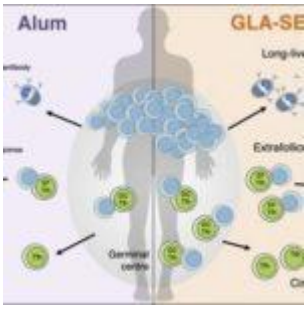
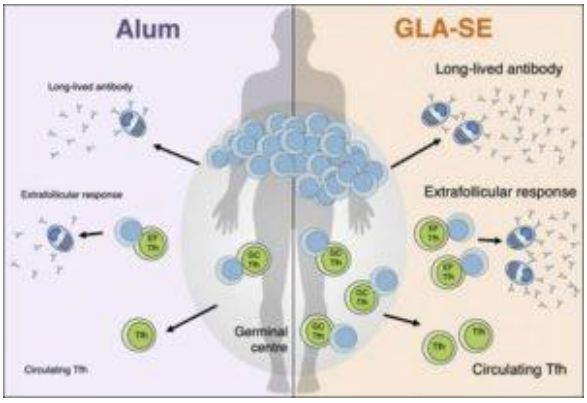
GLA-SE promotes superior Tfh expansion than Alum





Hill et al., Graphical Abstract. Source Hill et al., JEM)

After clean water, vaccination has contributed the most to reducing the prevalence of infectious diseases in the 21st century. The most successful vaccines induce durable long-term antibody (Ab) mediated immunity. Induction of such long-lived Abs requires antigen-experienced B cells to interact with follicular helper T (Tfh) cells in the lymphoid tissue facilitating B cell expansion, somatic hypermutation (SHM) and antibody class switching.

Since Tfh cells play a critical role in the generation of long-live Ab responses, targeting them using adjuvants is a potential way of improving vaccine strategies. Tfh cells are relatively understudied in human vaccine studies because sampling them can be challenging. Studying circulating Tfh

(cTfh) cells has been suggested as a suitable alternative because they can be isolated from blood, and phenotypically and functionally resemble Tfh cells. To determine if the type of adjuvant can alter vaccine-induced Ab-immunity in humans, Hill *et al.,* compared malaria-specific Ab immunity in phase 1b vaccine trials. Where Tanzanian male participants were vaccinated with three monthly doses of P27A malaria antigen adjuvanted with either GLA-SE (n=8) or Alhydrogel (Alum, n=8).

To ensure that cTfh cells are a suitable surrogate for studying Tfh cells, Hill *et al.,* showed that cTfh cells in the blood co-express ICOS+CD38+CXCR5+PD-1+ [phenotypic definition of Tfh cells] and positively correlate with the magnitude of vaccine-induced Ab responses. cTfh cells were transcriptionally similar to Tfh cells isolated with the lymphoid organs, and also shared TCRβ clonality. Thus making studying cTfh cells a suitable and more readily available surrogate for understanding vaccine-induced Tfh cells in humans. Hill *et al.,* showed that though both Alum and GLA-SE adjuvanted malaria vaccines induced detectable anti-P27A Ab responses, the GLA-SE adjuvant induced significantly higher proportions of Ab immunity than Alum. Additionally, vaccination with GLA-SE resulted in clonal expansion of TCRβ clones in 5 out of 8 vaccinated individuals. GLA-SE mediated enhancement of Ab immunity was not restricted to the germinal center, but also resulted in increased levels of extrafollicular plasmablast responses (short-lived Ab producing cells).

In summary, Hill *et al.,* demonstrate the type of adjuvant should be a key consideration in vaccine design. Using their study they were able to show that a malaria vaccine "adjuvanted" with GLA-SE induced superior Ab immunity than one "adjuvanted" with Alum. This superior Ab-mediated immunity was attributed to increased levels of cTfh and Tfh cells, and could be harnessed for other vaccine strategies that induced poor Ab immunity.

Journal Article: Hill et al., 2019. The adjuvant GLA-SE promotes human Tfh cell expansion and emergence of public TCRβ clonotypes. Jounral of Experimental Medicine