

Figure S1. Biological pathways and compounds triggering transcriptional signatures that mimic CS^S and CS^[sc]. (A) Similarity scores of the top biological pathways (CMap Classes) with associated transcriptional signatures that show a positive correlation to the CS^S. (B) Similarity scores of the top CMap Classes with associated transcriptional signatures that show a positive correlation to the CS^[sc]. (C) Gene Ontology analysis of the biological pathways that are significantly enriched among genes for which their downregulation triggers transcriptional signatures that positively correlate to the CS^S (Similarity score > 95). The panel represents those with a False Discovery Rate (FDR) < 0.05 and a fold enrichment > 25.1. Pathways related to female hormone signaling are highlighted in yellow. (D) Venn Diagram representing the overlap among the top compounds that trigger transcriptional signatures that positively correlate to COVID^{CS}, CS^S and CS^[sc]. The p-value was obtained with the *superexact* test.

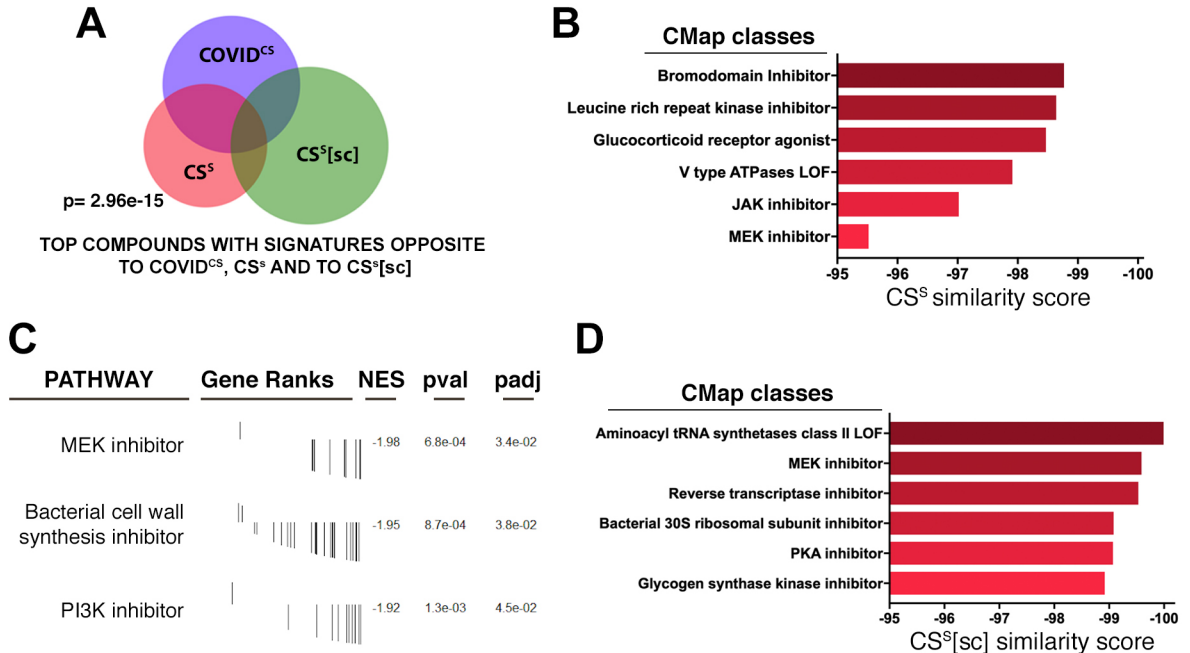


Figure S2. Compounds triggering transcriptional signatures opposite to CS^S and CS^S[sc]. (A) Venn Diagram representing the overlap among the top compounds that trigger transcriptional signatures that negatively correlate to COVID^{CS}, CS^S and CS^S[sc]. The p-value was obtained with the *superexact* test. (B) Similarity scores of the top CMap Classes with associated transcriptional signatures that show a negative correlation to the CS^S. (C) Drug GSEA analysis of compound classes with a transcriptional signature that negatively correlates to the CS^S[sc]. Enriched pathways as well as their gene ranks, Normalized Enrichment Scores (NES), p-values (pval) and adjusted p-values (padj) are shown. (D) Similarity scores of the top CMap Classes with associated transcriptional signatures that show a negative correlation to the CS^S[sc].

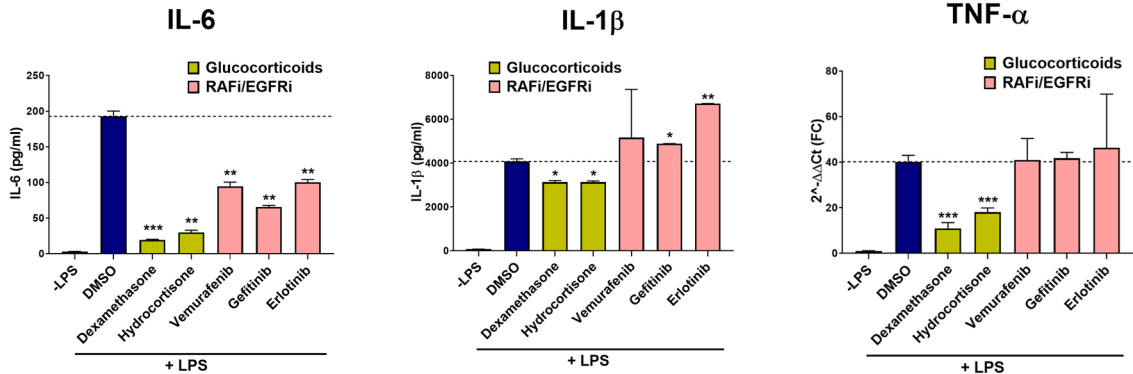


Figure S3. Effect of RAF and EGFR inhibitors in counteracting cytokine production. Cytokine expression in macrophages differentiated from THP1 cells upon exposure to LPS, with or without glucocorticoids (dexamethasone and hydrocortisone), a RAF inhibitor (vemurafenib) and EGFR inhibitors (gefitinib and erlotinib). IL-6 and IL-1 β levels were measured by ELISA (pg/ml), and TNF- α by qPCR (2^{- $\Delta\Delta$ Ct} (FC)). The experiment was repeated three times and a representative example is shown. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 (*t* test).