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The lncRNA Snhg1-Vps13D vesicle trafficking system promotes memory CD8 T cell establishment via regulating the dual effects of IL-7 signaling

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The efficient induction and long-term persistence of pathogen-specific memory CD8 T cells are pivotal to rapidly curb the reinfection. Recent studies indicated that long-noncoding RNAs expression is highly cell- and stage-specific during T cell development and differentiation, suggesting their potential roles in T cell programs. However, the key lncRNAs playing crucial roles in memory CD8 T cell establishment remain to be clarified. Through CD8 T cell subsets profiling of lncRNAs, this study found a key lncRNA-Snhg1 with the conserved naïvehi-effectorlo-memoryhi expression pattern in CD8 T cells of both mice and human, that can promote memory formation while impeding effector CD8 in acute viral infection. Further, Snhg1 was found physically interacting with the conserved vesicle trafficking protein Vps13D to promote IL-7Rα membrane location specifically. With the deep mechanism probing, the results show Snhg1-Vps13D regulated IL-7 signaling with its dual effects in memory CD8 generation, which not just because of the sustaining role of STAT5-BCL-2 axis for memory survival, but more through the STAT3-TCF1-Blimp1 axis for transcriptional launch program of memory differentiation. Moreover, we performed further study with finding the similar high-low-high expression pattern of human SNHG1/VPS13D/IL7R/TCF7 in CD8 T cell subsets from PBMC samples of the convalescent COVID-19 patients. The central role of Snhg1-Vps13D-IL-7R-TCF1 axis in memory CD8 establishment makes it a potencial target for improving the vaccination effects to control the ongoing pandemic.

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