Malaria (Poster Presentation)

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Malaria Treatment in African Folk Medicine: An Investigation on Medicinal Plant Products Used in Cameroon

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Malaria remains one of the leading public health problems in Cameroon as in other parts of Sub-Saharan Africa. In the past decades, this situation has been aggravated by the increasing spread of drug-resistant Plasmodium falciparum strains. New antimalarial drug leads are therefore urgently needed. Traditional healers have long used plants to prevent or cure infections. This article reviews the current status of botanical screening efforts in Cameroon as well as experimental studies done on antimalarial plants. Data collected from 53 references of various research groups in the literature up to June 2007 shows that 217 different species have been identified in Cameroon for their use as antimalarials in folk medicine. About a hundred phytochemicals have been isolated from 26 species some of which are potential leads for development of new antimalarials. Crude extracts and or essential oils prepared from 54 other species showed a wide range of activity on Plasmodium spp. Moreover, some 137 plants from 48 families that are employed by traditional healers remain uninvestigated for their presumed antimalarial properties. The present study shows that Cameroonian flora represents a high potential for new antimalarial compounds. Further ethno botanical surveys and laboratory investigations are needed to fully exploit the potential of the identified species in the control of malaria.

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Rna Interference Mediated Silencing of Hsp60 and 70 Genes in Human Monocytes Reveals Decreased Dengue Virus Multiplication

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Heat Shock Proteins (Hsps) or stress proteins are highly conserved molecules and expressed in all cell types under stressful conditions like heat, cold, hypoxia and infections. The objective of the present study was to determine the effect of Dengue virus infection on relative expression of stress proteins and their role in the progression of the infection. As macrophages are the primary host for Dengue, human promonocytic myeloblastoma U937 cells, monocytic THP1 cells and blood derived macrophages were infected with Dengue virus type 2 New Guinea strain for the evaluation of Hsp expression. A significant expression of Hsp60 was observed in virally infected U937 cells where as Hsp70 was predominantly expressed in blood derived macrophages and THP1 as compared to controls. In order to determine the correlation between Hsp60/70 expressions and viral multiplication in infected cells, expression of Hsp60 and 70 was down regulated by RNA interference. Viral multiplication was determined by quantification of viral RNA copy number using Real Time PCR and plaque formation assay in culture supernatants of Hsp60 and 70 silenced cells. Intracellular quantification of viral load was also determined by flow cytometry. It was observed that down regulation of Hsp60 and 70 in virally infected cells resulted into decrease in viral RNA copy number and intracellular viral load. At the same time down regulation of Hsp60 and 70 expressions also resulted in increased IFN-α level which mediate its antiviral effect through double stranded RNA induced protein kinase (PKR). These observations suggest that, elevation of Hsp60 and 70 expressions in virally infected cells may help in viral multiplication and could be possible therapeutic targets for the management of Dengue virus infection.

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Comparison of the Genetic Diversity and Natural Selection in the Apical Membrane Antigen 1 of Plasmodium falciparum and P. vivax

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Apical membrane antigen 1 (AMA1) is a promising vaccine candidate, and a number of vaccines based on this molecule are currently at different stages of clinical trials. Prior information of the genetic repertoire of the natural Plasmodium populations helps in the development of malaria vaccines. Accumulating evidence suggests that allelic variations in the antigens may influence immunogenicity and protective effect of a vaccine. In a comprehensive and comparative study we have analyzed extent of polymorphisms and natural selection at P. falciparum and P. vivax AMA1 among Indian populations. We sequenced domain I of P. falciparum AMA1 while both domain I and II of P. vivax AMA1. Sequencing data were analyzed using DnaSP and MEGA3 packages. Signatures of selection on these antigens were estimated by the ratio of non-synonymous (dN) and synonymous (dS) mutations as well as Tajima’s D and McDonald-Kreitman test statistics. Three-dimensional structures of AMA1 were made using MODELLER routine incorporated in Discovery studio. A total of 57 AMA1 haplotypes with 29 polymorphic residues were found among 157 P. falciparum isolates. Whereas 49 haplotypes with 25 polymorphic residues were found among 61 P. vivax isolates. Most of the observed haplotypes from both species were new as they have not been reported from any other regions. The dN-dS difference for PfAMA1 domain I and PvAMA1 domain II were found to be positive, indicating that they are under positive natural selection while, it was negative for PvAMA1 domain I. Results from PfAMA1 show moderate level of genetic differentiation and limited gene flow between populations. Three-dimensional structures of both antigens predicted that all polymorphic residues were found to be distributed at only one surface of the molecule.