Exploring the fate of microparticles in cerebral malaria using 3D reconstruction

Amy Cohen, Sharissa Latham, Valery Combes, and Georges E.R. Grau

Vascular Immunology Unit, University of Sydney, NSW 2006

Microparticles (MP) are submicron plasma membrane-derived vesicles involved in coagulation, inflammation and cell-cell communication. MP numbers are increased in cerebral malaria (CM) patients and in the corresponding murine model of the disease. In the latter, we showed that genetically or pharmacologically blocking MP release confers protection against CM, suggesting a role of MP in neuropathogenesis. Here, we evaluated the in vivo production, fate, and localisation of MP during Plasmodium berghei-ANKA (PbA) infection of CM-susceptible (CM-S) and CM-resistant (CM-R) mice.

Upon infection, CM-S but not CM-R mice had raised plasma levels of MP. When adoptively transferred, fluorescent MP from CM-S mice into uninfected or infected CM-R mice were quickly cleared from the circulation. Wide-field fluorescence imaging showed arrested MP lining the endothelium of brain vessels of infected mice. Following this, multi-photon microscopy on 100 µm sections was used to create 3D reconstructions of the vasculature. This greatly improved our examination of the localisation of MP, as well as defining the sequestration of parasitised and non-parasitised red blood cells within the vessels, the intravascular accumulation of platelets and monocytes, the increased perivascular/parenchymal cellularity, haemorrhages and signs of oedema, typical of CM pathology.

These initial experiments highlight the importance of these techniques in allowing us to scrutinize not only at sites of interest within pathological analysis, but also the downstream effects of this pathology in order to gain a greater insight into the mechanisms of CM pathogenesis, as well as the localisation of MP in vivo during pathological processes.

References: