

In order of Importance, list of 10 best papers of the applicant highlighting the important discoveries/contributions described in them briefly:

- 1. Awasthi A, Mathur R, Khan A, Joshi BN, Jain N, Sawant S, Boppana R, Mitra D, Saha B. CD40 signalling is impaired in L. major-infected macrophages and is rescued by a p38MAPK activator establishing a host-protective memory T cell response. *Journal of Experimental Medicine* 2003; 197: 1037-43.**

In this study, we have shown the CD40-induced p38MAPK phosphorylation, iNOS2 expression and anti-leishmanial function were impaired in Leishmania-infected macrophages but were restored by anisomycin. Anisomycin's effects were reversed by SB203580 emphasizing the role of p38MAPK in CD40-induced iNOS2-dependent leishmanicidal function. Anisomycin administration in L. major-infected BALB/c mice resulted in significant reduction in the parasite load and established a host-protective Th1-type memory response. Also implicated in these findings is a scientific rationale to define novel anti-parasite drug targets and to bypass the problem of drug resistance.
- 2. Awasthi A, Carrier Y, Peron JP, Bettelli E, Kamanaka M, Flavell RA, Kuchroo VK, Oukka M, Weiner HL. A dominant function for interleukin 27 in generating interleukin 10–producing anti-inflammatory T cells. *Nature Immunology* 2007; 12:1380-9.**

In this publication, we have identified the role of cytokine IL-27 in inducing type 1 regulatory T cells (Tr1). Tr1 cells produce copious amounts of the anti-inflammatory cytokine IL-10, which is crucial for maintaining immune homeostasis and regulating tissue inflammation in inflammatory diseases.
- 3. Lee Y#, Awasthi A*#, Yosef N, Quintana F, Xiao S, Kunder S, Regev A, Sobel R, Kuchroo VK. Induction and molecular signature of pathogenic TH17 cells. *Nature Immunology* 2012; 13:991-9.**

In this publication, we have demonstrated and identified the signature of pathogenic and nonpathogenic Th17 cells. Th17 cells are associated with the induction of tissue inflammation in autoimmune diseases. We reported that Th17 cells generated with TGF- β 1 and IL-6 produce IL-17 and are non-pathogenic. TGF- β 3 production by developing Th17 cells upon IL-23 exposure leads to the generation of pathogenic Th17 cells. TGF- β 3-induced Th17 cells are functionally and molecularly distinct from TGF- β 1-induced Th17 cells.
- 4. Karwacz K, Miraldi ER, Pokrovskii M, Madi A, Yosef N, Wortman I, Chen X, Watters A, Carriero N, Awasthi A, Regev A, Bonneau R, Littman D, Kuchroo VK. The critical role of IRF1 and BATF in preparing the chromatin landscape during Tr1 differentiation. *Nature Immunology* 2017, 18(4):412- 421.**

In this publication, we have identified the role of two transcription factors, IRF-1 and Batf, which are essential for the differentiation and function of Type 1 regulatory T cells. They shape the epigenetic landscape by regulating chromatin accessibility and are the pioneer factors for the differentiation of Tr1 cells.
- 5. Malik S, Sadhu S, Elesela S, Pandey R, Rathod D, Amanpreet Chawla, Sharma D, Ghosh B, Ahuja V, Awasthi A. Transcription factor Foxo1 essential for differentiation of IL-9+ T helper cells. *Nature Communications* 2017, 8(1):815. doi: 10.1038/s41467-017-00674-6.**

In this publication, we have demonstrated for the first time that Foxo1 acts as a key transcription factor in the differentiation of Th9 (IL-9-producing T cells). Foxo1 is required for the induction of IL-9 and suppressing IL-17 in Th17 cells. Since Th9 cells play a pro-inflammatory role in allergic inflammation, autoimmunity, and tumor immunity; the identification of Foxo1 as a crucial transcription factor for IL-9 could prove beneficial in designing targeted drug therapies and alleviate the course of autoimmune diseases and anti-cancer therapy.
- 6. Roy, Rizvi ZA, Clarke A, Macdonald F, Pandey A, Zaiss D, Dr. Simon KA, Awasthi A. EGFR-HIF1 α signaling positively regulates the differentiation of IL-9 producing T helper cells. *Nature Communication* 2021, 12(1):3182. doi: 10.1038/s41467-021-23042-x.**

In this publication, we have demonstrated the role of the Areg-EGFR-HIF1 α signaling pathway in the differentiation and functions of Th9 cells. This pathway could be further used for targeting Th9 cells mediated anti-tumor response.

7. **Thiruvengadam R, Awasthi A, Medigeshi GR, Bhattacharya S, Mani S, Sivasubbu S, Shrivastava S, Samal S, Murugesan DR, Desiraju BK, Kshetrapal P, Pandey R, Scaria V, Malik PK, Taneja J, Binayke A, Vohra T, Zaheer A, Rathore D, Khan NA, Shaman H, Ahmed S, Kumar R, Deshpande S, Subramani C, Wadhwa N, Gupta N, Pandey AK, Bhattacharya J, Agrawal A, Vratil S, Bhatnagar S, Garg PK. Cellular Immune Responses are Preserved and may Contribute to Vaccine Effectiveness of ChAdOx1 nCoV-19 vaccine against SARS-CoV-2 infection during the delta (B.1.617.2) variant surge in India: a test-negative, case-control study and a mechanistic study of post-vaccination immune responses. Lancet Infectious Disease 2021, Nov 25:S1473-3099(21)00680-0. doi: 10.1016/S1473-3099(21)00680-0.**

In this publication, we have reported independent, real-world effectiveness, humoral and cellular immune responses post COVISHIELD vaccine during the delta surge in India. Our group performed the T cells assays and observed that although neutralizing antibodies are substantially reduced against the Delta variant, the T cell response is largely conserved.

8. **Rizvi ZA, Dalal R, Sadhu S, Binayke A, Dandotiya J, Kumar Y, Shrivastava T, Gupta SK, Aggarwal S, Tripathy M, Rathore DK, Yadav AK, Medigeshi GR, Pandey A, Samal S, Asthana A, Awasthi A. Golden Syrian hamster as a model to study cardiovascular complications associated with SARS-CoV2 infection. eLife 2022, Jan 11;11:e73522. doi: 10.7554/eLife.73522.**

In this publication, we have reported the Golden Syrian hamsters as a suitable animal model to study SARS-CoV-2 infection. We showed that the early phase of Covid disease leads to lung inflammation and pathology, while the late stage of infection leads to cardiovascular complications.

9. **Rizvi ZA, Dalal R, Sadhu S, Kumar Y, Kumar S, Gupta SK, Tripathy MR, Rathore DK, Awasthi A. High salt diet mediates interplay between NK cells and gut microbiota to induce potent tumor immunity. Science Advances 2021, 7(37):eabg5016. doi: 10.1126/sciadv.abg5016.**

In this publication, we have shown for the first time how table salt triggers anti-tumor immunity by modulating the gut microbiome and by enhancing the anti-tumor functions of Natural killer cells.

10. **Sadhu S, Dalal R, Dandotia J, Binayke A, Vinayak KV, Shakti K, Singh V, Goswami S, Tripathy MR, Rizvi ZA, Awasthi A. IL-9 exacerbates SARS-CoV2 infection and associated airway inflammation. Manuscript ID: NCOMMS-22-28241C, Nature Communication 2023.**

In this publication we provides mechanistic insight into an important inflammatory pathway in SARS-CoV-2 infection, and thus represents proof of principle for the development of host-directed therapeutics to mitigate disease severity.



Dr. Amit Awasthi,
Senior Professor,
Translational Health Science & Technology Institute,
Faridabad, Haryana