Cortisol and epinephrine control opposing circadian rhythms in T cell subsets

April 2009 · Blood 113(21):5134-43

DOI: 10.1182/blood-2008-11-190769

Source · PubMed

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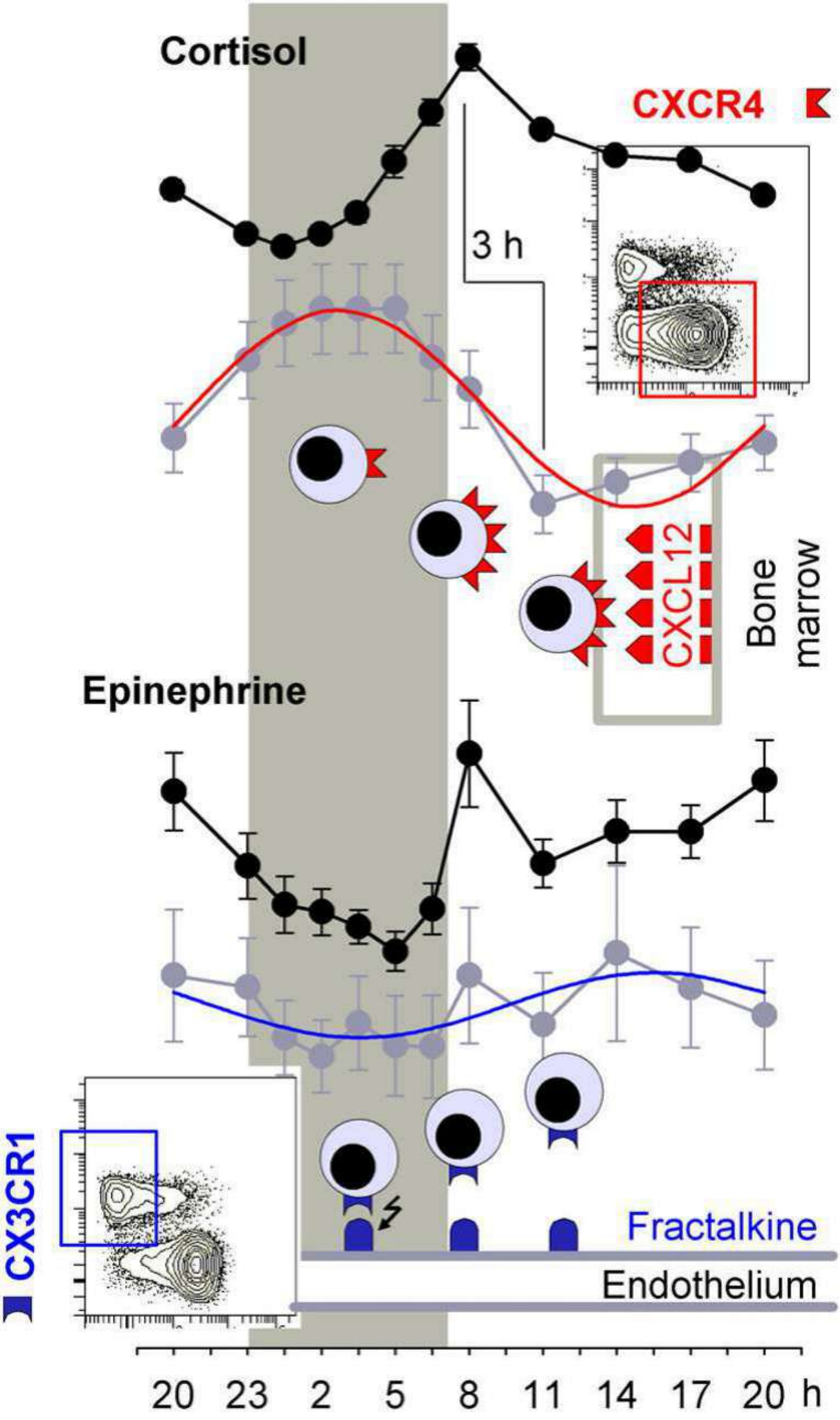
Cortisol
CXCR4
3 h
CXCL12
Bone marrow
Epinephrine
CX3CR1
Fractalkine
Endothelium
20 23 2 5 8 11 14 17 20 h

Pronounced circadian rhythms in numbers of circulating T cells reflect a systemic control of adaptive immunity whose mechanisms are obscure. Here, we show that circadian variations in T cell subpopulations in human blood are differentially regulated via release of cortisol and catecholamines. Within the CD4(+) and CD8(+) T cell subsets, naive cells show pronounced circadian rhythms with a daytime nadir, whereas (terminally differentiated) effector CD8(+) T cell counts peak during daytime. Naive T cells were negatively correlated with cortisol rhythms, decreased after low-dose cortisol infusion, and showed highest expression of CXCR4, which was up-regulated by cortisol. Effector CD8(+) T cells were positively correlated with epinephrine rhythms, increased after low-dose epinephrine infusion, and showed highest expression of beta-adrenergic and fractalkine receptors (CX3CR1). Daytime increases in cortisol via CXCR4 probably act to redistribute naive T cells to bone marrow, whereas daytime increases in catecholamines via beta-adrenoceptors and, possibly, a suppression of fractalkine signaling promote mobilization of effector CD8(+) T cells from the marginal pool. Thus, activation of the major stress hormones during daytime favor immediate effector defense but diminish capabilities for initiating adaptive immune responses.

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