

THE DIAGNOSTIC POTENTIAL OF GLYCAN SPECIFIC ANTIBODIES IN SCHISTOSOMIASIS ASSESSED BY GLYCAN MICROARRAYS

Anna O. Kildemoes¹, Angela van Diepen¹, Tom Veldhuizen¹, Linh Nguyen¹, Mio Tanaka², Govert J. van Dam¹, Meta Roestenberg¹, Shinjiro Hamano², Cornelis H. Hokke¹

¹Leiden University Medical Center, Leiden, Netherlands, ²Institute of Tropical Medicine (NEKKEN), Nagasaki, Japan

During *Schistosoma* infections, antibodies specific for numerous antigens are induced by parasite larvae, adult worms and eggs. A large proportion of these antibodies are directed against antigenic glycans, which are part of the parasite's glycoprotein and glycolipid repertoire. It remains poorly understood whether these anti-glycan antibodies play a role in immunity to schistosomiasis or contribute to parasite immune evasion. Irrespective of the function of antibodies to defined schistosome glycans in infection, they may constitute a valuable so far untapped potential in a diagnostic context. As animal experimental work has shown that these anti-glycan antibody responses are highly dynamic, we aim to identify specific glycan targets of the antibody response in schistosome infection. After glycomics analyses of *Schistosoma mansoni* life stages and other helminths, we have isolated and identified hundreds of glycans of which several are unique to blood flukes. These native *S. mansoni* glycans combined with synthetic glycans relevant to schistosomes and other helminths were used to construct a glycan microarray. As such the antigenic repertoire on the microarray represent targets uniquely present in schistosomes as well as targets cross-reactive with other organisms: helminths, other invertebrates, food stuff of plant origin or the mammalian host. We have used this microarray to screen sera from a controlled human *S. mansoni* infection model and from schistosomiasis cohorts from both low and high transmission endemic areas, pre- and post-treatment, in order to identify targets with diagnostic potential. We focus on elucidating anti-glycan antibody responses, which are not only specific to schistosomes but also provide grounds for distinction between current infection and prior exposure/infection. Additionally, we aim to identify differences between responses to *S. mansoni* and *S. haematobium* infection. Development of an antibody based diagnostic tool with such properties would be a useful addition to the diagnostic toolbox available for monitoring treatment efficacy and in schistosomiasis control/elimination programs.

PERSISTENCE OF AFEBRILE SUBMICROSCOPIC PLASMODIUM SPP. INFECTIONS IN AN ENDEMIC AREA FOR MALARIA IN COLOMBIA

Jehidys E. Montiel Ramos¹, Luisa F. Carbal Reyes¹, Lina M. Zuluaga Idarraga¹, Ana M. Vasquez Cardona¹, Daniel C. Aguirre Acevedo¹, Berlin Londoño Rentería², Alberto Tobón Castaño¹

¹Universidad de Antioquia, Medellín, Colombia, ²Kansas State University, Manhattan, KS, United States

In malaria endemic regions, many of *Plasmodium* infections are below the level of detection by microscopy (submicroscopic) which is the standard test for malaria diagnosis. Submicroscopic infections (SI) persist undetectable and could contribute to malaria transmission. Understanding of dynamic and duration of SI is indispensable to develop control strategies. Afebrile and SI detected in an endemic Colombian population were longitudinally followed for 60 days. The clearance time of SI and associated factors were estimated. Inhabitants of 4 endemic villages in Tumaco (Pacific Coast) were enrolled between August/2017-March/2018. SI were defined as those detected by LAMP (Loop-mediated isothermal amplification) but not by microscopy with an axillary temperature lower than 37,5°C. An ELISA test was performed to evaluate Antiplasmodial IgG Antibody levels at zero day. SI people were followed up for two months by LAMP and microscopy in at least 6 measurements to estimate the parasite positivity in time. A survival analysis was performed to calculate the survival function and a log rank test to compare the survival distributions

regarding malaria history. A cox regression model was done to identify risk factor associated to the persistence. SI in the community were detected in 64/958 individuals (6,7%), 67,2% were *P. falciparum* and 32,8% were *Plasmodium* spp. The median persistence was 53 days and 47,5% had at least three negative consecutive LAMP results with a clearance rate of 0,013/100 SI/day. The median survival was higher in individuals with history of malaria (58 days) compared to individuals without history of malaria (31 days) but there were not statistically significant differences (p 0,205). On the other hand, an increase in the antibody levels against Pf-msp was associated with a decrease in the clearance *Plasmodium* risk (HR 0,14; CI 95%: 0,043- 0,475). There is a high proportion of SI which can persist over time and this persist is related with antibody levels Pf-msp. It is suggested that a cumulative exposure to *Plasmodium* antigens is associated with protection from future clinical malaria episodes and therefore with SI.

FALCIPARUM BUT NOT VIVAX MALARIA DURING EARLY GESTATION IS ASSOCIATED WITH INCREASED RISK OF SUBSEQUENT HYPERTENSIVE DISORDERS OF PREGNANCY

Whitney E. Harrington¹, Aung Myat Min², Mary Ellen Gilder², Nay Win Tun², Kerryn Moore³, Moo Kho Paw², Jacher Wiladphaingern², Kesinee Chotivanich⁴, Nicholas J. White⁵, Francois Nosten², Rose McGready²

¹Seattle Children's / University of Washington, Seattle, WA, United States, ²Shoklo Malaria Research Unit, Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Mae Sot, Thailand, ³Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Australia, ⁴Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, ⁵Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Old Road Campus, Oxford, United Kingdom

Malaria and hypertensive disorders of pregnancy (HDoP) continue to affect millions of pregnancies world-wide, particularly those of young, first-time mothers. Prior research suggests a link between the two conditions, but to date, no large, prospective analysis has considered the effect of peripheral falciparum or vivax malaria on risk of HDoP, by gestational age of infection. Using data from the Thai-Myanmar border collected between 1986 and 2016, we evaluated the relationship between (1) any falciparum or vivax malaria and (2) gestational age of first falciparum or vivax infection and the risk of gestational hypertension (GH), pre-eclampsia (PRE-EC), and eclampsia (EC). 23,262 singleton, live-born pregnancies were considered, in which women were enrolled during first trimester and followed fortnightly with data recorded on blood smear positivity, blood pressure, and proteinuria. Logistic regression models were adjusted for maternal age, first trimester weight, weight gain, chronic hypertension, number of consultations, place of delivery, refugee status, and year of delivery. Among all women, any falciparum infection was associated with risk of any HDoP (AOR 1.63, 95%CI: 1.13-2.37), with strongest effect for GH (AOR 1.84, 95%CI: 1.18-2.87). When stratified by gravidity, falciparum malaria predicted risk of PRE-EC among primigravidae (AOR 4.11, 95%CI: 1.35-12.49) and risk of GH among multigravidae (AOR 2.16, 95%CI: 1.33-3.51). Falciparum infection between 0-11 weeks gestation (AOR 2.51, 95%CI: 1.40-4.50) or 12-21 weeks gestation (AOR 1.75, 95% CI: 1.00-3.05) was associated with risk of HDoP. There was no association between vivax malaria and HDoP. In this large, prospectively followed cohort we observed a strong association between early peripheral falciparum malaria and HDoP. The data suggest that falciparum but not vivax malaria during a key period of placental development may result in chronic placental hypoxia, eventually progressing to clinical GH or PRE-EC. These data highlight the critical need to prevent malaria early in gestation, during a window when many women may not yet be aware of the pregnancy.