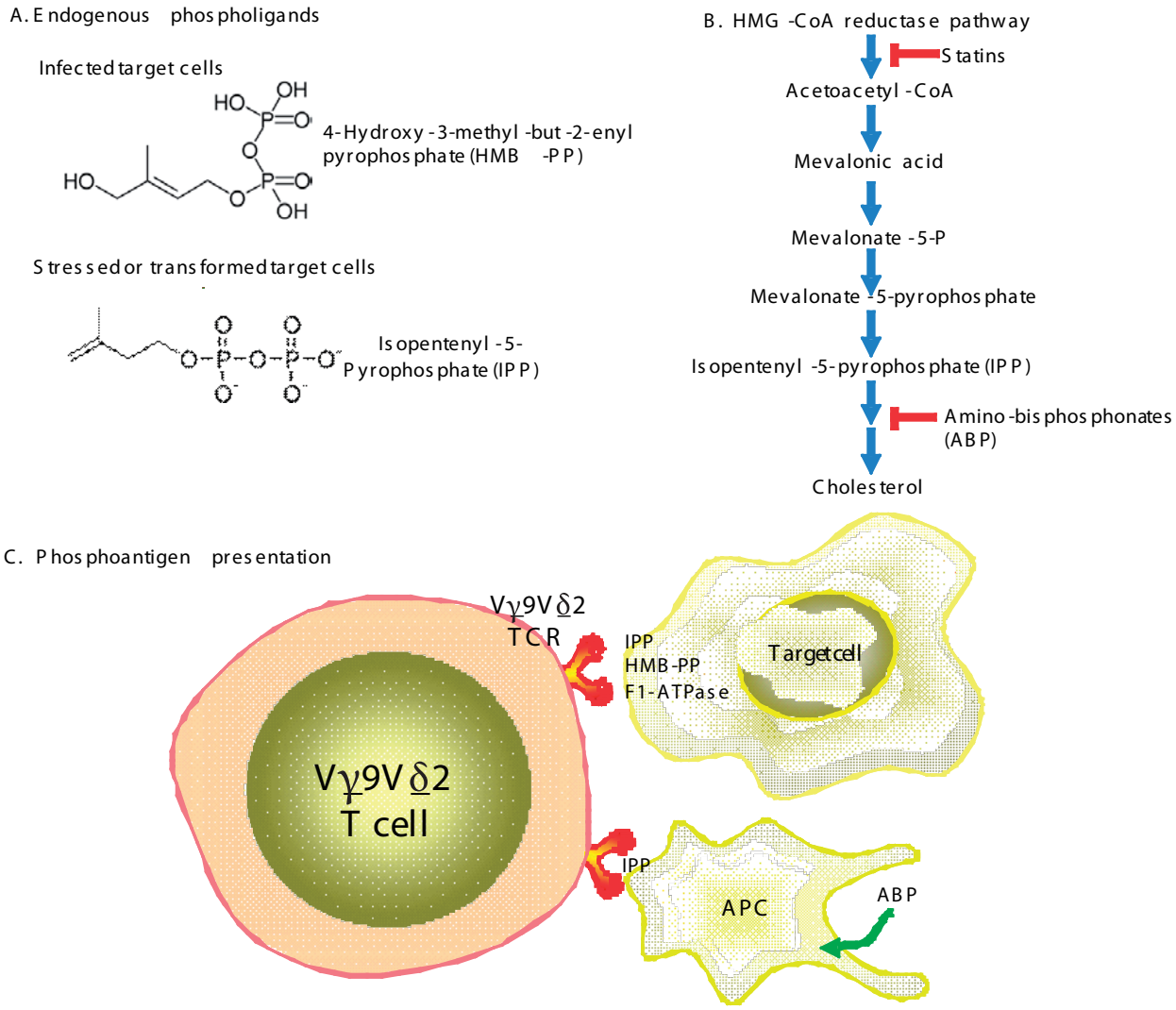
In format provided by June *et al.* (OCTOBER 2009)



Supplementary information S1 (figure)
Metabolic pathways that guide activation of human Vγ9Vδ2 T cells. A | Vγ9Vδ2 T cell receptors (TCRs) recognize the phosphoantigen HMB-PP (4-hydroxy-3-methyl-but-2-enyl pyrophosphate), a natural intermediate of the non-mevalonate pathway of isopentenyl pyrophosphate (IPP) biosynthesis that is found in some bacterial and protozoan pathogens. IPP is an intermediate product in the classical mevalonate pathway and is structurally closely related to HMB-PP. IPP is present in all human cells, and may be a physiological danger signal of stressed or transformed cells. The potency of HMB-PP is 10,000 fold greater than IPP. **B** | The HMG-CoA reductase pathway is upstream of cholesterol biosynthesis. IPP is formed from acetyl-CoA via mevalonic acid. The abundance of IPP is decreased by the addition of statins and increased by the addition of amino biosphosphonates. **C** | The molecular details of phosphoantigen presentation to Vγ9Vδ2 T cells are beginning to emerge. MHC independent presentation by infected target cells of the high affinity HMB-PP ligand and the low affinity IPP ligand to the Vγ9Vδ2 TCR occurs via an unknown mechanism. The membrane bound F1-ATP synthase can also trigger Vγ9Vδ2 TCR activation[1]. In tumour cells and antigen-presenting cells (APCs) the amount of agonistic IPP can be augmented by briefly culturing with amino biosphosphonates.

1. Scotet, E. *et al.* Tumor recognition following Vγ9Vδ2 T cell receptor interactions with a surface F1-ATPase-related structure and apolipoprotein A-I. *Immunity* **22**, 71-80 (2005).