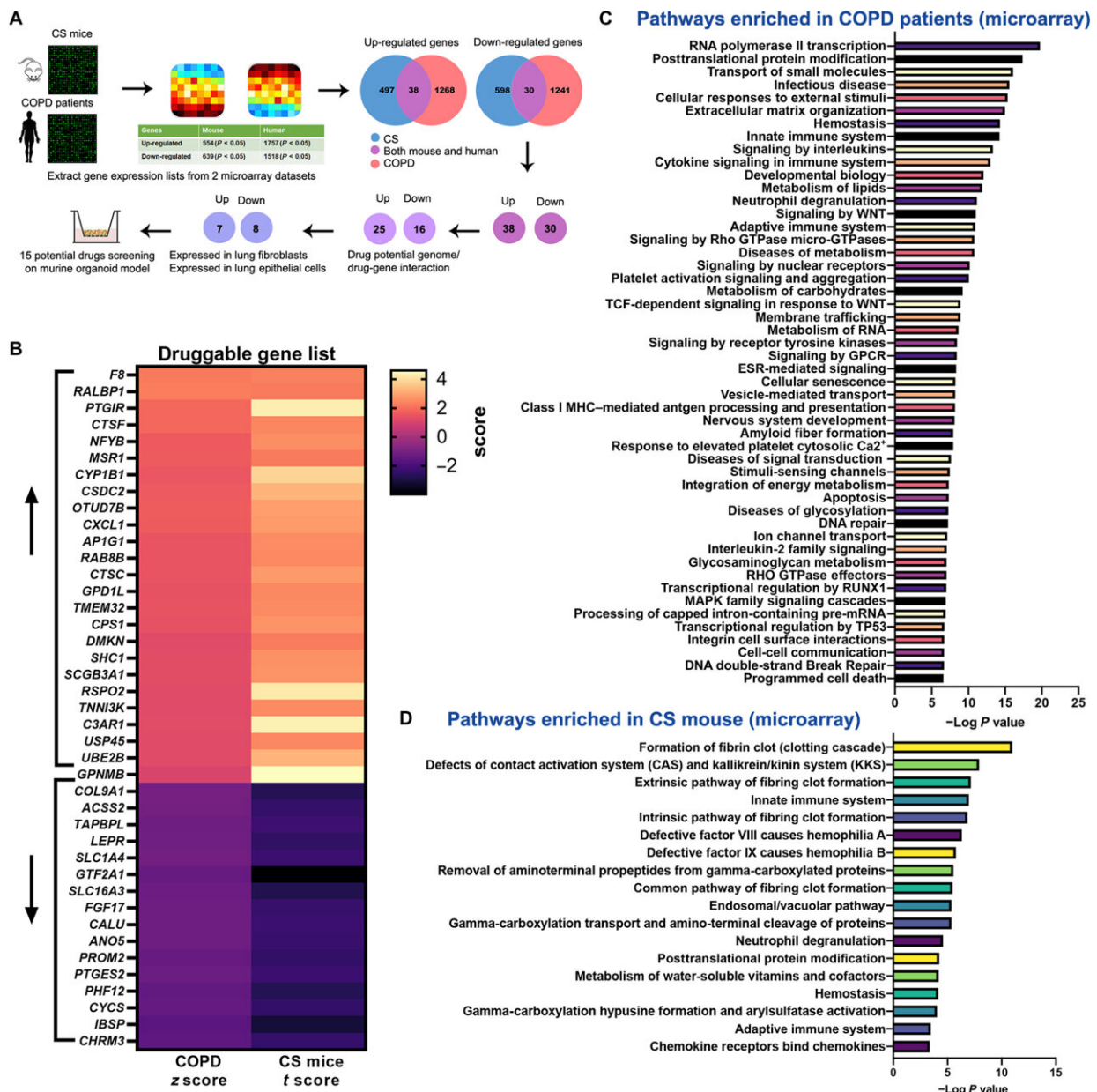


Two drugs show promise in rejuvenating lung epithelial progenitor cells damaged by COPD

March 24 2022, by Bob Yirka



Overview of the transcriptomics-guided drug discovery strategy. (A) Schematic outline of the drug screening strategy. (B) Heatmap shows the gene expression pattern of the druggable genes (www.dgidb.org) identified both in CS-exposed mice and patient with COPD databases. (C) Reactome pathway enrichment analysis of genes differentially expressed from patients with COPD (8) using gene set enrichment analysis (GSEA); the top 50 pathways enriched are presented. TCF, T cell factor; GPCR, G protein–coupled receptor; ESR, estrogen receptor; MHC, major histocompatibility complex; RUNX1, runt-related transcription factor 1. (D) Reactome pathway enrichment analysis of differentially genes differentially expressed from CS-exposed mice (9) using GSEA (www.gsea-msigdb.org/gsea/msigdb/annotate.jsp). Credit: *Science Advances* (2022). DOI: 10.1126/sciadv.abj9949

A team of researchers from the Netherlands, Germany and the U.S. reports that two drugs show promise in rejuvenating lung epithelial progenitor cells damaged by chronic obstructive pulmonary disease (COPD). In their study, published in the journal *Science Advances*, the group identified certain proteins involved in epithelial generation for targeting with prostanoids and tested them under different scenarios. Sean Fortier, Loka Penke and Marc Peters-Golden with the University of Michigan have published a Focus piece in the same journal issue that gives a short history of the use of prostanoids in medical endeavors and outlines the work done by the team in Michigan.

COPD is a [disease of the lungs](#) that develops when the [immune system](#) overreacts to conditions, such as [smoke inhalation](#), and damages epithelial progenitor cells in the lungs. The job of epithelial progenitor cells is to produce new cells lining the lungs to keep them healthy. In their absence, patients experience shortness of breath and excess mucus production. Therapies have been developed to reduce the symptoms of

COPD, but there is no cure. In this new effort, the researchers have identified two drugs that show promise in rejuvenating lung epithelial progenitor cells.

The work involved obtaining and analyzing data from prior studies using human and mouse lung tissue damaged by COPD due to smoking. In comparing the data with similar data from healthy patients, the researchers were able to isolate genes that became less active due to damage, which resulted in less production of two proteins. They then conducted a search of existing drugs that might be used to restore normal levels of the two proteins. They found two: iloprost, which has been used to treat [high blood pressure](#) in arteries in the lungs, and mioprostol, which has been used to treat stomach ulcers.

Testing of the drugs in mice showed them both able to restore the regenerative capacity of the progenitor cells. The researchers suggest this is because they worked to restart the circadian clocks in the cells that had been disrupted by long-term exposure to smoke. More work is required to find out if the regenerated cells actually result in new cells lining the lungs.

More information: Xinhui Wu et al, A transcriptomics-guided drug target discovery strategy identifies novel receptor ligands for lung regeneration, *Science Advances* (2022). [DOI: 10.1126/sciadv.abj9949](https://doi.org/10.1126/sciadv.abj9949). www.science.org/doi/10.1126/sciadv.abj9949

Sean M. Fortier et al, Illuminating the lung-regenerative potential of prostanoids, *Science Advances* (2022). [DOI: 10.1126/sciadv.abp8322](https://doi.org/10.1126/sciadv.abp8322). www.science.org/doi/10.1126/sciadv.abp8322

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