

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

- 1. 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.
- 2. 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.
- 3. 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.
- 4. 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.
- 5. 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. Nat Commun. 2023 Jul 10;14(1):4060. doi: 10.1038/s41467-023-39815-5**
 - 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.
- 6. Rizvi ZA, Sharma K, Srikanth S, Dandotiya J, Khatri R, Singh V, Adhikari N, Das V, Mani S, Samal S, Awasthi A*. Omicron sub-lineage BA.5 infection causes attenuated pathology and results in robust protection in Omicron-recovered hACE2 transgenic mice. Commun Biol. 2023 Sep 13;6(1):935. doi: 10.1038/s42003-023-05263-6**
 - In this article we have shown that mice recovered from B.1.1.529 infection showed robust protection against BA.5 infection associated with reduced lung viral load and pathology. Together, our data provide insights as to why BA.5 infection escapes previous SARS-CoV-2 exposure induced-T cell immunity but may result in milder immuno-pathology and alleviated chances of re-infectivity in Omicron-recovered individuals.

7. Sadhu S, Dandotiya J, Dalal R, Khatri R, Anna Z. Mykytyn, Aashima Batra, Manpreet Kaur, Rucha Chandwaskar, Virendra Singh, Aarzoo Kamboj, Mitul Srivastava, Shailendra Mani, Shailendra Asthana, Sweetey Samal, Zaigham Abbas Rizvi, Deepak B. Salunke, Bart L. Haagmans, Awasthi A. Fangchinoline inhibits SARS-CoV-2 and MERS-CoV entry. *Antiviral Res.* 2023 Dec;220:105743. doi: 10.1016/j.antiviral.2023.105743
- In this publication we have shown that Fangchinoline (Fcn), a bisbenzylisoquinoline alkaloid, inhibits replication of SARS-CoV, SARS-CoV-2, and MERS-CoV in a range of in vitro assays, by blocking entry. Therapeutic use of Fcn inhibited viral loads in the lungs, and suppressed associated airway inflammation in hACE2. Tg mice and Syrian hamster infected with SARS-CoV-2. Combination of Fcn with remdesivir (RDV) or an anti-leprosy drug, Clofazimine, exhibited synergistic antiviral activity. Compared to Fcn, its synthetic derivative, MK-04-003, more effectively inhibited SARS-CoV-2 and its variants B.1.617.2 and BA.5 in mice. Taken together these data demonstrate that Fcn is a pan beta coronavirus inhibitor, which possibly can be used to combat novel emerging coronavirus diseases.
8. Rizvi ZA, Sadhu S, Dandotiya J, Sharma P, Binayke A, Singh V, Das V, Khatri R, Kumar R, Samal S, Kalia M, Awasthi A. SARS-CoV-2 infection induces thymic atrophy mediated by IFN γ in hACE2 transgenic mice. *Eur J Immunol.* 2024 Jul;54(7):e2350624. doi: 10.1002/eji.202350624
- Thymic atrophy was notably higher in male hACE2-Tg mice than in females and involved an upregulated de-novo synthesis pathway of thymic glucocorticoid. Further, IFN- γ was crucial for thymic atrophy, as anti-IFN- γ -antibody neutralization blunted thymic involution. Therapeutic use of Remdesivir also rescued thymic atrophy. While the Omicron variant and its sub-lineage BA.5 variant caused marginal thymic atrophy, the delta variant of SARS-CoV-2 exhibited severe thymic atrophy characterized by severely depleted DP T-cells. Recently characterized broadly SARS-CoV-2 neutralizing monoclonal antibody P4A2 was able to rescue thymic atrophy and restore the thymic maturation pathway of T-cells. Together, we report SARS-CoV-2-associated thymic atrophy resulting from impaired T-cell maturation pathway which may contribute to dysregulated T cell response during COVID-19.
9. Madan U, Verma B, Awasthi A. Ceniviroc, a CCR2/CCR5 antagonist, promotes the generation of Type 1 regulatory T cells. *Eur J Immunol.* 2024 Jul;54(7):e2350847. doi: 10.1002/eji.202350847
- This study is the first to report that Ceniviroc promotes Tr1 cell generation by up-regulating the signature of Tr1 cell transcription factors such as c-Maf, Prdm1, Irf-1, Batf, and EGR-2. Ceniviroc displayed a protective effect in experimental colitis models by preventing body weight loss and intestinal inflammation and preserving epithelial barrier integrity. We show that Ceniviroc induced IL-10 and inhibited the generation of pro-inflammatory cytokines IFN- γ , IL-17, IL-6, and IL-1 β during colitis. Based on our data, we propose Ceniviroc as a potential therapeutic in controlling tissue inflammation by inhibiting the generation and functions of effector T cells and promoting the induction of anti-inflammatory Tr1 cells.
10. Binayke A, Zaheer A, Vishwakarma S, Sharma P, Dandotiya J, Raghavan S, Gosain M, Singh S, Chattopadhyay S, Kaushal J, Madan U, Kshetrapal P, Batra G, Wadhwa N, Pandey A.K, Bhatnagar S, Garg P.K, Awasthi A* Understanding the landscape of the SARS-CoV-2-specific T cells post Omicron Surge. *J Med Virol* 2024 Aug;96(8):e29877. doi: 10.1002/jmv.29877
- This study investigated the durability, magnitude, and breadth of SARS-CoV-2-spike-specific T cell responses in 216 two-dose vaccinated individuals pre- and post-omicron surge. Post-surge samples showed enhanced T cell responses, indicating widespread asymptomatic exposure to omicron. Further analysis of 105 individuals with multiple exposures to SARS-CoV-2 through boosters or infections showed that post-omicron, two-dose vaccinated individuals had T cell responses comparable to those of COVID-19 convalescents or boosted individuals. Additionally, we report cross-reactive T cell responses against omicron sub-variants, including BA2.86, remained strong, with preserved frequencies of spike-specific stem-cell-like memory T cells. In silico prediction indicates that mutated epitopes of JN.1 and KP.2 retain over 95.6% of their HLA binding capability. Overall, our data suggests that T cell responses are sustained, enhanced, and cross-reactive against emerging SARS-CoV-2 variants following symptomatic or asymptomatic omicron infection.

