# Abstract

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 (naive 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.