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Abstract (oral session)

Effect of malaria pigment (haemozoin) on infection and immunity

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Several studies on the role of hemozoin (Hz), which is released during plasmodium blood stage, show that it can have an immunosuppressive effect (disruption of macrophage/dendritic cell function), although findings are still controversial. This project aims to study the possible effects of Hz on infection and immunization. Objectives: First we studied the kinetics of Hz in a rodent model. Then the effect of Hz on the immune response to vaccination with irradiated malaria sporozoites was investigated. Methods: C57BL/6 mice were infected with Plasmodium berghei NK65 and treated with chloroquine (CQ). Mice were sacrificed and organs (liver, spleen, bone marrow and blood) investigated for the presence of Hz. To look at the interference of Hz in vaccination, C57BL/6 mice were infected with P. berghei NK65 followed by treatment with CQ (mice cleared parasite but Hz still remains in the organs). Mice were then immunized with whole irradiated sporozoites and after 10 days challenged with live sporozoites. Liver infection load was determined 42 hours after challenge by real-time PCR. In parallel mice were injected with Hz and then immunized followed by challenge. Native and synthetic Hz was produced and characterized by several methods. Results: Our results showed that Hz was detectable in the host for up to 200 days with the spleen as the major organ for Hz deposition. Immunized mice which had a previous malaria infection seemed to have a reduced protection relative to naïve immunized mice. Also, mice injected with Hz at time of vaccination had undetectable levels of antibodies against sporozoites. Hz characterization by SEM showed that Hz produced by us is structurally equivalent to others, with crystals in the size range of 0.7-1.6 µm. Conclusions: In highly endemic areas continuous infections with malaria can potentially lead to a certain level of Hz accumulation in host organs. Thus if Hz has a role in immunosuppression it can potentially interfere with the response to other infections or to vaccination. Our results seem to indicate that this maybe the case, because Hz appeared to cause a degree of immunosuppression capable of reducing the protective efficacy of a malaria vaccine, using whole irradiated parasites. This was shown by a higher liver infection on mice with a previous blood stage and undetectable antibody production against sporozoites when immunization was given together with hemozoin.