List of Ten papers related to important findings by the research group:

1. Recombinant antigens of Leishmania donovani inducing IFN-g release from Leishmania specific cell line, Arora SK, Pal NS & S.Mujtaba. Exp Parasit 2005; 109:163-170.
2. Vaccination with a novel recombinant Leishmania antigen along with MPL provides partial protection against L. donovani challenge in experimental model of visceral leishmaniasis. Bhardwaj S, Vasishta RK and Arora SK. Exp Parasit 2009; 121:29–37.
3. Efficacy of Leishmania donovani ribosomal P1 gene as potential DNA vaccine in experimental visceral leishmaniasis. Masih S, Arora SK and Vasishta RK. Exp Parasit 2011; 129: 55-64.
4. Leishmania recombinant antigen modulates macrophage effector function facilitating early clearance of intracellular parasites. Ratna A; Arora SK. Trans Roy Soc Trop Med Hyg 2016 110 (10): 610-619. doi: 10.1093/trstmh/trw068.
5. A T-Cell Epitope-Based Multi-Epitope Vaccine Designed Using Human HLA Specific T Cell Epitopes Induces a Near-Sterile Immunity against Experimental Visceral Leishmaniasis in Hamsters. Arya A, Arora SK. Vaccines 2021, 9, 1058. https://doi.org/10.3390/vaccines9101058.
6. Prediction of drug-resistance in HIV-1 Subtype C based on protease sequences from ART naïve and first line therapy failures in North India using genotypic and docking analysis. Toor JS, Verma R, Gupta P, Garg P, Sharma A and Arora SK. ANTIVIRAL RESEARCH 2011; 92:213-18.
7. Prediction of NRTI drug resistance in HIV-1 subtype C among first line antiretroviral-experienced virological failure patients from North India using genotypic and docking analysis. Toor JS, Kumar R, Garag P, Sharma A, Arora SK. J AIDS CLIN RES 2012, S5: 005. doi:10.4172/2155-6113.S5-005.
8. Differential expression of Rac-1, CxCR4 and CCR5 on CD4 T-cells at different stages of HIV-1 disease relate to its progression in therapy-naïve individuals. Toor JS, Sharma A, Kamboj SS and Arora SK. J AIDS CLIN RES. 2013; 4:207. doi:10.4172/2155-6113.1000207.
9. Human Immunodeficiency virus-1 (HIV-1) subtype-C genetically diversify to acquire higher replication competence in human host with co-morbidities. Mehta G, Sharma A, Arora SK. AIDS Res Hum Retroviruses. 2021 Jan 7. doi: 10.1089/AID.2020.0118. Online ahead of print.
10. Acquisition of additional NFκB binding sites in LTR of genetically evolving HIV-1 subtype C viral species in host with co-morbidities. Mehta G, Sharma A, Arora SK. AIDS Res Hum Retroviruses. 2021 Jan 13. doi: 10.1089/AID.2020.0195. Online ahead of print

Our lab has been interested in developing a vaccine against a tropical parasitic disease, Visceral leishmaniasis which is also called kala azar in India. This disease is highly endemic in many parts of the world mainly Latin America, eastern Europe and Indian subcontinent. In India it is more prevalent in Eastern states of West Bengal and Bihar. The parasite is transmitted by the sand fly vector. Clinically the disease is characterized by hepato-splenomegaly, anaemia, hyper gamma-globulineamia due to poly-clonal B-cell activation, weight loss, darkening of skin and death if not treated well in time. Chemotherapy is available but most of the drugs are highly toxic and prone to development of resistance. Development of immunity against reinfection indicates that the vaccine approach is feasible. There have been many trials by various groups but a vaccine that can induce a sterile immunity in humans is still not available. We started with identifying novel clones from a cDNA library that we generated initially and carried on to evaluate the protective efficacy of novel vaccine candidates (1). We identified three novel clones which expressed

proteins that could induce expression of high level of Interferon gamma (IFNg) from immune T-cells isolated from individuals who had recovered from kala azar. But in order to pick up clones that could induce T-cell activation we developed a Leishmania specific CD4 T-cell line from a healthy individual and used this cell line to screen the cDNA clones for identifying T-cell stimulating proteins. We checked the protective efficacy of these three recombinant proteins in a model of experimental visceral leishmaniasis in hamsters and found these to have a protective efficacy varying from 60-85% (2, 3). We even checked the immunotherapeutic potential of one of these antigens and showed that this protein could induce production of high level of ROS and NO when used ex vivo culture of peritoneal macrophages. The macrophages stimulated with this protein cleared the intracellular parasites more efficiently due to increased oxidative burst. We also showed that when used in conjunction with the anti-leishmanial drugs like miltefosine and Ambisome, the protein stimulation facilitated the clearance of parasites with half the therapeutic dose of the drug and at much earlier time point (4). This indicated that the recombinant protein was a potential immunomodulator and when used as a immunotherapeutic agent along with existing anti-leishmania drugs will reduce the toxic effects of the drug due to reduced dose of drugs being effective at shorter time points. We worked diligently and consistently to find ways to improve the efficacy of this vaccine. After years of hard work and scientific enquiry, the group has proposed ‘multi-epitope constructs’ as vaccine candidates including the select T-cell based epitopes mapped from their previously cloned genes using immune-informatic tools. They found that one of these multi-epitope peptides was able to induce ‘sterile immunity’ in the hamster model of experimental visceral leishmaniasis. The animals were nearly 100% protected to a lethal challenge with the virulent parasite. This study has recently been published in Vaccines (5). This is a remarkable progress in the field of vaccine development against this tropical disease, which indicates a consistent and focused approach by our group in this area of research. The proposed approach of selective epitope mapping and designing of multi-epitope constructs as vaccine candidate may not remain restricted to leishmaniasis but would be highly translatable to epitope-based vaccine designing for other emerging infections as well.

In the area of HIV and HCV, our lab has been interested in understanding the immune-defects leading to immunocompromised state in the advanced stage of these two chronic viral infections. These two viral infections have common transmission mode and both lead to chronic infection in the infected individuals. While HIV-1 infection leads to severe immunocompromised state in the individual in due course of time due to gradual loss of CD4+ T-cells, which are the host cells for this virus. The cell death is not only because of infection but also because of the immune response generated against the virus and the CD8+ cytotoxic T-cells kill not only the infected cells but the by-stander uninfected cells are also found to be dying because of strong immune activation. But surprisingly as the disease progresses a state of severe immune-deficiency sets in and the infected individual gets prone to many opportunistic infections like pneumocystis carinii, Mycobacterium tuberculosis etc. So, the lab hypothesised that there are more immune defects in the infected individuals than only the T-cell number getting depleted. Since the myeloid dendritic

cells are the major antigen presenting cells for generation of immune response, we wanted to check the functional state of these cells in infected individuals at different stage of infection. We reported that the mDCs loose the capacity to mature in response to the antigenic stimulation in the advanced stage of disease (when the CD4 count drops below 250 cells/cmm). Similarly in the chronic HCV infection we reported the maturation defects in mDCs due to upregulation of negative factors which even effects the response to anti-viral treatment in these individuals. My lab has reported an HIV-1 subtype-C specific drug-docking prediction model for assessment of drug-resistant mutations based on binding energy to RT and PR genes (6, 7). Very interesting studies from my lab have shown that the *Mycobacterium tuberculosis* (Mtb), the most common opportunistic co-infection among HIV-1 infected individuals, modulates many genes in the co-infected host cells to facilitate the replication and HIV-1, leading to faster disease progression in such individuals (8). More recently we further delineated the molecular mechanisms and described the genetic evolution of HIV-1 in the co-infected host in terms of accumulation of DR mutations and acquisition of additional NF-kB binding sites in the LTR region that turns the virus into more fit and replication competent in such individuals (9, 10). Our work on molecular pathways leading to maturation defective myeloid dendritic cells in the advanced HIV disease and chronic viral hepatitis (CHC) is phenomenal and has received great attention.