ECD
81.3
7.97
D
Frequency / %
% CD28dimCD95- of CD45RA+
% CD28+CD95+ of CD45RA-
% CD45RA+ of CD28dimCD95-
% CD45RA- of CD28+CD95+
E
CD45RA+
Spearman r = 0.8079
p = 0.0072
CD28dimCD95-
CD45RA-
Spearman r = 0.7212
p = 0.0234
CD95+CD28+

**Figure S1.** Validation of using CD45RA as marker to differentiate naïve and memory CD4+ T cells from pigtail macaque tissues. **A.** Representative histograms of two gating strategies to discriminate macaque tissue naïve and memory CD4+ T cells. Naïve and memory cells can be defined as CD45RA+ and CD45RA- cells (left) or $CD28^{dim}$CD95- and CD28+CD95+ cells (right). It can be seen that the antibody CD45RA-ECD (clone 2H4) clearly separated CD4+ T cells into CD45RA+ and CD45RA- populations whereas the separation by CD95 (clone DX2) was relatively poor. **B.** Representative staining of macaque tissue CD4+ T cells with CD45RA and CD27. Within CD45RA+ cells, median frequency of CD27+ cells was 97.2% (n=8) and CD27- cells only account for less than 3% of CD45RA+ cells. **C.** Representative histograms of CD4+ T cell subsets' phenotypes. In the top row, CD4+ T cells were plotted against CD45RA, and CD45RA+ and CD45RA- cells were gated (top left) (unclear). CD28 and CD95 expression of CD45RA+ and CD45RA- CD4+ T cells was then examined. Most CD45RA+ cells were $CD28^{dim}$CD95- (top middle) and about three quarters of CD45RA- cells were CD28+CD95+ (top right). In the bottom row, expression of CD28 and CD95 on CD4+ T cells was examined and $CD28^{dim}$CD95- and CD28+CD95+ cells gated (bottom left). The CD45RA expression within $CD28^{dim}$CD95- and CD28+CD95+ CD4+ T cell populations was then examined. Most CD28+CD95+ cells were CD45RA+ (bottom right) and about 65% of $CD28^{dim}$CD95- cells were CD45RA- (bottom middle). The discordance appears to be mainly due to the dimness of CD95 staining so that cells expressing CD95 may appear CD95-. **D.** Summary of CD4+ T cell subset phenotypes based on the two gating strategies as described in B (n=8). **E.** Correlation of frequencies of naïve CD4+ T cells defined as CD45RA+ or $CD28^{dim}$CD95- (left: Spearman $r = 0.81$, $p = 0.007$)

and correlation of frequencies of memory CD4+ T cells defined as CD45RA- or CD28+CD95+ (right: Spearman $r = 0.72$, $p = 0.02$).

Fig S2

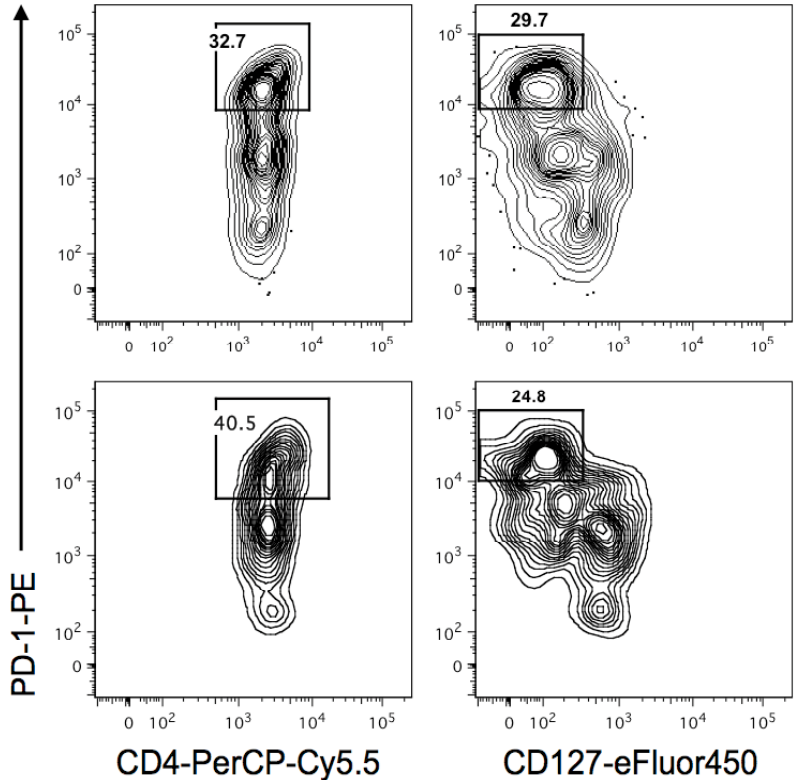


**Figure S2.** Identification of PD-1$^{high}$ cells with or without CD127. Memory CD4+ T cells were plotted on PD-1 vs CD4 histogram (left) or PD-1 vs CD127 histogram (right). In most cases, PD-1-PE (clone EH12.2H7) separated memory CD4+ T cells into 3 populations (top left) and most PD-1$^{high}$ cells lack expression of CD127 (top right). However, in some cases, the cut-off between PD-1$^{high}$ and PD-1$^{med}$ cells is unclear using this strategy alone (bottom left). The addition of CD127 allowed us to gate out PD-1$^{high}$ cells from the rest (bottom right).

Fig S3


Translation of SIVmac239 gp120
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PD-1medCD127low-132
1.0
CD45RA+-76
2.0
CD45RA+-66
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1.0
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CD127+-153
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CD45RA+-64
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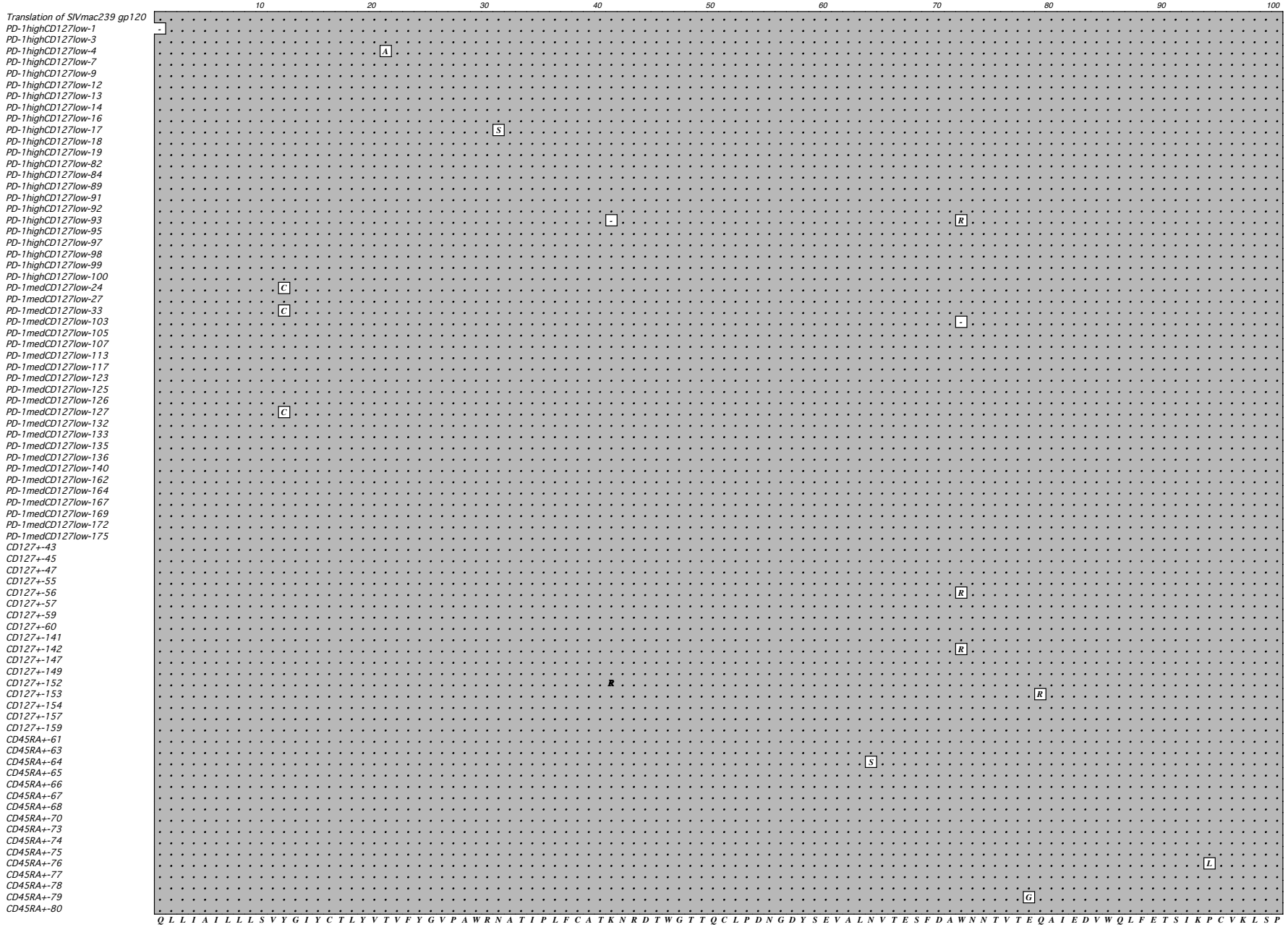
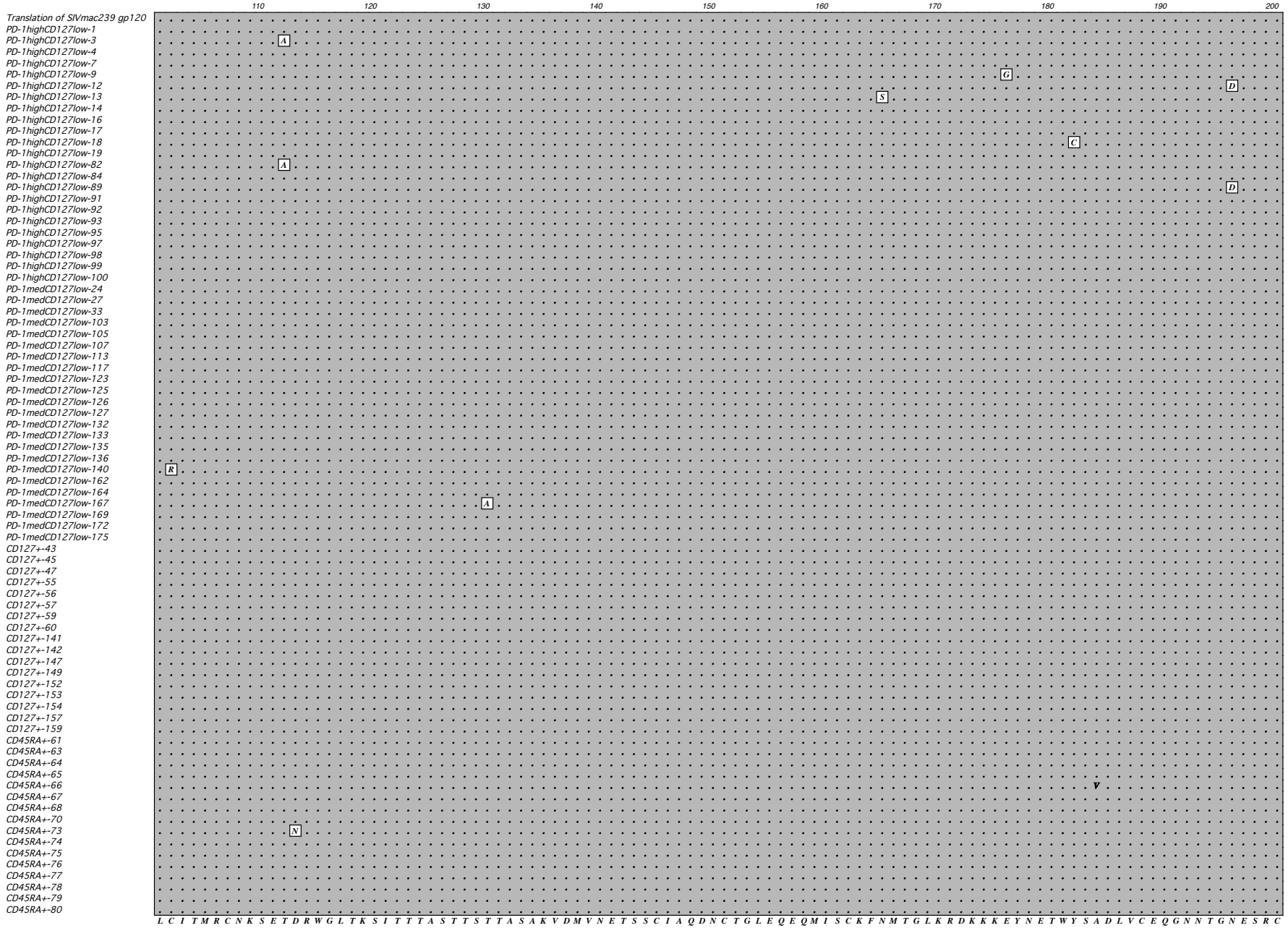
1.0
PD-1highCD127low-17
1.0
PD-1highCD127low-18
1.0

**Figure S3.** Neighbour-joining tree of gp120 amino acid sequences from each clone amplified from CD4+ T cell subsets (PD-1$^{high}$CD127$^{low}$, PD-1$^{med}$CD127$^{low}$, and CD127+ memory CD4+ T cells, and CD45RA+ naïve CD4+ T cells) of a macaque infected with SIVmac239 for 28 days. SIVmac239 envelope sequence, downloaded from GeneBank (accession: AAA47637) was assigned to be the root of the tree. Sample name shows the subset and ID of each clone. Branches are scaled in absolute number of differences, according to the scales at the bottom of the trees.

## Formatted Alignments

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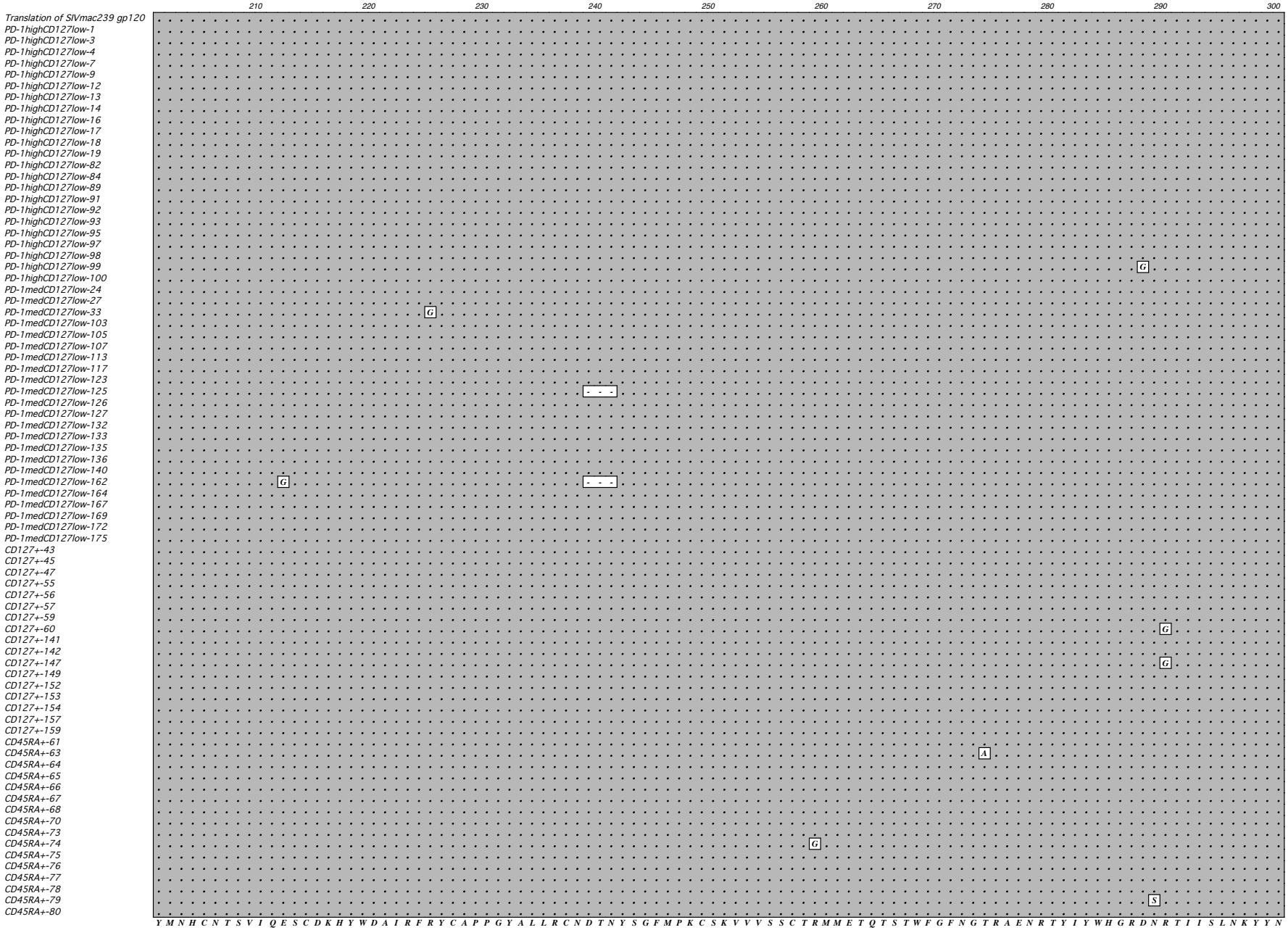
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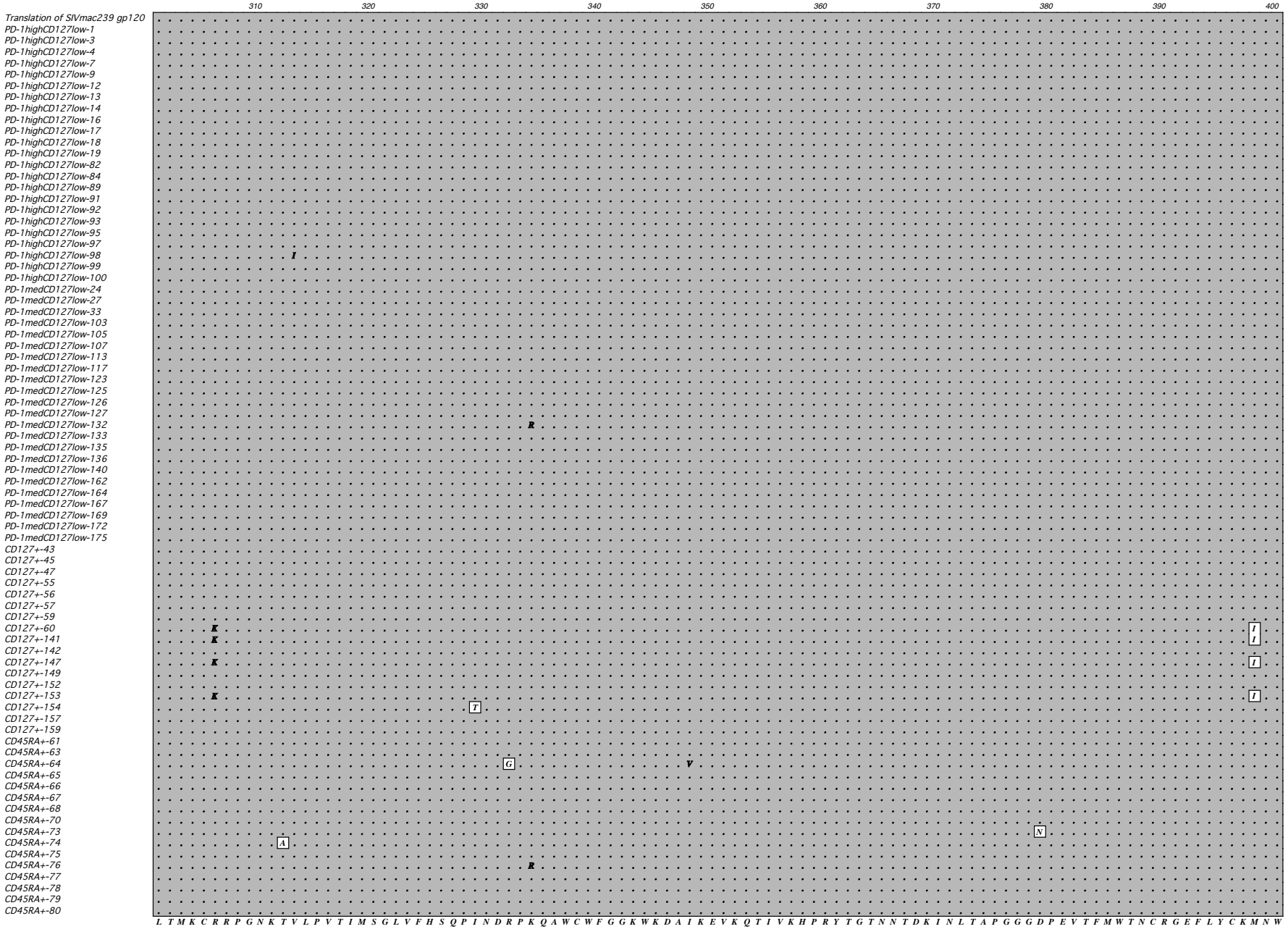
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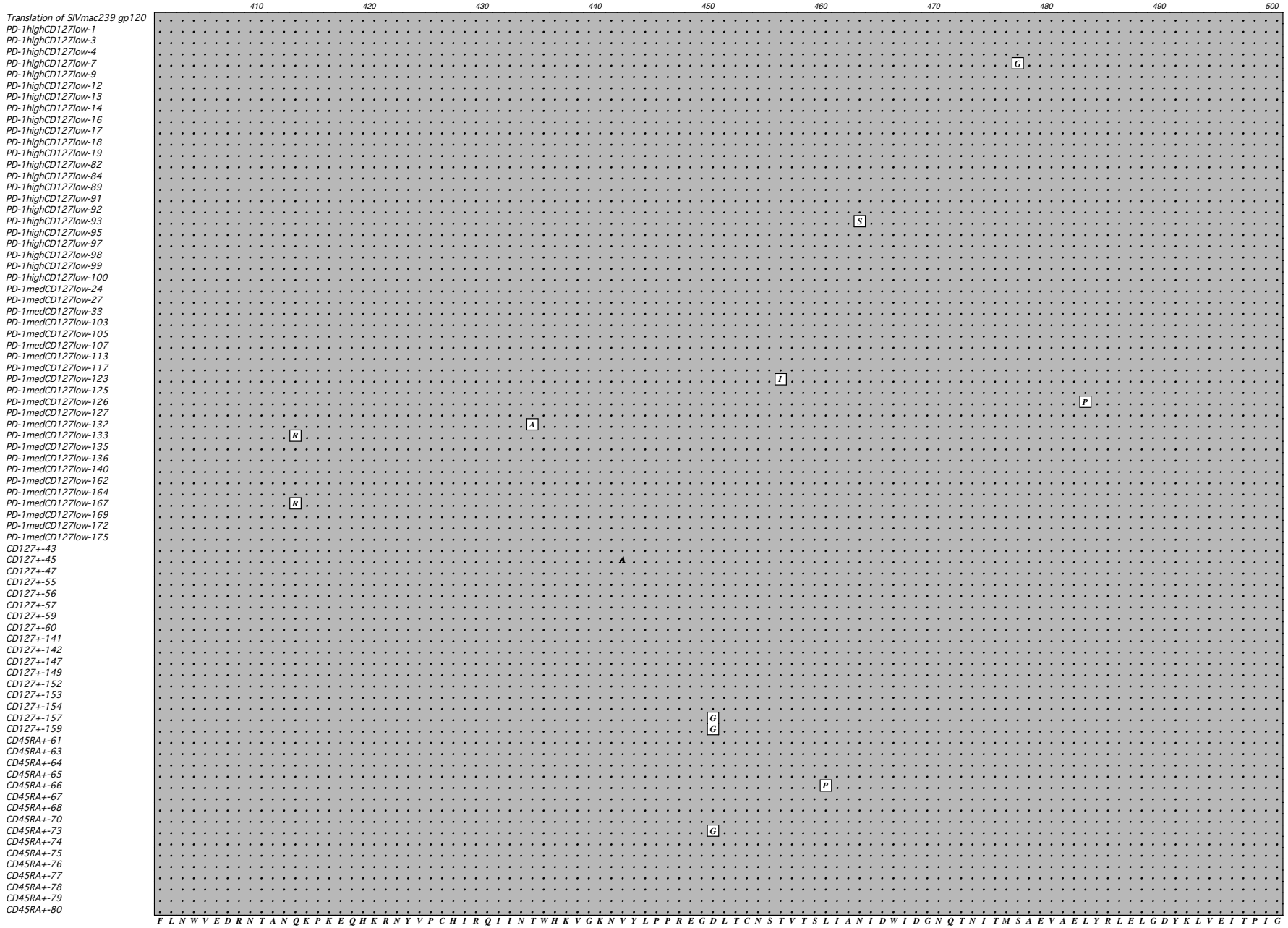
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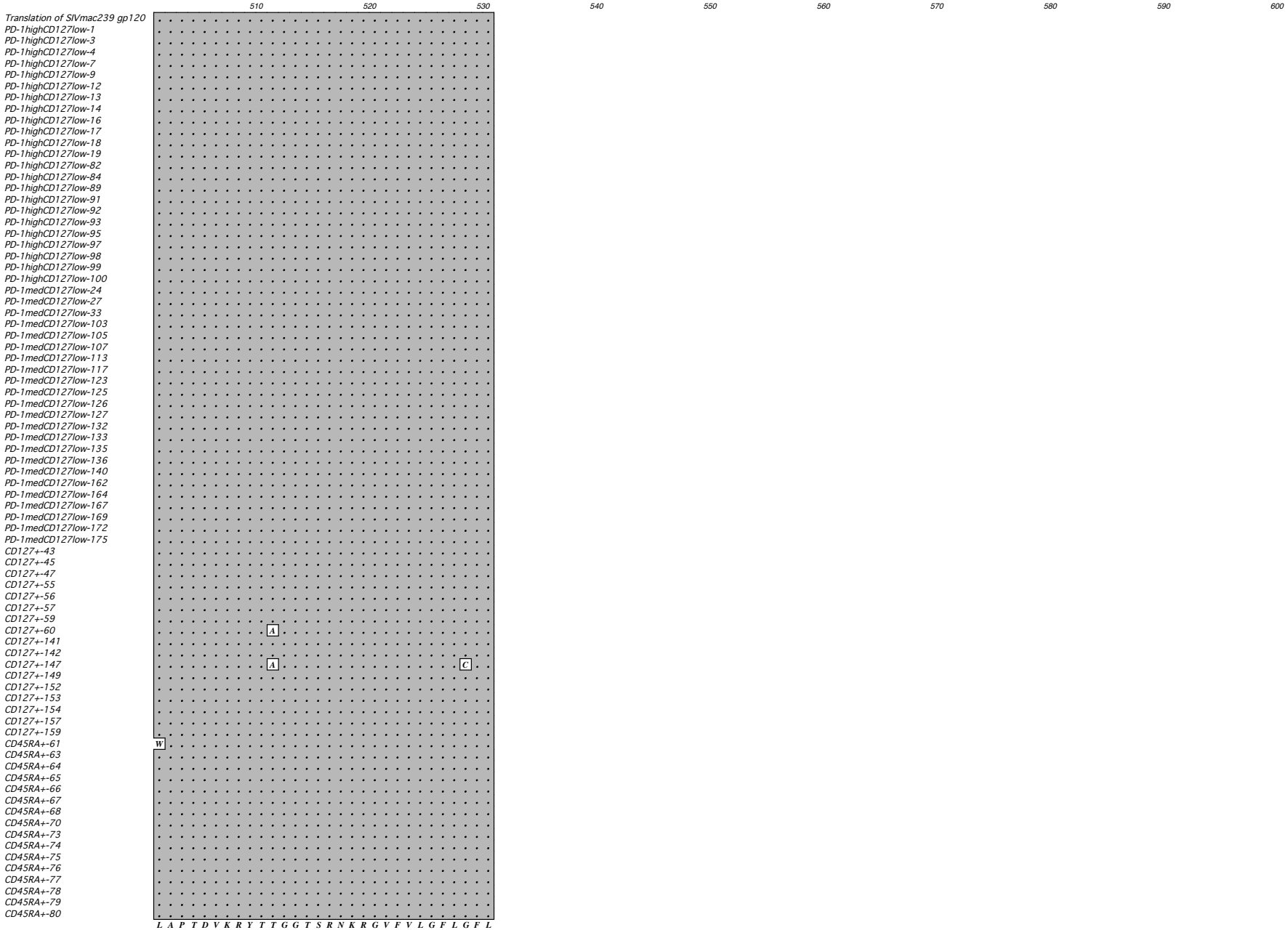
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