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Title:	Differentiation of effector and memory CD8+ T cells during HSV1 infection
Authors:	Kumar, Dhaneshwar (/jspui/browse?type=author&value=Kumar%2C+Dhaneshwar)
Keywords:	Biology HSV1 infection Herpes Simplex Virus Infection
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Abstract:	<p>All human population worldwide is infected with herpesviruses and most individuals develop one or the other immunopathological conditions manifested in critical organs. Such reactions are generally treated using glucocorticoids but their effects on virus-specific CD8 + T cells remain less well explored. CD8 + T cells are crucial for viral control. We show a dichotomy in the effects of dexamethasone, a synthetic analogue of glucocorticoid, on virus-specific quiescent (naïve and memory) and effector CD8 + T cells. Accordingly, dexamethasone induced apoptosis in naïve as well as virus-specific memory CD8 + T cells but spared effector cells from killing as the latter population downregulated Nr3c1, a specific receptor for the glucocorticoids. Dexamethasone induced attrition of naïve and memory CD8 + T cells compromised anti-viral CD8 + T cells immunity against a subsequent infection but at the same time its transient exposure of effector cells augmented their function, inflammatory tissue homing potential as well as their transition into memory cells. The effects observed were generic as the differentiating CD8 + T cells during both α-HSV1 and γ-MHV68 herpesvirus infections downregulated their Nr3c1. Surprisingly, dexamethasone also activated CD8 + T cells in the absence of an overt TCR stimulation. Our study therefore calls into question the logic of corticosteroid therapy used for managing persistent inflammatory reactions. At the same time we also described a strategy to harness their untapped potential in promoting immunological memory. In the second part of the study, we identified and characterized HSV1 specific CD8 + T cells in experimentally infected zebrafish, a model system that offers a real time tracking of cellular dynamics in vivo. We generated class I MHC tetramer for probing the kinetics of virus-specific CD8 + T cells during HSV1 infection and demonstrated a rapid expansion of virus-specific CD8 + T cells both in the acute stage as well as upon their recall with a secondary homologous challenge. The expanded cells upregulated effector molecules and helped control the viral growth. Therefore, zebrafish could potentially serve as a model system to decipher the differentiation pathways of antigen-specific CD8 + T cells and their dynamics in live animals. Our results further suggest for an evolutionary conserved and functional adaptive immune cell homeostatic mechanisms activated during viral infection across vertebrates.</p>
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