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Progressive CD4$^+$ central–memory T cell decline results in CD4$^+$ effector–memory insufficiency and overt disease in chronic SIV infection

Afam Okoye, Martin Meier-Schellersheim, Jason M. Brenchley, Shoko I. Hagen, Joshua M. Walker, Mukta Rohankhedkar, Richard Lum, John B. Edgar, Shannon L. Planer, Alfred Legasse, Andrew W. Sylwester, Michael Piatak, Jr., Jeffrey D. Lifson, Vernon C. Maino, Donald L. Sodora, Daniel C. Douek, Michael K. Axthelm, Zvi Grossman, and Louis J. Picker

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Please note that the x axis labeling in Fig. 6 (D and E) was inadvertently cropped. The html and pdf versions are correct. The corrected figure is shown below.

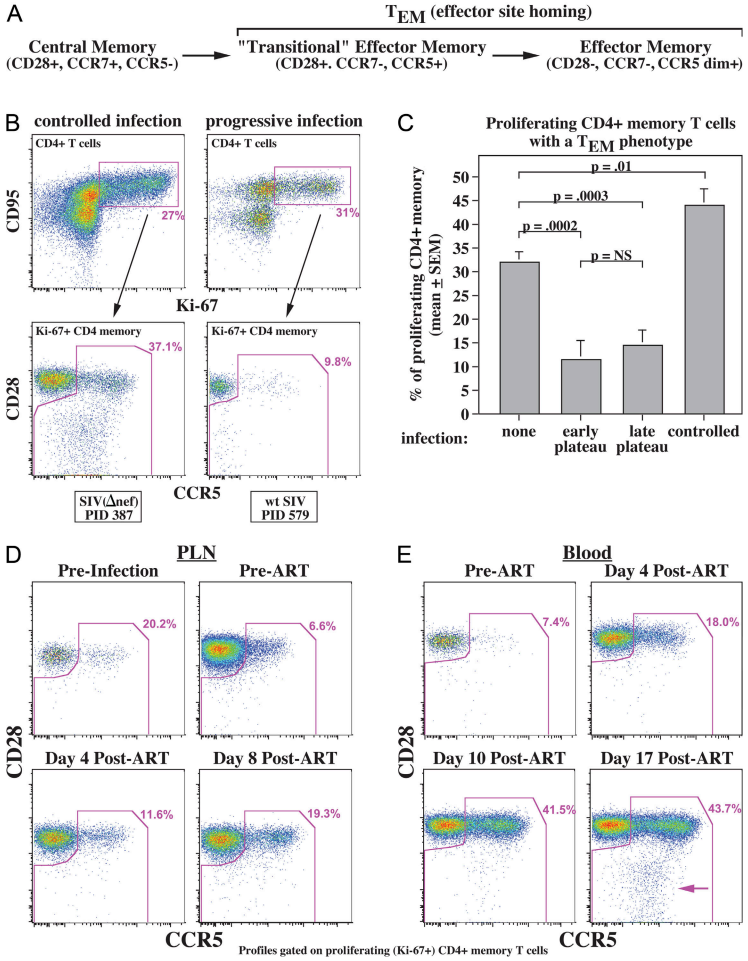

Figure 6. Effect of infection on CD4$^+$ T$_{EM}$ cell differentiation from proliferating T$_{CM}$ cell precursors. (A) Schema of memory T cell differentiation in RMs (18). (B) The top profiles show CD4$^+$ T cells from one RM with attenuated SIVmac239(Δnef) infection (PID 387; pvl = 5,200 copies/ml) and one with progressive SIVmac239 infection (PID 579; pvl = 3,800,000 copies/ml), indicating the gating of proliferating (Ki-67$^+$) CD4$^+$ memory T cells. The bottom profiles show the representation of T$_{CM}$ cells (CD28$^+$; CCR5$^-$) versus total T$_{EM}$ cells (including CD28$^+$, CCR5$^+$ transitional T$_{EM}$ cells, and CD28$^-$/CCR5^{dim+} mature T$_{EM}$ cells) within the proliferating CD4$^+$ memory compartment. (C) The figure shows cross-sectional analysis of the fractional representation of total T$_{EM}$ cells (as in A) in 10 SIV$^-$ RMs, 7 RMs with early plateau-phase SIVmac239 infection (PID 105; median pvl = 5,300,000 copies/ml), 8 RMs with late plateau-phase SIVmac239 infection (PID 533–878; median pvl = 660,000 copies/ml), and 12 RMs with controlled SIV infection: 9 infected with SIVmac239(Δnef) (PID 154–390; pvls < 400 copies/ml) and 3 spontaneous controllers of SIVmac239 (PID 105–147: pvls < 4,000 copies/ml). Differences were assessed by unpaired *t* test. (D) The profiles show the fractional representation of T$_{EM}$ cells among proliferating (Ki-67$^+$) CD4$^+$ memory T cells from PLNs from an RM 5 d before SIVmac239 infection, at PID 150 (immediately before ART; pvl = 4,400,000 copies/ml), and at 4 (pvl = 180,000) and 8 d (pvl = 87,000) after ART initiation. (E) The profiles show the fractional representation of T$_{EM}$ cells among proliferating (Ki-67$^+$) CD4$^+$ memory T cells from the blood of an SIVmac239-infected RM at PID 105 (immediately before ART; pvl = 3,000,000 copies/ml) and days 4 (pvl = 220,000 copies/ml), 10 (pvl = 170,000 copies/ml), and 17 (pvl = 24,000 copies/ml) after ART. The arrow indicates the development of a fully mature CD4$^+$ T$_{EM}$ cell population.