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Title:

"Identifying a Genetic Signature from Murine Acute Respiratory Distress Models – a Meta-Analysis."

Abstract :

Introduction:

Acute Respiratory Distress Syndrome (ARDS) is a non-cardiogenic pulmonary oedema causing respiratory failure and acute hypoxaemia [1] ; the aetiology of the syndrome is diverse, and the underlying pathophysiology is poorly understood. Studies have sought to overcome this challenge by identifying a genetic signature unique to ARDS [2]. Pre-clinical models are central to research and mice are often used. This research utilises meta-analysis by information content (MAIC) to synthesise the genetic data form currently published omics studies and create one comprehensive ranked ARDS gene and protein list.

Methods:

Data was extracted from published research, formatted, and subsequently used to run MAIC in RStudio, where a novel ranked gene list was generated. Functional enrichment analysis using external databases took place and findings were compared with Millar et al's [3] research investigating the ARDS genetic signature in humans.

Results:

A set of 131 genes and proteins were identified as differentially expressed in ARDS mice, with the role of CDKN1a, and LCN2 most robustly evidenced.

Conclusion:

Apart from cytokines IL-4, IL-10, and IL-13, much of the functional enrichment analysis revealed different biological processes in murine models compared to humans. This calls into question the role of mice as pre-clinical models in ARDS research.

Diagrams:

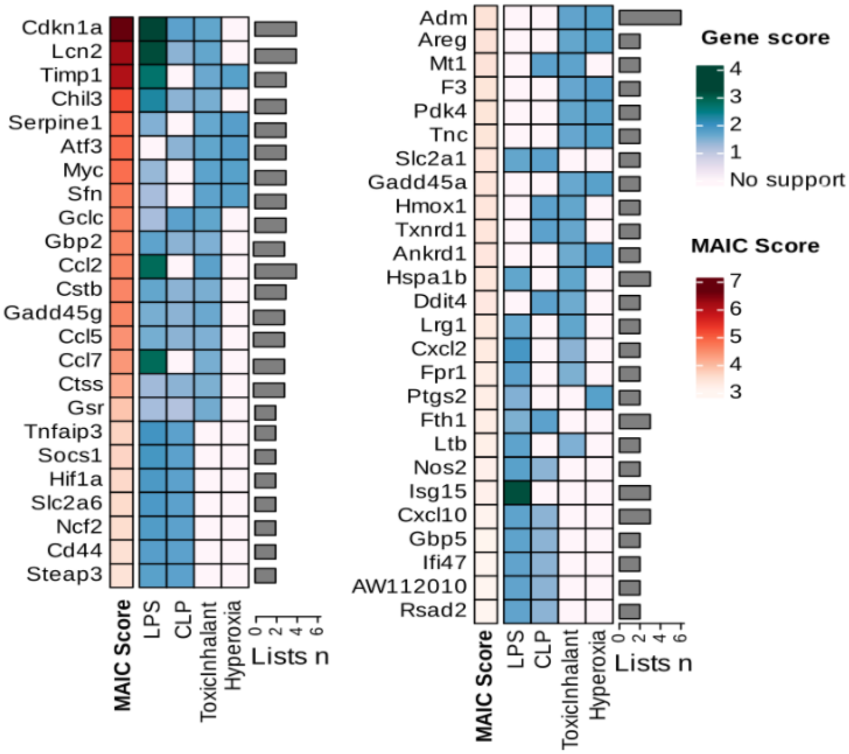

Figure 1. Heatmap showing the top 50 genes and proteins ranked as significant in ARDS mice.

Figure 2. Euler Diagram Representing Number of Prioritised Genes and Proteins Identified in ARDS Mice or Humans, and Any Identified in Both.

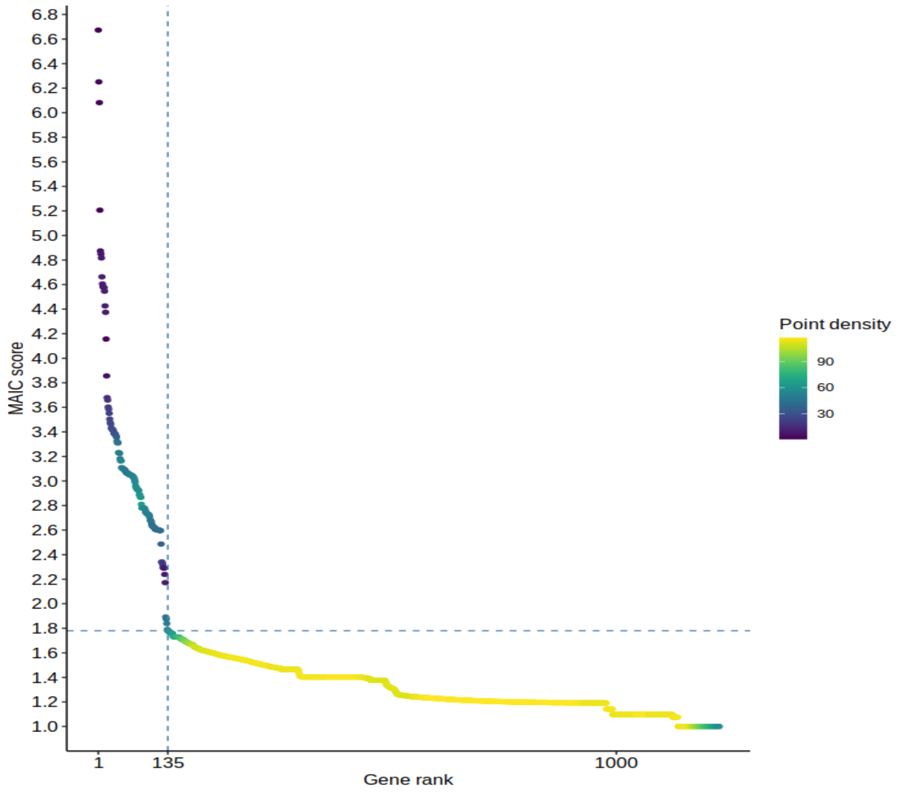

Figure 3. A Scatter Plot Representing Gene Prioritisation Curve.

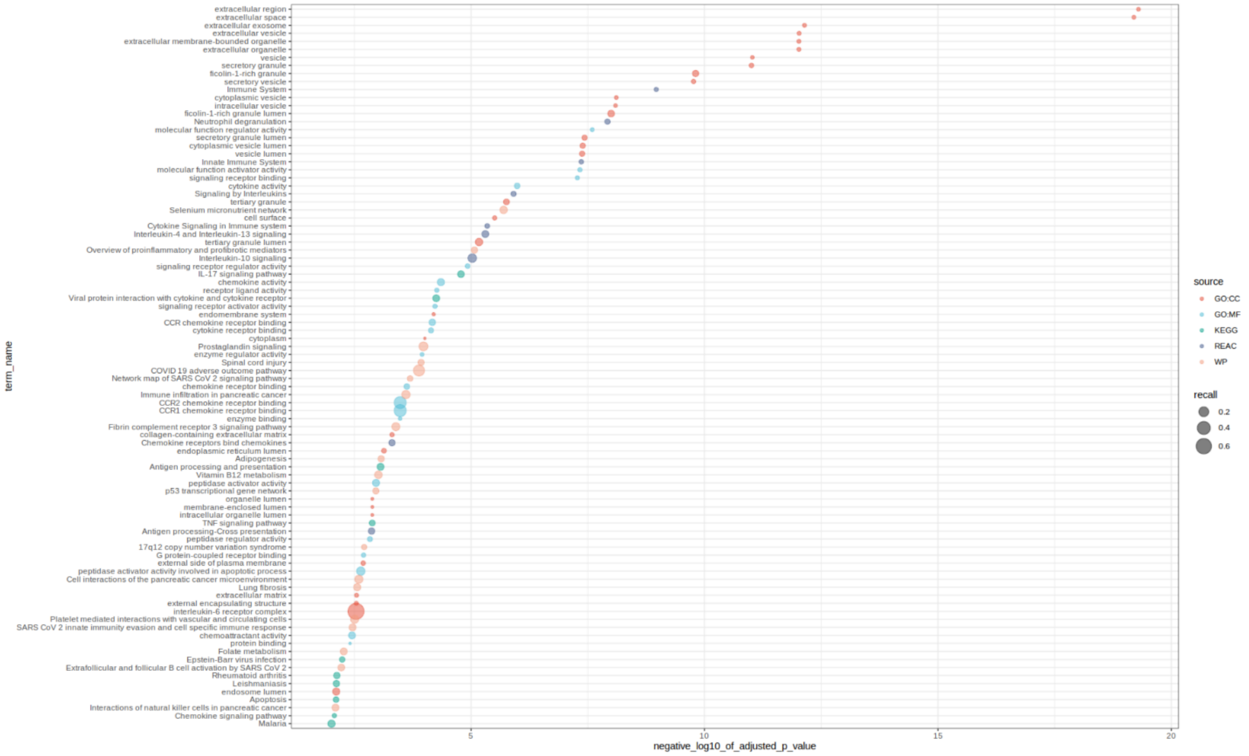

Figure 4f. Bubble Plot Showing the Combined Functional Enrichment Analysis of WikiPathways, Genome Ontology: Cellular Component, Reactome, Genome Ontology: Molecular Function, and Kyoto Encyclopaedia of Genes and Genomes.

Reference List:

1. Clark SB, Soos MP. Noncardiogenic Pulmonary Edema [Internet]. PubMed. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2024 Apr 4]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542230/#:~:text=Arguably%20the%20most%20recognized%20form
2. Battaglini D, Al-Husinat L, Gabriela A, Adriana Paes Leme A, Franchini KG, Morales MM, et al. Personalized medicine using omics approaches in acute respiratory distress syndrome to identify biological phenotypes. Respiratory Research [Internet]. 2022 Nov 19 [cited 2024 Apr 4];23(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9675217/
3. Millar JE, Clohisey-Hendry S, McMannus M, Zechner M, Wang B, Parkinson N, et al. The genomic landscape of Acute Respiratory Distress Syndrome: a meta-analysis by information content of genome-wide studies of the host response. [cited 2024 Apr 14]; Available from: https://www.medrxiv.org/content/10.1101/2024.02.13.24301089v1