



Figure S1: Cartoon model showing the conceptual advance provided by this work. The *Toxoplasma* CD4⁺ T cell eliciting 15-mer peptide, AS15, administered with the IDRI adjuvant GLASE, an Avanti polar lipid Toll Receptor 4 ligand GLA emulsified in the IDRI adjuvant SE, can be both harmful (lethal causing intestinal, hepatic and spleen pathology associated with a storm of IL6) or helpful resulting in robust protection against subsequent challenge with Type II strain *T. gondii* depending on the accompanying peptides administered with it. The addition of the universal CD4⁺ T cell epitope, PADRE, as well as epitopes eliciting CD8⁺ T cells, abrogates the harmful phenotype of AS15. This suggests a cross-reactive pool of precursor cells that respond to PADRE and to AS15, which reduces the pathogenic response. In addition, this peptide elicits CD4⁺ T cells after immunization against challenge with *Toxoplasma* parasites at early but not at later times.