List of Ten Best Papers

1. **Alveolar macrophage-expressed Plet1 is a driver of lung epithelial repair after viral pneumonia.** ***Nat Commun. 2024 Jan 2;15(1):87.*** PMID: 38167746.

   Contribution: Shared First author

   The study titled "Alveolar Macrophage-Expressed Plet1 is a Driver of Lung Epithelial Repair after Viral Pneumonia" investigates the role of the protein Plet1, expressed by alveolar macrophages, in the repair of lung epithelial tissue following viral pneumonia. Key discoveries from the study include:

   1. **Plet1 Function in Repair**: The research identifies Plet1, a protein expressed by alveolar macrophages, as a crucial mediator in the repair process of lung epithelial cells after viral pneumonia. Plet1 is shown to drive the repair and regeneration of lung tissues by promoting epithelial cell proliferation and migration.
   2. **Mechanistic Insights**: The study elucidates the mechanisms by which Plet1 facilitates repair. Plet1 influences several signaling pathways that are critical for epithelial cell function and tissue regeneration. It appears to modulate the local immune environment, ensuring an optimal balance between inflammation and repair.
   3. **Macrophage Role**: Alveolar macrophages are essential for maintaining lung homeostasis and responding to injury. This research highlights how these macrophages, through the expression of Plet1, play a direct role in orchestrating the repair of lung epithelium post-infection.
   4. **Therapeutic Implications**: The findings suggest that targeting Plet1 or enhancing its function could offer new therapeutic strategies for treating viral pneumonia and other conditions involving lung epithelial damage. By harnessing or mimicking Plet1's effects, it may be possible to improve recovery and repair in affected patients.
   5. **Experimental Evidence**: The study employs various experimental approaches, including genetic and pharmacological manipulation, to demonstrate the role of Plet1. These methods provide robust evidence supporting the involvement of Plet1 in the repair process.

Overall, the research underscores the significant role of alveolar macrophage-expressed Plet1 in lung epithelial repair following viral pneumonia, presenting potential avenues for therapeutic intervention to enhance lung tissue recovery and improve patient outcomes. This research also highlights the potential of targeting Plet1 as a therapeutic strategy for improving lung recovery after viral infections, such as influenza and COVID-19.

2. **Macrophage-epithelial paracrine crosstalk inhibits lung edema clearance during influenza infection.** ***J Clin Invest. 2016 Apr 1;126(4):1566-80.*** PMID: 26999599.

   Contribution: Co-author

   The study titled "Macrophage-Epithelial Paracrine Crosstalk Inhibits Lung Edema Clearance During Influenza Infection" investigates how interactions between macrophages and epithelial cells affect lung edema during influenza infection. Key findings include:

   1. **Paracrine Crosstalk**: The research reveals that macrophage-epithelial cell interactions, specifically through paracrine signaling (where cells communicate via secreted factors), play a critical role in modulating lung edema during influenza infection.
   2. **Impact on Edema Clearance**: The study demonstrates that this paracrine crosstalk inhibits the clearance of lung edema. Lung edema, or fluid accumulation in the lungs, is a common complication of influenza, and the study shows that macrophage-epithelial interactions contribute to prolonged edema by interfering with normal fluid clearance mechanisms.
   3. **Inflammatory Mediators**: The research identifies specific inflammatory mediators involved in this process. The signaling molecules secreted by macrophages impact epithelial cell function and contribute to impaired resolution of edema, highlighting the role of inflammatory pathways in disease progression.
   4. **Mechanistic Insights**: The study provides mechanistic insights into how macrophage-derived factors alter epithelial cell responses, affecting the balance between inflammation and tissue repair. This crosstalk disrupts normal clearance processes, exacerbating lung edema.
   5. **Therapeutic Implications**: Understanding this crosstalk opens potential therapeutic avenues for managing influenza-induced lung edema. Targeting the interactions between

macrophages and epithelial cells or modulating the inflammatory signals involved might improve edema resolution and overall lung function.

6. **Experimental Evidence**: The study employs both in vivo and in vitro models to demonstrate how macrophage-epithelial cell interactions influence edema clearance, providing robust evidence for the identified mechanisms.

   Overall, the study highlights the complex interplay between macrophages and epithelial cells in influenza infection, underscoring how paracrine signaling can inhibit the resolution of lung edema and suggesting potential targets for therapeutic intervention.

3. **Intestinal macrophages in pathogenesis and treatment of gut leakage: current strategies and future perspectives.** ***J Leukoc Biol. 2024 Mar 29;115(4):607-619.*** PMID: 38198217
   Contribution: First author

   The paper "Intestinal macrophages in pathogenesis and treatment of gut leakage: current strategies and future perspectives," published in *Journal of Leukocyte Biology* in 2024, sheds light on the crucial role of intestinal macrophages in both the development and potential treatment of gut leakage. Key discoveries include the identification of distinct macrophage populations that either promote or mitigate intestinal permeability. The study reveals that pro-inflammatory macrophages contribute to gut barrier disruption by releasing cytokines that weaken tight junctions between epithelial cells, thereby exacerbating gut leakage. Conversely, anti-inflammatory macrophages are shown to support barrier integrity by promoting tissue repair and maintaining homeostasis. The paper also explores emerging therapeutic strategies that target macrophage polarization to enhance gut barrier function, including the use of specific cytokines, small molecules, and probiotics. These findings suggest that modulating intestinal macrophage activity could be a promising approach to treating conditions associated with gut leakage, such as inflammatory bowel disease and metabolic disorders.

4. **Resident alveolar macrophages are master regulators of arrested alveolarization in experimental bronchopulmonary dysplasia.** ***J Pathol. 2018 Jun;245(2):153-159.*** PMID: 29574785.

   Contribution: Second Co-author

   The paper "Resident alveolar macrophages are master regulators of arrested alveolarization in experimental bronchopulmonary dysplasia," published in *The Journal of Pathology* in June 2018, explores the role of resident alveolar macrophages in the pathogenesis of bronchopulmonary dysplasia (BPD), a chronic lung disease in preterm infants. The study reveals that these macrophages are key regulators of impaired alveolarization, a process critical for lung development. In experimental models of BPD, the researchers found that alveolar macrophages contribute to the arrest of alveolar growth by releasing pro-inflammatory cytokines and growth factors that disrupt normal lung development. This disruption leads to fewer and larger alveoli, characteristic of the structural abnormalities seen in BPD. The study suggests that targeting the activity of alveolar macrophages may be a potential therapeutic approach to prevent or mitigate the arrested alveolarization and associated lung damage in infants at risk for BPD, offering new insights into the management of this debilitating condition.

5. **Acid Aspiration Impairs Antibacterial Properties of Liver Macrophages.** ***Am J Respir Cell Mol Biol. 2021 May;64(5):641-643.*** PMID: 33929292.

   Contribution: Co-author

   The study titled "Acid Aspiration Impairs Antibacterial Properties of Liver Macrophages," investigated how acid aspiration, a condition where acidic stomach contents are inhaled into the lungs, affects the immune function of liver macrophages, also known as Kupffer cells. The research demonstrates that acid aspiration leads to systemic inflammation, which compromises the antibacterial capabilities of Kupffer cells. This impairment is characterized by a reduced ability of these liver macrophages to phagocytose and kill bacteria, making the host more susceptible to infections. The study suggests that the inflammatory mediators released during acid aspiration travel from the lungs to the liver, disrupting the normal

function of Kupffer cells. This finding is significant because it links lung injury to impaired liver immune function, highlighting the potential for increased bacterial infections in patients who experience acid aspiration, such as those with gastroesophageal reflux or during anesthesia. The study underscores the importance of addressing systemic effects in the treatment of acid aspiration.

6. **IRE1 Signaling as a Putative Therapeutic Target in Influenza Virus-induced Pneumonia**. ***Am J Respir Cell Mol Biol. 2019 Oct;61(4):537-540.*** PMID: 31573336.

   Contribution: Co-author

   The article "IRE1 Signaling as a Putative Therapeutic Target in Influenza Virus-induced Pneumonia" discusses how the IRE1 (Inositol-Requiring Enzyme 1) signaling pathway plays a critical role in the pathogenesis of influenza virus-induced pneumonia. Key discoveries include:1.Pathway Activation: IRE1 signaling is activated in response to endoplasmic reticulum (ER) stress during influenza infection, contributing to inflammatory responses and disease severity. 2. Inflammatory Response: This pathway is crucial for the regulation of inflammatory cytokines and contributes to lung damage. 3. Therapeutic Potential: Targeting IRE1 signaling could offer new therapeutic strategies to mitigate inflammation and improve outcomes in influenza virus-induced pneumonia. Overall, the study suggests that modulating IRE1 signaling might help in developing novel treatments for influenza-induced respiratory illnesses by reducing inflammation and improving patient outcomes.

7. **Nicotine promotes e-cigarette vapour-induced lung inflammation and structural alterations.** ***Eur Respir J. 2023 Jun 22;61(6):2200951.*** PMID: 37105573

   Contribution: Co-author

   The study titled "Nicotine Promotes E-Cigarette Vapour-Induced Lung Inflammation and Structural Alterations" explores the impact of nicotine on lung health in the context of e-cigarette use. Here are the key discoveries from the research:

   1. **Nicotine's Role**: Nicotine, a primary component of e-cigarette vapor, is found to exacerbate lung inflammation and damage. The study highlights that nicotine not only

contributes to the harmful effects of e-cigarette vapor but may also independently drive inflammation in the lungs.

2. **Inflammatory Response**: The research demonstrates that nicotine enhances the inflammatory response in the lungs, leading to increased production of pro-inflammatory cytokines and recruitment of immune cells to the lung tissue. This suggests that nicotine plays a critical role in the inflammatory processes triggered by e-cigarette use.
3. **Structural Alterations**: E-cigarette vapor, particularly in the presence of nicotine, induces structural changes in the lung tissue. These alterations include damage to the epithelial lining and disruptions in normal lung architecture, which can compromise lung function and contribute to respiratory diseases.
4. **Mechanistic Insights**: The study provides insights into the mechanisms through which nicotine exacerbates inflammation and structural damage. It involves increased oxidative stress and alterations in cellular signaling pathways related to inflammation and tissue repair.
5. **Implications for E-Cigarette Use**: The findings underscore the health risks associated with e-cigarette use, particularly concerning nicotine. The study suggests that nicotine not only contributes to the harmful effects of e-cigarette vapor but may also be a key factor in promoting lung inflammation and structural damage.
6. **Potential Interventions**: Understanding the role of nicotine in e-cigarette-induced lung damage could inform strategies for reducing harm associated with e-cigarette use. This includes developing nicotine-free or lower-nicotine alternatives and implementing public health measures to mitigate lung damage.

   Overall, the study highlights the detrimental effects of nicotine on lung health in the context of e-cigarette use, revealing its role in promoting inflammation and structural damage.

8. **Increased blood immune regulatory cells in severe COVID-19 with auto antibodies to type I interferons.** ***Sci Rep. 2023 Oct 13;13(1):17344.*** PMID: 37833265

   Contribution: Co-author

   The study titled "Increased Blood Immune Regulatory Cells in Severe COVID-19 with Autoantibodies to Type I Interferons" provides critical insights into the immunological characteristics associated with severe COVID-19, particularly in patients with autoantibodies against type I interferons (IFNs). Here are the key discoveries from the research:

   1. **Role of Autoantibodies Against Type I IFNs:** The study confirms that autoantibodies against type I interferons are prevalent in severe COVID-19 cases. These autoantibodies neutralize the antiviral effects of type I IFNs, which are crucial for the body's initial immune response to viral infections. This impairment is linked to more severe disease progression.
   2. **Increased Regulatory Immune Cells:** The research shows a significant increase in immune regulatory cells, such as regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs), in the blood of patients with severe COVID-19 who also have these autoantibodies. These cells generally act to suppress immune responses, which could contribute to an inadequate immune reaction against the virus.
   3. **Immune Dysregulation:** The presence of autoantibodies against type I IFNs, combined with the increase in immune regulatory cells, suggests a state of immune dysregulation in these patients. This dysregulation may prevent the body from effectively controlling the viral infection, leading to worse outcomes.
   4. **Clinical Implications:** The study highlights the potential for using the presence of autoantibodies against type I IFNs as a biomarker for identifying patients at higher risk of severe COVID-19. It also suggests that therapies targeting immune regulatory pathways might be beneficial for these patients by restoring an appropriate immune response.
   5. **Pathophysiological Insights:** The research provides new insights into the pathophysiology of severe COVID-19, emphasizing the importance of type I IFNs in antiviral defense and the impact of their inhibition by autoantibodies. This finding is significant for understanding why certain individuals develop more severe forms of the disease.

Overall, the study underscores the complex interplay between autoimmunity, immune regulation, and disease severity in COVID-19, offering new avenues for research and potential therapeutic interventions.

9. Development of allergic asthma emerge with gut leakage and associated inflammatory manifestations. ***Adv Biol (Weinh). 2024 Jan;8(1):e2300350***. PMID: 37752729

Contribution: First author

The study titled “Development of Allergic Asthma Emerges with Gut Leakage and Associated Inflammatory Manifestations” explores the link between gut permeability and the development of allergic asthma. Key findings from the research include:

1. **Gut Leakage**: The study identifies gut leakage (increased intestinal permeability) as a significant factor in the development of allergic asthma. It suggests that when the gut barrier is compromised, allergens and other antigens can cross into the bloodstream, triggering systemic immune responses.
2. **Immune Activation**: Gut leakage leads to the activation of systemic inflammation. The study highlights how this increased permeability contributes to the activation of immune cells and the production of inflammatory cytokines, which play a role in the pathogenesis of asthma.
3. **Inflammatory Manifestations**: The research demonstrates that gut leakage is associated with various inflammatory manifestations that contribute to asthma development. This includes heightened immune responses and increased production of Th2 cytokines, which are known to be involved in allergic reactions and asthma.
4. **Pathophysiological Link**: The study establishes a pathophysiological link between gut health and respiratory conditions. It shows that disturbances in gut barrier function can influence the immune system's response in the lungs, leading to asthma.
5. **Potential Interventions**: The findings suggest that interventions aimed at improving gut barrier function or reducing gut permeability might have therapeutic potential for preventing or managing allergic asthma. Probiotics, dietary changes, and other strategies to support gut health could be explored as part of asthma management.

6. **Experimental Evidence**: The research utilizes various experimental models and clinical data to support its conclusions, providing a comprehensive view of how gut leakage impacts asthma development.

Overall, the study highlights the critical role of gut permeability in the onset and progression of allergic asthma, suggesting that maintaining gut health might be a key strategy in managing or preventing asthma. The findings also suggest that therapeutic strategies targeting gut leakage could be beneficial in reducing asthma-related inflammation and symptoms.

10. NS Segment of a 1918 Influenza A Virus-Descendent Enhances ReplicaIon of H1N1pdm09 and Virus-Induced Cellular Immune Response in Mammalian and Avian Systems. ***Front Microbiol. 2018 Mar 22;9:526.*** PMID: 29623073.

Contribution: Co-author

The paper "NS Segment of a 1918 Influenza A Virus-Descendent Enhances Replication of H1N1pdm09 and Virus-Induced Cellular Immune Response in Mammalian and Avian Systems," published in *Frontiers in Microbiology* on March 22, 2018, investigates the impact of the non-structural (NS) segment from the 1918 influenza virus on the replication and immune response of the H1N1pdm09 virus. The study reveals that the NS segment from the 1918 pandemic virus significantly enhances the replication efficiency of the H1N1pdm09 virus in both mammalian and avian cells. This segment also amplifies the virus-induced cellular immune response, leading to increased production of pro-inflammatory cytokines and interferons. The research demonstrates that the presence of the 1918 NS segment contributes to the heightened pathogenicity and immune activation of the virus, which may have implications for understanding the mechanisms behind severe influenza outbreaks. These findings provide insights into how historical viral elements can influence the behavior of contemporary influenza strains, potentially guiding future vaccine and antiviral development.