

## 4<sup>th</sup> International Conference and Exhibition on **Immunology**

September 28-30, 2015 Crowne Plaza Houston River Oaks, Houston, TX, USA

### Pro-inflammatory CCL3, 4 cytokines and B – follicular T cell interactions in the regulation of T-dependent humoral immune response

Irina Grigorova

University of Michigan Medical School, USA

B cell receptor crosslinking has been shown to induce production of proinflammatory chemokines CCL3/CCL4 in the native and germinal center (GC) B cells. Consistent with previous data we found that CCL3/4 expression in GC centrocytes is upregulated compared to native B cells and centroblasts. However, the role of CCL3/4 for GC B cell interactions with follicular T cells and the regulation of humoral immunity are poorly understood. We found that B cell intrinsic production of CCL3/4 is required for both their selection and control in GCs. In addition, intravital imaging analysis revealed that B-cell intrinsic production of CCL3/4 promotes GC B cell interactions with follicular regulatory and helper T cells. Further studies are under the way to address whether CCL3/4 forms local chemotactic gradients within GCs to promote recruitment of follicular T cells to a subset of GC B cells.

[igrigor@umich.edu](mailto:igrigor@umich.edu)

### Multiple clinical episodes of *Plasmodium falciparum* malaria in a low transmission intensity setting: Exposure versus immunity

Josea Rono<sup>1,2</sup>, Anna Färnert<sup>2</sup>, Linda Murungi<sup>1</sup>, John Ojal<sup>1</sup>, Gathoni Kamuyu<sup>1</sup>, Fatuma Guleid<sup>1</sup>, George Nyangweso<sup>1</sup>, Juliana Wambua<sup>1</sup>, Barnes Kitsao<sup>1</sup>, Ally Olotu<sup>1</sup>, Kevin Marsh<sup>1,3</sup> and Faith H A Osier<sup>1</sup>

<sup>1</sup>Center for Geographical Medicine Research-Coast, Kenya

<sup>2</sup>E&K Health Consulting, Kenya

**Background:** Epidemiological studies indicate that some children experience many more episodes of clinical malaria than their age mates in a given location. Whether this is as a result of the micro-heterogeneity of malaria transmission with some children effectively getting more exposure to infectious mosquitoes than others, or reflects a failure in the acquisition of immunity needs to be elucidated. Here, we investigated the determinants of increased susceptibility to clinical malaria by comparing the intensity of exposure to *Plasmodium falciparum* and the acquisition of immunity in children at the extreme ends of the over-dispersed distribution of the incidence of clinical malaria.

**Methods:** The study was nested within a larger cohort in an area where the intensity of malaria transmission was low. We identified children who over a five-year period experienced 5 to 16 clinical malaria episodes (children at the tail-end of the over-dispersed distribution, n=35), remained malaria-free (n=12) or had a single episode (n=26). We quantified antibodies against seven *Plasmodium falciparum* merozoite antigens in plasma obtained at six cross-sectional surveys spanning these five years. We analyzed the antibody responses to identify temporal dynamics that associate with disease susceptibility.

**Results:** Children experiencing multiple episodes of malaria were more likely to be parasite positive by microscopy at cross-sectional surveys (X2 test for trend 14.72 P=0.001) and had a significantly higher malaria exposure index, than those in the malaria-free or single episode groups (Kruskal-Wallis test P=0.009). In contrast, the five-year temporal dynamics of anti-merozoite antibodies were similar in the three groups. Importantly in all groups, antibody levels were below the threshold concentrations previously observed to be correlated with protective immunity.

**Conclusions:** We conclude that in the context of a low malaria transmission setting, susceptibility to clinical malaria is not accounted for by anti-merozoite antibodies but appears to be a consequence of increased parasite exposure. We hypothesize that intensive exposure is a prerequisite for protective antibody concentrations, while little to modest exposure may manifest as multiple clinical infections with low levels of antibodies. These findings have implications for interventions that effectively lower malaria transmission intensity.

[josea.rono@gmail.com](mailto:josea.rono@gmail.com)