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Biography: Dr. Prakasha Kempaiah is a Research Assistant Professor at the Center for Global Health (CGH), Department of Internal Medicine. Dr. Kempaiah received his PhD from the Institute for Human Genetics, University of Goettingen, Germany. During his PhD dissertation, he worked on areas caused by genetic disorders using animal models. Dr. Kempaiah's PhD thesis work on protein transduction domain mediated recombinant protein supplementation therapy for Rett-syndrome resulted in two disclosures being filed, one for *MECP2* synthetic gene and other for the approach used to produce the recombinant protein for substitution therapy [(US 2009/0233856 A1). He also has completed one year of certificate course in Clinical and Translational Research (CTR) at UNM with an emphasis on biostatistics, global health and clinical research. He is trained in the field of genetics, cell biology, biochemistry, animal models and infectious diseases with skills set in the areas of genetic diagnostics, cloning, cell culture, parasite culture, protein expression, flow cytometry, genotyping, functional genomics, genome wide association study (GWAS), gene expression arrays, custom array design, high density data analysis, pathways network analysis and biostatistics. Dr. Kempaiah is also well versed in using several genetics and genomics analysis tools such as SPSS, HPlus, Haploview, GeneSpring, Golden Helix SVS suite, GeneGo, analyzing genotypes, haplotypes, and high density GWAS and gene expression data. Dr. Kempaiah is an editorial board member of Open Journal of Apoptosis, Human Parasitic Diseases, Journal of Life Medicine, AIMS Genetics, Asian Council of Science Editors and Journal of Public Health & Epidemiology. He is also an invited peer-reviewer for Human Parasitic Diseases, Gene Regulation and Systems Biology, Cancer Cell International,Breast Cancer, Biotechnology Progress, Journal of Cell Death, Immunology and Immunogenetics Insights, Gene Expression to Genetical Genomics and Cancer Informatics and other journals.

Teaching: Evidence based practice (EBP), Infectious diseases, Immunology, Genetics & Neoplasia, Global and Emergining Infections.

Research Interest: Dr. Kempaiah currently overseas the research activities of malaria and co-infections at the CGH. He is primarily involved in investigating the genetic basis of infectious disease outcome, specifically host-mediated pathogenesis in children with severe malarial anemia (SMA, Hb<5.0g/dL). His research projects includes: (1), determining the relationship between the immunomodulatory aspect of immune response genes and promoter polymorphism (SNPs and VNTRs), functional changes, downstream effects on modulator production, and SMA manifestation; (2), determining the suitability of Glutamine as a therapeutic agent in children with malaria to target HSP70 production and improve the therapeutic effects of anti-malarials in combination with glutamine; (3), GWAS using Illumina Omni-2.5 array, human Immunochip and whole genome transcriptome arrays to identify important markers, CNVs and candidates gene pathways that condition development of SMA; (4), malaria parasite cultures for anti-malarial drug screening and to isolate hemozoin (*Pf*Hz) and testing its immunomodulatory activities using *in-vitro* cultures; (5), elucidating the molecular mechanisms of inflammatory-derived inefficient erythropoiesis using CD34+ hematopoietic progenitor's cells isolated from umbilical specimens; (6), Identifying natural and pharmacological compounds to stimulate inflammatory mediators altered during SMA such as interlukin-12 using *in-vitro* cultures treated with *Pf*Hz. In addition, his interest also includes Following themes are his the primary research interest.

Theme 1: Identifying the genetic basis of severe anemia outcomes.

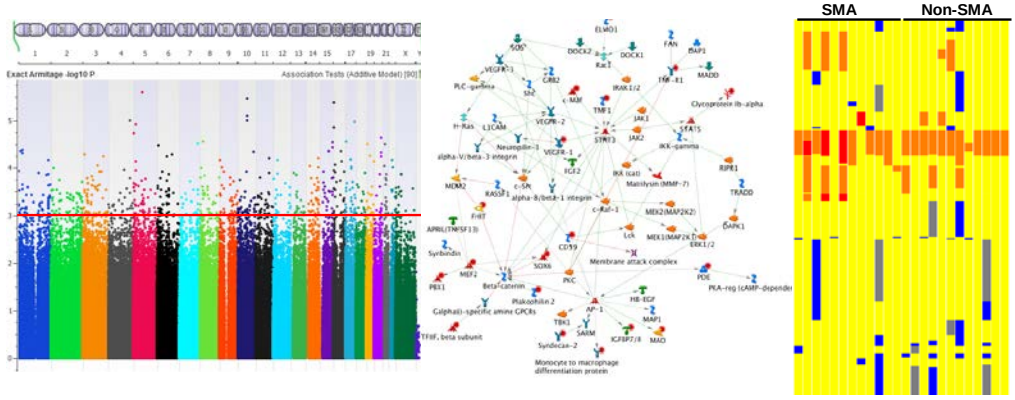

Figure 1. Manhattan plot of SNPs from GWAS in SMA children. Biomolecular networks generated from the findings placed into existing canonical gene pathways. CNV analysis: Genomic heat map showing amplified or deleted regions on chr.1 in the non-SMA and SMA groups [Blue=0 (deletion); Grey=1; Yellow=2 (normal); Orange=3; Red=4 copies and above].

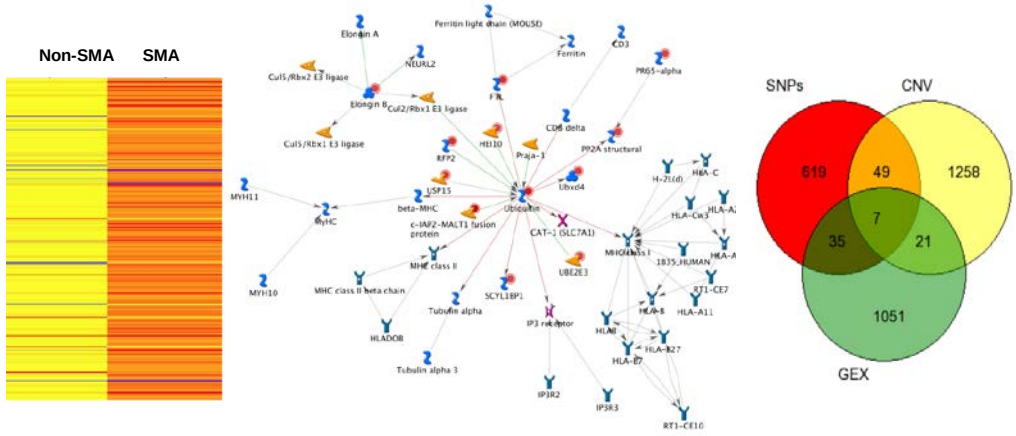

Figure 3. Global Gene Expression Profiles in the non-SMA and SMA groups. Fold-change: yellow= no change; blue= decrease >1; grey= decrease <1; orange= 1.5-2.0 increase; and red= increase >2. Biomolecular networks generated from the findings placed into existing canonical gene pathways. Integration of data from different arrays to identify the overlapping genes.

Dr. Kempaiah's primary interest is to continue to identify the genetic basis of diseases (i.e. monogenic, complex multigenic, heritable and infectious diseases). Recent advances in genomics, bioinformatics and high-throughput technologies such as the whole genome sequencing, GWAS, RNASeq and global microarray gene expression profiling are bringing about a revolution in our understanding of genetic and molecular mechanisms underlying normal and dysfunctional biological process. In order to develop new therapeutic interventions for any genetic disorders or a vaccine testing for infectious diseases influenced by genetic make-up of an individual, it is critical to understand the underlying host molecular and genetic factors. This can be achieved by following steps including: 1) knowledge of the genetic variants (SNPs/VNTRs, CNVs, microsatellites, chromosomal aberrations such as deletion, translocation, duplication, and epigenetic) associated with disease susceptibility and clinical outcomes; 2) knowledge of the gene expression profiles; and 3) knowledge of the critical biological pathways and factors that mediate disease outcomes. Currently, genetic variations are known to cause about 20-30% of all infant deaths, 12% of all hospital admissions, 50% of all mental retardation, 15% of all cancers, and 10% of all chronic diseases.

Theme 2: Genotyping to validate polymorphic variations identified from GWAS in the larger population.

After generating the list of significant markers (i.e., GWAS) and expression

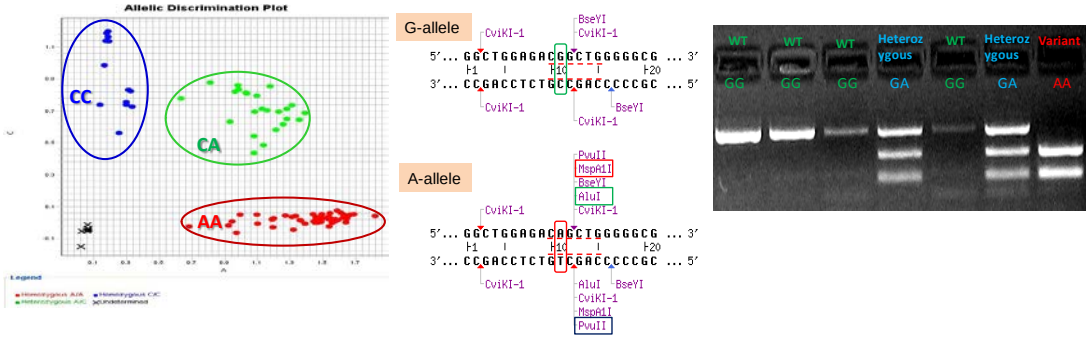

Figure 2. Genotyping of SNPs through allelic discrimination assay in pediatric malaria samples. Selection strategy of restriction enzyme. Genotyping of SNPs through RFLP method in pediatric malaria samples.

profiles (transcriptome) of the intersected genes, we will select candidate genes to further validate in the larger population. Following genotyping, association tests will be performed with cross-sectional as well as longitudinal follow-up data set controlling for appropriate covariates.

Theme 3: Role of HSP70 and autophagy in SMA pathogenesis.

Human malaria parasite *P. falciparum* polymerizes free heme into hemozoin (*Pf*Hz) crystals as a byproduct of hemoglobin digestion. Freely circulating *Pf*Hz from ruptured RBCs is taken-up by phagocytes causing dysregulation in immune response. In order for these phagocytes to survive and function, adverse effect of *Pf*Hz needs to be circumvented by cellular mechanisms. In recent years, studies have focused on delineating mechanisms in clearing toxins, damaged and unwanted cellular components to maintain the homeostasis through autophagy process. Considering its role in other diseases, autophagy induction could be beneficial in controlling the parasite and clearing parasitic products (*Pf*Hz) in children with severe malarial anemia. Dr. Kempaiah has identified several ATG genes associated with SMA outcome using transcriptomics and GWAS. He is interested in delineating the molecular process associated in clearing the *Pf*Hz through autophagy process. In addition, we have also found association of markers from *HSP70* genes with SMA. Since heat shock proteins (Hsp's) 70 are major stress-inducible proteins known to play dual role as molecular chaperones and immunogenic molecules, we will expand our investigation to characterize its role in the pathogenesis of malaria.

Theme 4: Development of in-vitro model for small molecules, herbal and pharmacological compounds screening.

Dr. Kempaiah is using Disease Systems Chemical Biology approach to identify target compounds and develop high-throughput *in vitro* assays to screen. We have assembled paediatric specific FDA approved compounds/drugs library to include in the screening for immunomodulation properties using *in-vitro* PBMCs and CD34+ based hematopoietic stem cell model. He is currently using these models for screening pharmacological compounds to overcome the inhibitory effect of inflammatory-derived inefficient erythropoiesis and also from *Pf*Hz. In this process we have identified several neem derived compounds having immunomodulatory and anti-parasitic properties using PBMC and parasite cultures. In future, we will source for additional compounds for screening derived from either herbal origin or FDA approved. For broader application, CD34+ model can be used to screen compounds or drugs to overcome inefficient erythropoiesis seen in many chronic inflammatory and infectious diseases.

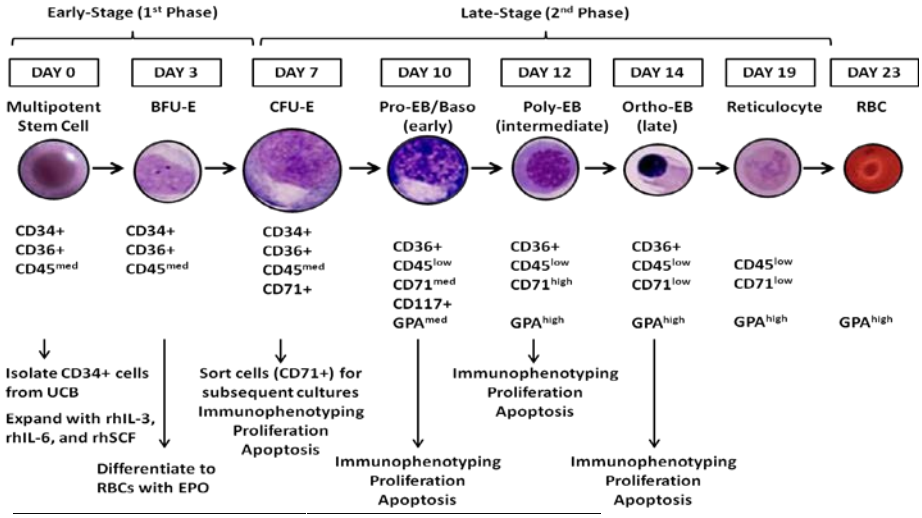

Figure 3. Erythropoiesis Model for understanding the anemia's. Stages of erythroid development in the *in-vitro* model.

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