memory T cells of only immunized mice. Sterile protection was abrogated when CD8+ T cells were depleted whereas CD4+ T cells played a minor role.

Conclusions: Based on these data we suggest that the increase in protective immunity observed after immunization and subsequent challenge infection is the sum of different antiparasitic mechanisms including CD8+ and CD4+ T cells as well as neutralizing antibodies, with CD8+ effector-memory T cells playing the major role. Our results indicate that a vaccine which induces a short-lived liver-stage specific immunity that prevents disease within a certain time span would allow the induction of naturally acquired immunity upon repeated sporozoite infections.

P1111
Pathogenesis and therapy of malaria-associated acute respiratory distress syndrome
Rega Institute, Katholieke Universiteit Leuven, Leuven, Belgium

Purpose/Objective: Malaria-associated acute respiratory distress syndrome (MA-ARDS) is a lethal complication of malaria. No efficient treatment is available for this complication and its pathogenesis remains poorly understood. We studied the disease mechanisms and evaluated candidate treatments in a new mouse model.

Materials and methods: We established a novel mouse model of MA-ARDS by infection with Plasmodium berghei NK65 (PbNK65). Histology, FACS analysis, RT-PCR, bronchoalveolar lavages, cell depletions and anti-inflammatory treatment with dexamethasone were performed. A new method for the extraction and quantification of hemozoin (malaria pigment) in tissues was optimized.

Results: PbNK65 infection resulted in leukocyte accumulation, extensive edema and hemorrhage in the lungs. The pulmonary expression of several cytokines and chemokines was increased to a higher level than in mice infected with P. chabaudi AS, a parasite strain which does not cause MA-ARDS. CD8+ T lymphocytes were shown to be pathogenic and high doses of dexamethasone (DEX) blocked MA-ARDS through inhibition of lymphocyte proliferation and expression of chemotacticants for monocytes/macrophages, even when given after appearance of the pathology. On tissue sections, we noticed the presence of hemozoin or malaria pigment in the lungs. In view of the important inflammatory potential of this hemoglobin degradation product, we optimized a novel method to quantify hemozoin in tissues and measured the Hz content in different organs of mice infected with parasites of different pathogenicity. Significantly higher amounts of hemozoin were detected in the lungs and may contribute to the pathogenesis.

Conclusions: Based on these data we suggest that the increase in protective immunity observed after immunization and subsequent challenge infection is the sum of different antiparasitic mechanisms including CD8+ and CD4+ T cells as well as neutralizing antibodies, with CD8+ effector-memory T cells playing the major role. Our results indicate that a vaccine which induces a short-lived liver-stage specific immunity that prevents disease within a certain time span would allow the induction of naturally acquired immunity upon repeated sporozoite infections.

P1112
Abstract withdrawn.

P1113
The immuno-stimulatory and protective effect of the novel nanoparticle-coated Plasmodium yoelii merozoite surface protein (PyMSP-1)
M. S. Cherif,* M. N. Shuaibu,† T. Kurotschi,‡ Y. Kodama,§ H. Sasaki,∥ K. Yui,∥ G. K. Helegbe,† M. Kikuchi,† T. Yanagi∥ & K. Hirayama§
*Immunogenetics, Institut National de Sante´ Publique, Universite´ de Conakry (Guinea) & Institute of Tropical Medicine, Nagasaki, Japan,
†Immune genetics, Institute of Tropical Medicine, Nagasaki, Japan,
‡Hospital Pharmacy Department, Nagasaki University, Nagasaki, Japan,
§Division of Immunology, Department of Molecular Microbiology and Immunology, Nagasaki University, Nagasaki, Japan,
∥Institute of Tropical Medicine, Animal Research Center for Tropical Medicine, Nagasaki, Japan

Purpose/Objective: In malaria DNA vaccine development, for induction of an efficient and protective immunity against parasite, there exists a critical need for additional delivery vehicles. We analyzed the immuno-stimulatory effect of PEI/γ-PGA nanoparticle (NP)-coated PyMSP-1 plasmid and investigated its in vivo stimulatory effect on dendritic cells.

Materials and methods: Groups of C57BL/6 mice were immunized either with 100 μg/mouse of nanoparticle-coated plasmid (pVR1020-MSP-1/PEI/γ-PGA), naked (pVR1020-MSP-1) or coated control group (pVR1020/PEI/γ-PGA) using different routes of administration. Mice were prime-immunized at day 0 and subsequently, two boosters given with 3 weeks intervals. Two weeks after the last boost, specific IgG and their subtype’s titres measured by ELISA. Cytokine (IL-12 and INF-γ) levels were measured in the supernatants of antigen stimulated spleen cells and sera from immunized mice using procarta-immunnoassays kit. Flow cytometric analysis of various activated DC markers was also carried out.

Results: Protection against P. yoelii lethal challenge, specific IgG and its subtypes and INF-γ producing cell number were observed to be significantly higher in the coated-MSP-1 group than the naked group. Also, there were a significantly increased proportion of activated DCs and their elevated CD40 expression in the NP-coated immunized group as compared to naked plasmid. In the coated group, the co-stimulatory molecule CD80 was significantly increased when immunized subcutaneously, while CD86 molecule was increased when immunized intraperitoneally. In vivo and ex-vivo production of IL-12 were observed in the sera and the spleen cells stimulated with recombinant MSP-1.

Conclusions: These data indicates that nanoparticle-coated PyMSP-1 DNA vaccine protected mice and induced activated DCs either with CD80 or CD86, and the activated DCs produced IL-12 when stimulated by iMSP-1.