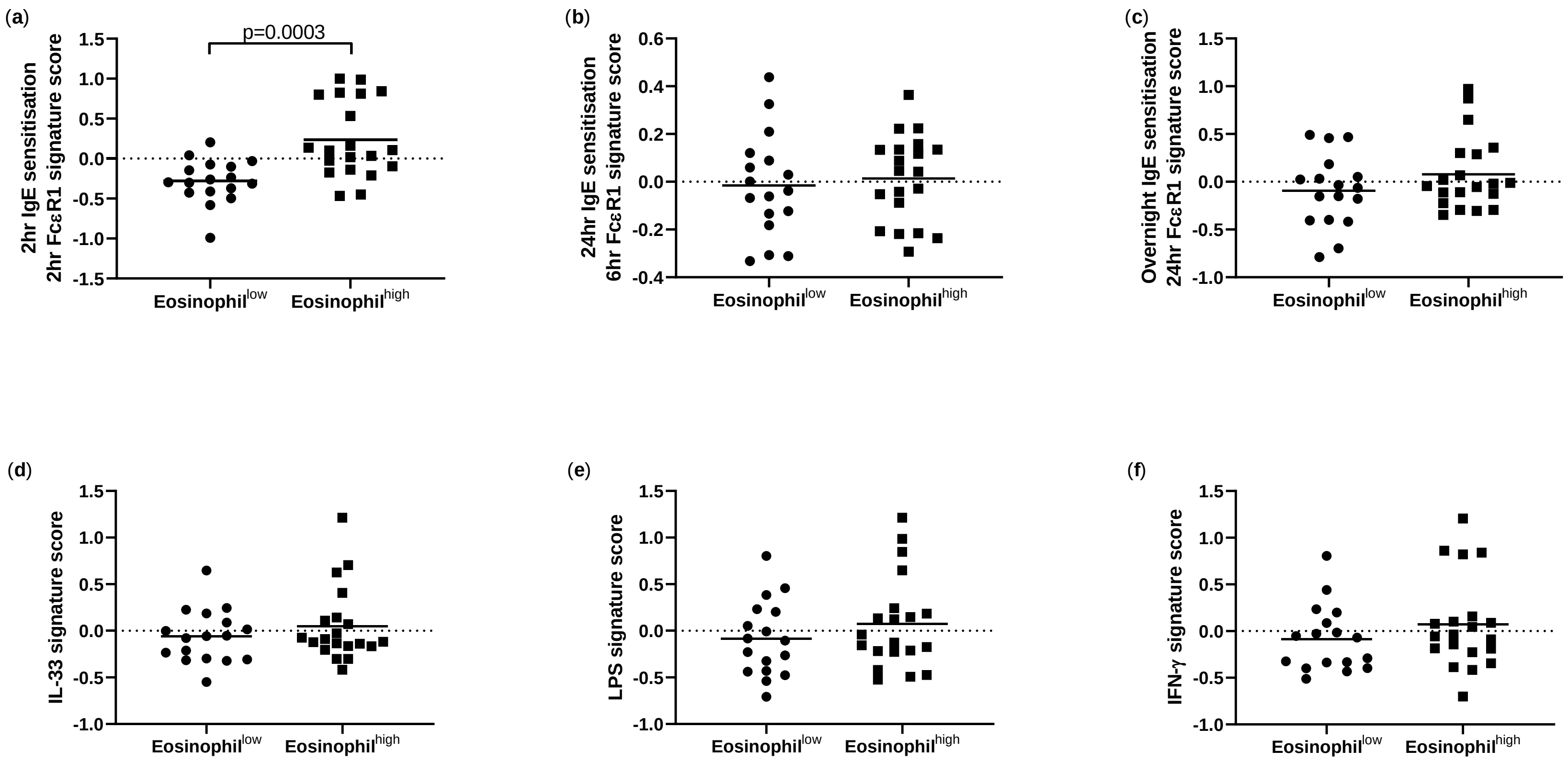
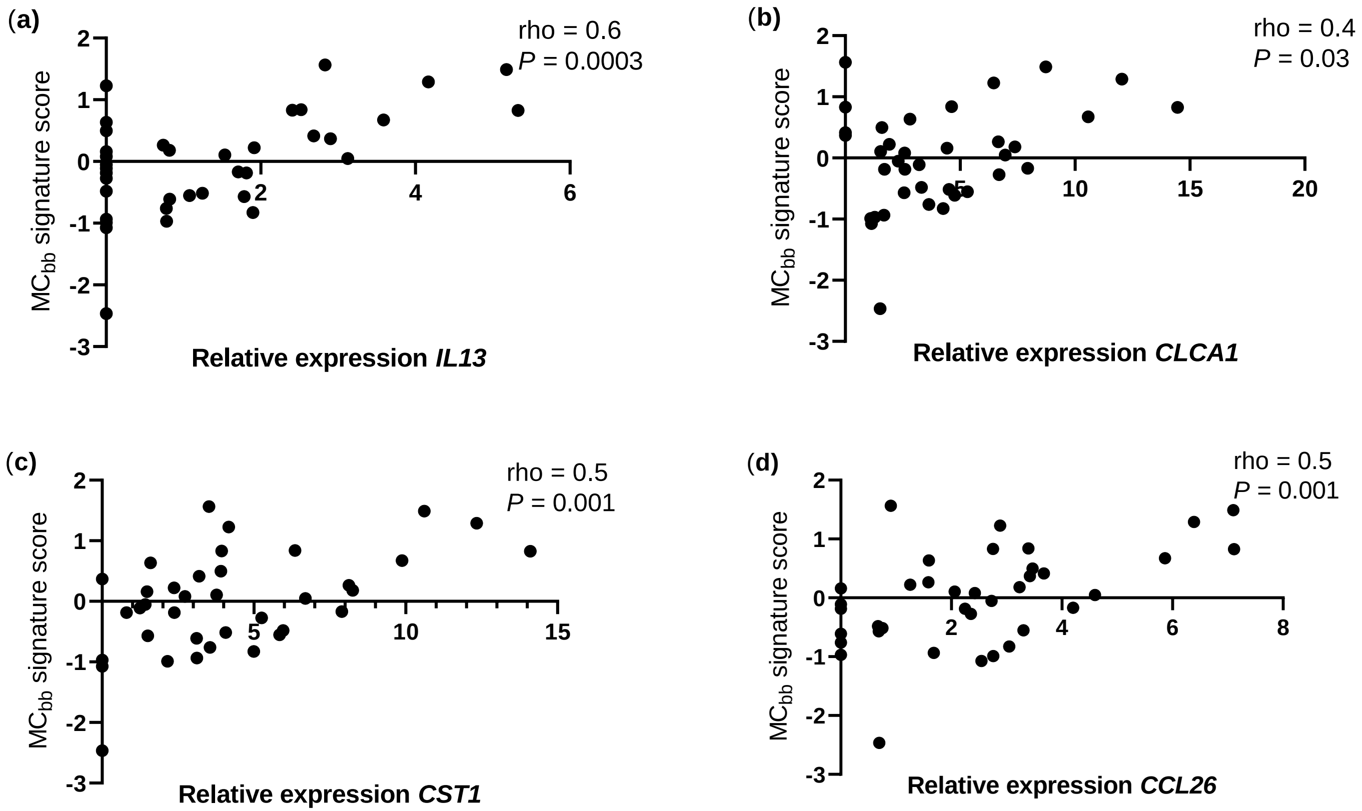
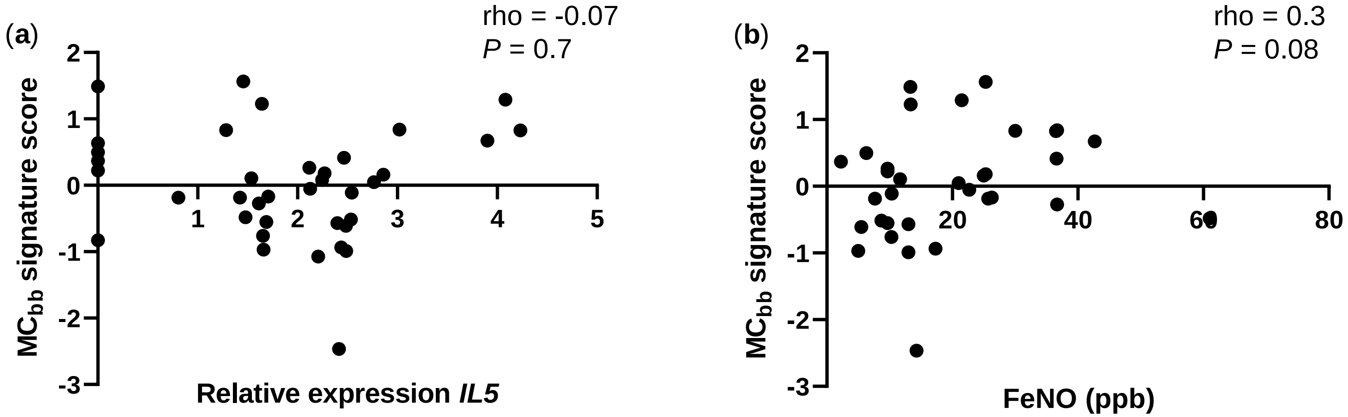


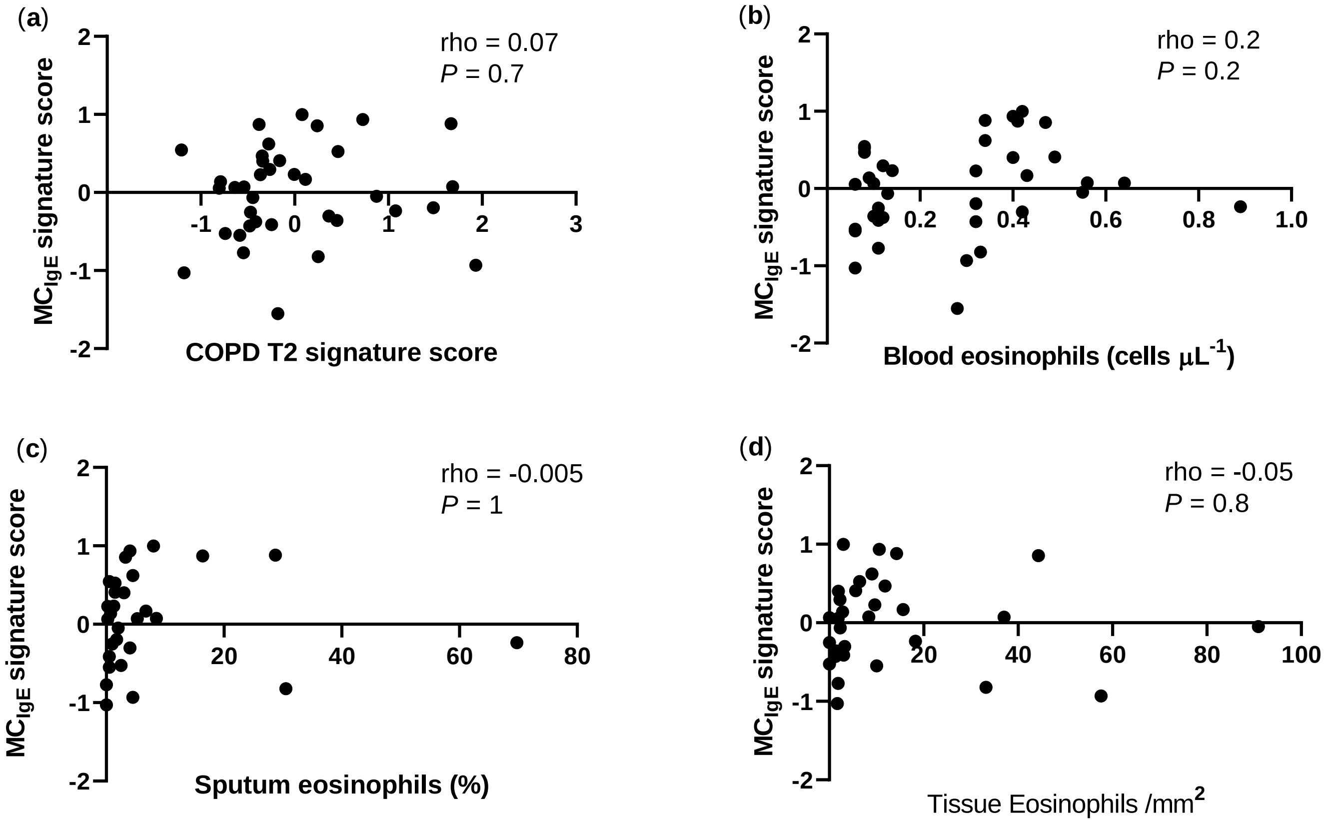
Supplementary figure 1. Bronchial brushing mast cell gene expression in eosinophil^{low} and eosinophil^{high} COPD patients. RNA sequencing was used to examine the expression of (a - c) acute IgE signatures, (d) IL-33 signature, (e) LPS signature, and (f) IFN-γ signature in n = 17 eosinophil^{low} and n = 20 eosinophil^{high} COPD patients. Data presented as individual values where the black horizontal line represents the median.



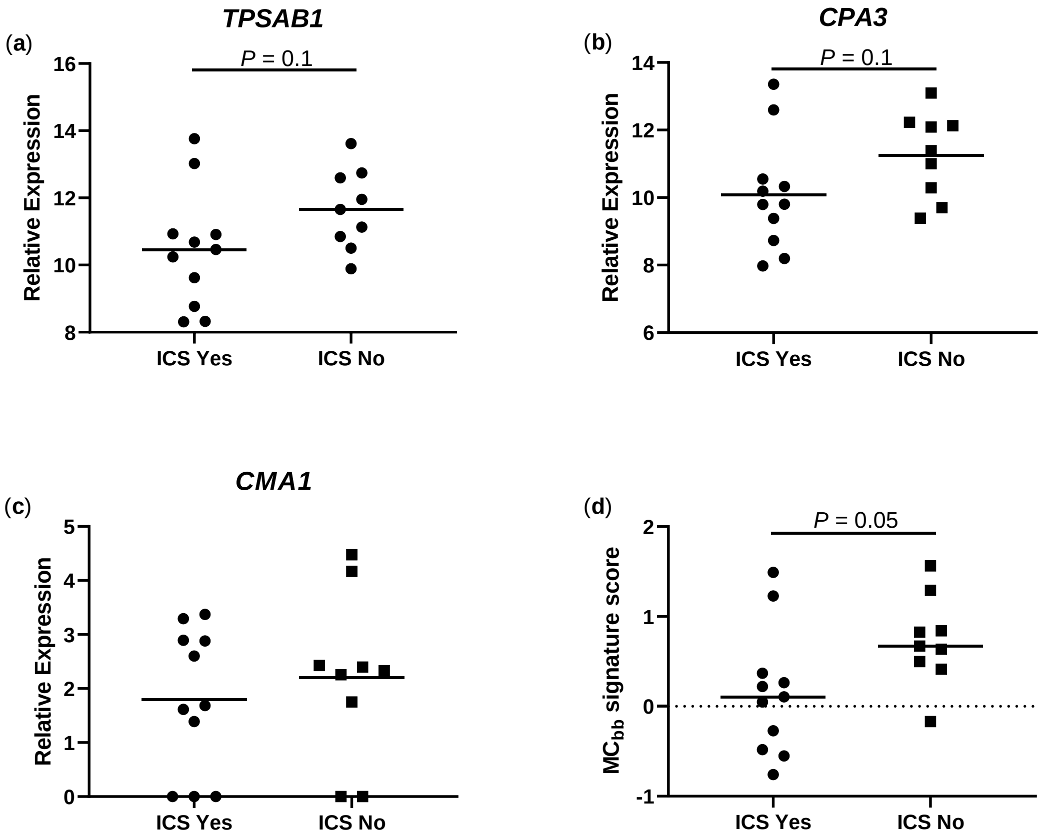
Supplementary figure 2. Correlations between bronchial brushing mast cell gene expression and T2 biomarkers. RNA sequencing was used to examine correlations between the MC_{bb} signature and (**a**) *IL13*, (**b**) *CLCA1*, (**c**) *CST1*, and (**d**) *CCL26*. Data analysed by Spearman correlation.



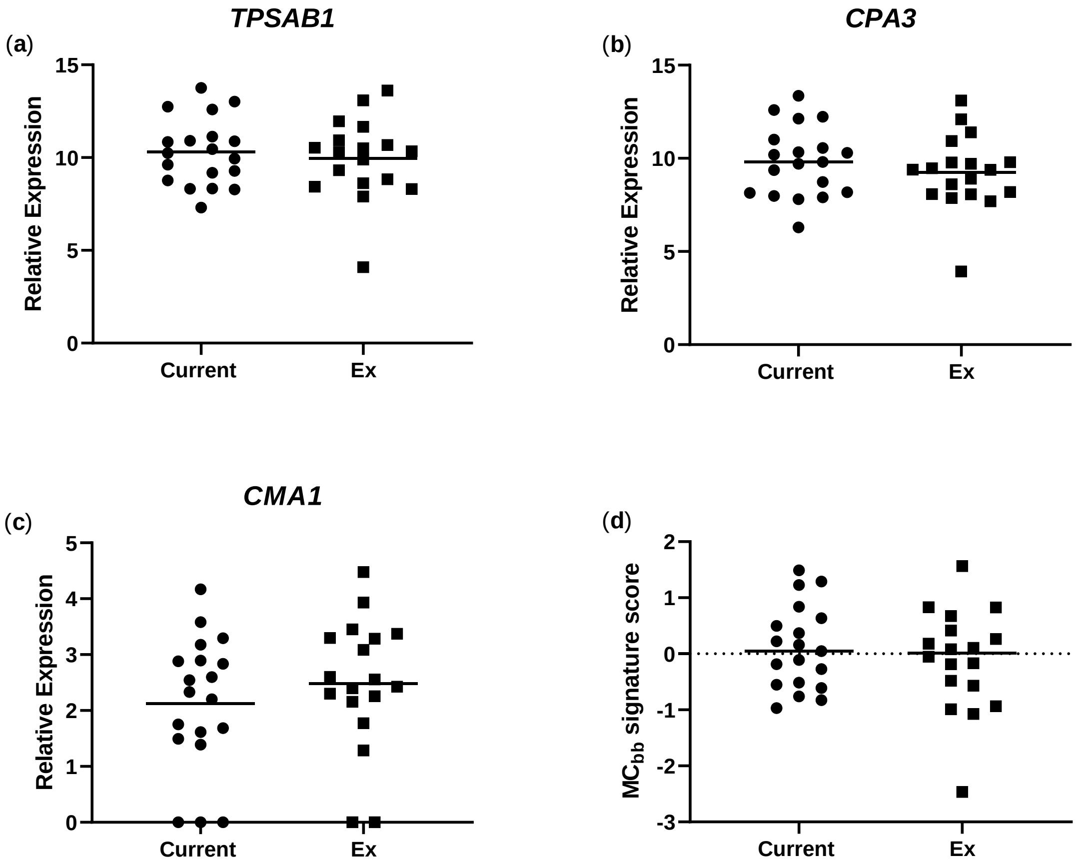
Supplementary figure 3. Correlations between bronchial brushing mast cell gene expression and T2 biomarkers. RNA sequencing was used to examine correlations between the MC_{bb} signature and (**a**) *IL5* and (**b**) FeNO. Data analysed by Spearman correlation.



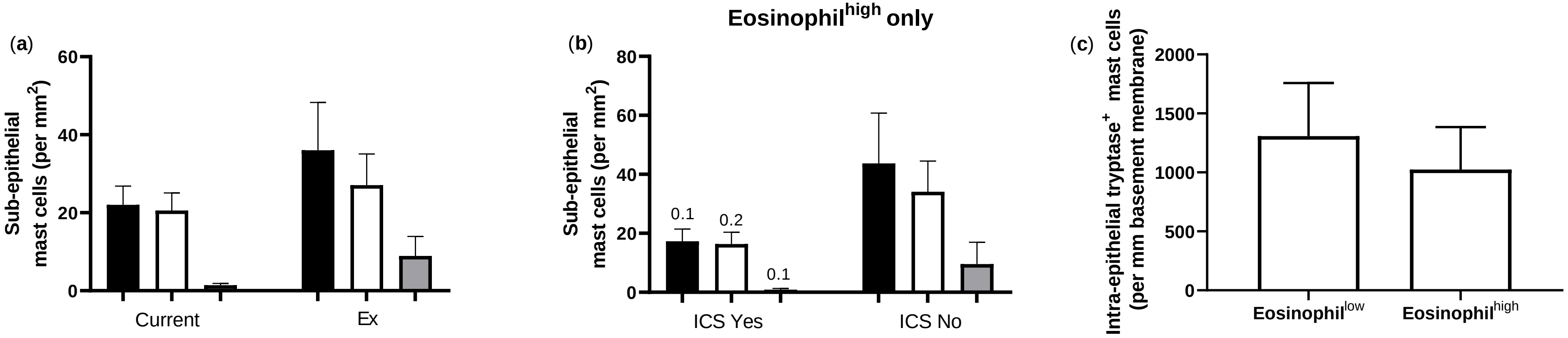
Supplementary figure 4. Correlations between bronchial brushing mast cell gene expression and T2 biomarkers. RNA sequencing was used to examine correlations between the MC_{IgE} signature and (**a**) COPD T2 signature, (**b**) blood eosinophils, (**c**) sputum eosinophils, and (**d**) bronchial biopsy eosinophils. Data analysed by Spearman correlation.



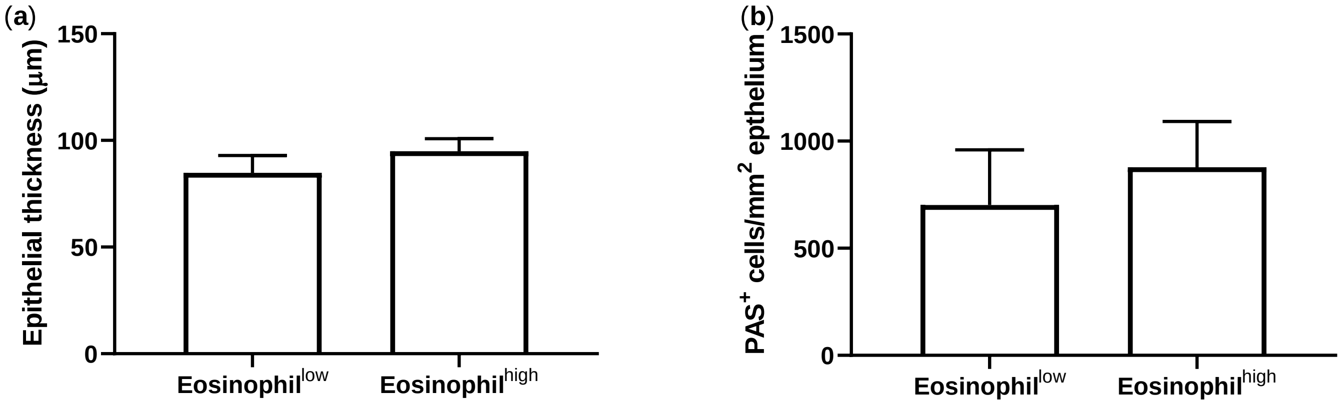
Supplementary figure 5. Bronchial brushing mast cell gene expression in ICS users and non-users in the eosinophil^{high} group only. RNA sequencing was used to examine the expression of (**a**) *TPSAB1*, (**b**) *CPA3*, (**c**) *CMA1*, and (**d**) MC_{bb} signature in ICS users (ICS yes; n=11) vs non-users (ICS no; n=9). Data presented as individual values where the black horizontal line represents the mean (**a** – **c**) or median (**d**).



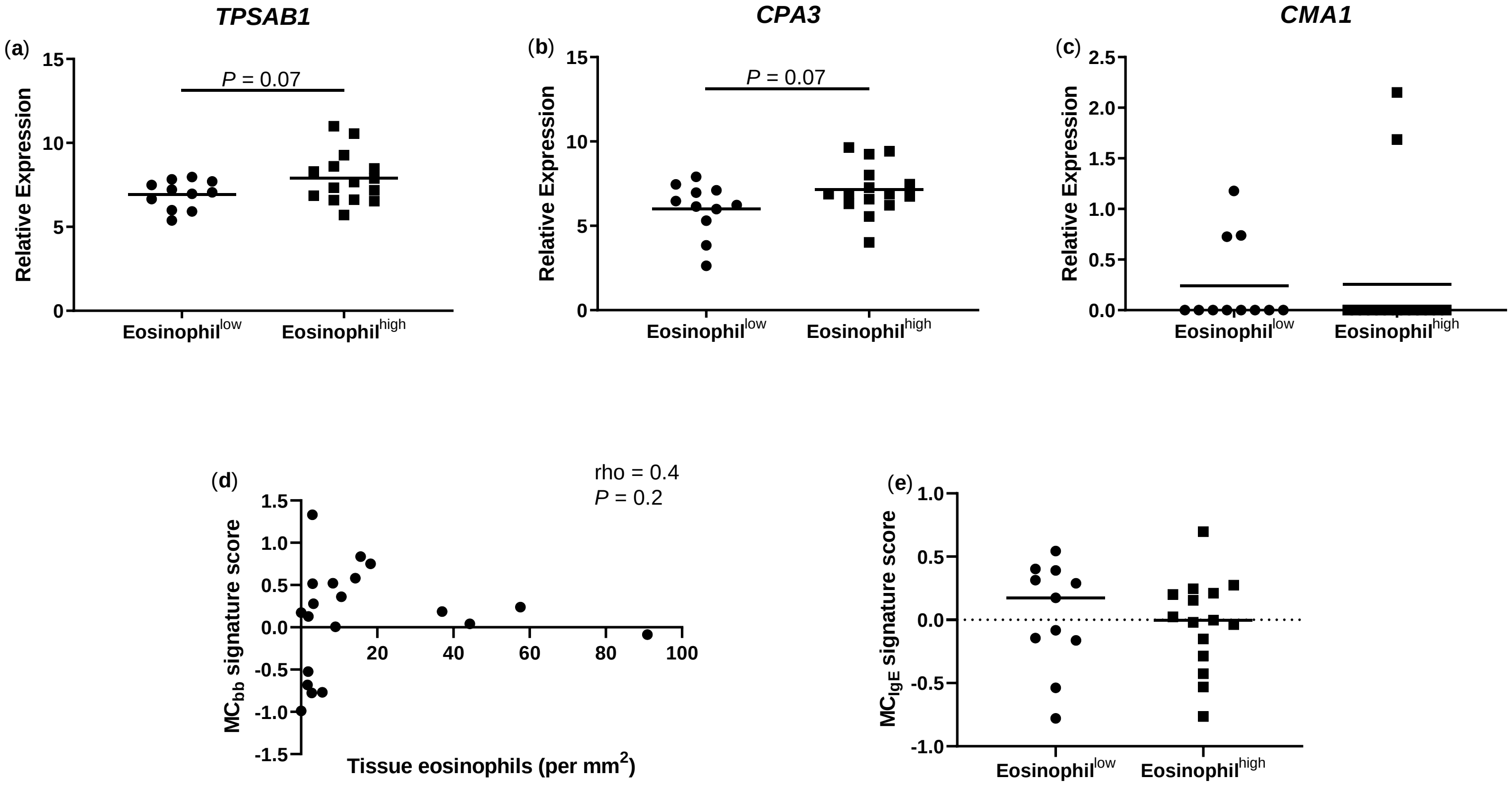
Supplementary figure 6. Bronchial brushing mast cell gene expression in current vs ex-smokers. RNA sequencing was used to examine the expression of (**a**) *TPSAB1*, (**b**) *CPA3*, (**c**) *CMA1*, (**d**) MC_{bb} signature signature in current smokers (n=19) vs ex-smokers (n=18). Data presented as individual values where the black horizontal line represents the mean (**a** – **c**) or median (**d**).



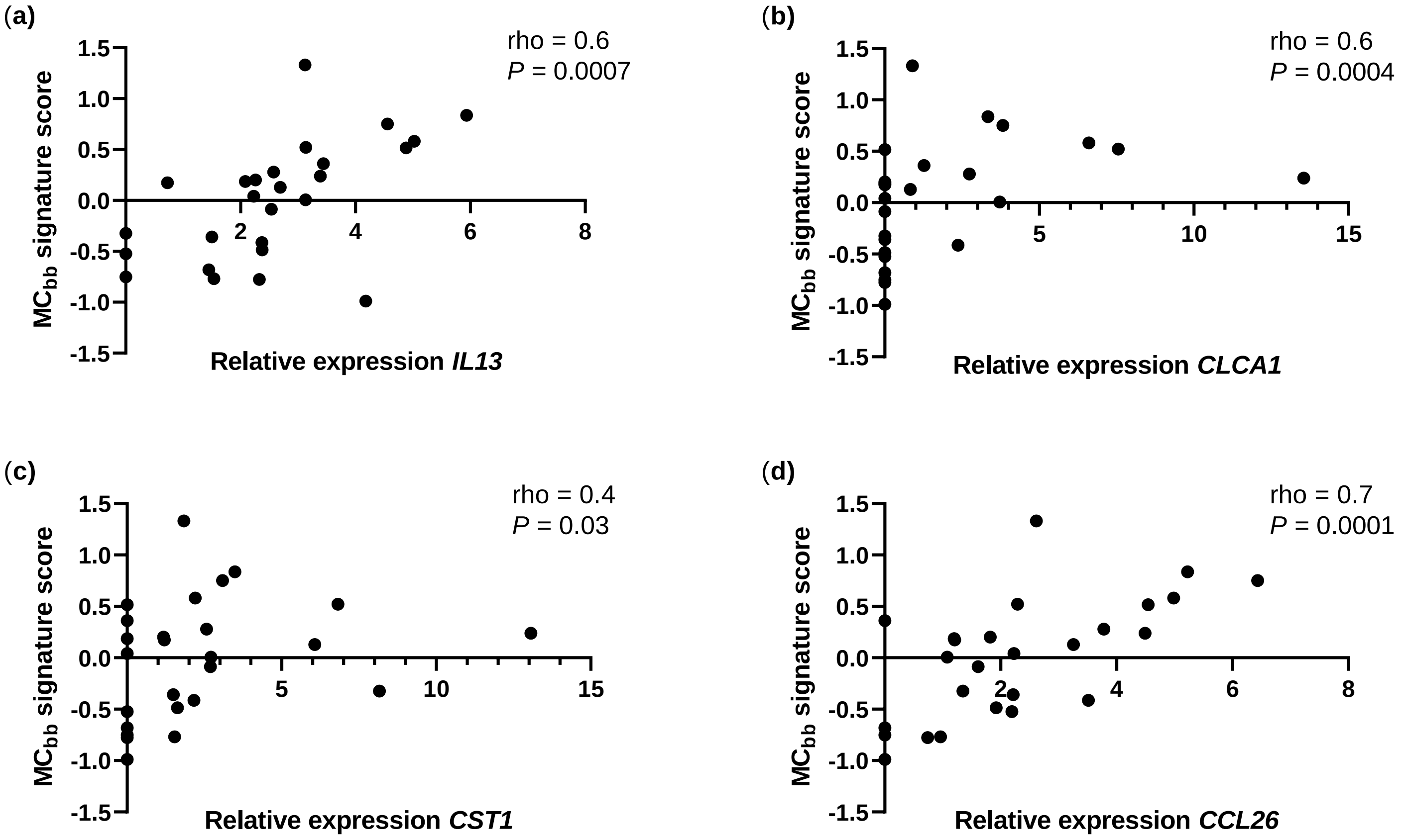
Supplementary figure 7. Mast cell quantification in bronchial biopsies. The number of sub-epithelial tryptase$^+$ (M_T), tryptase$^+$chymase$^+$ (M_{TC}) and the total number of mast cells (M_T + M_{TC}) were quantified by immunofluorescence and counts were normalised to area. Comparisons were made between current vs ex-smokers (**a**; n=12 vs n=11) ICS users vs non-users in the eosinophil^{high} group only (**b**; n=7 vs n=6). The number of intra-epithelial tryptase$^+$ mast cells were quantified by immunohistochemistry and counts were normalised to basement membrane length (c).



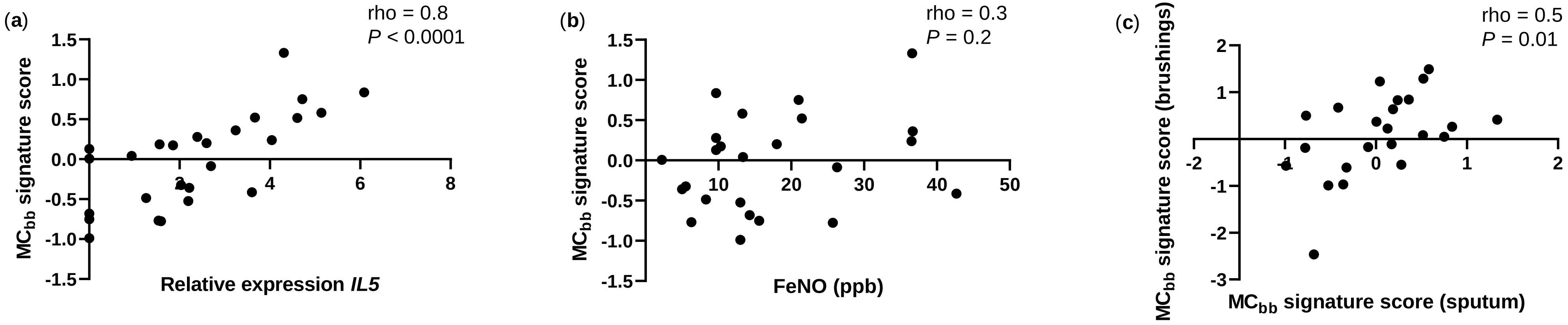
Supplementary figure 8. Other histological measures in bronchial biopsies. The epithelial thickness (**a**) and the number of PAS$^+$ cells (**b**) were compared between groups.



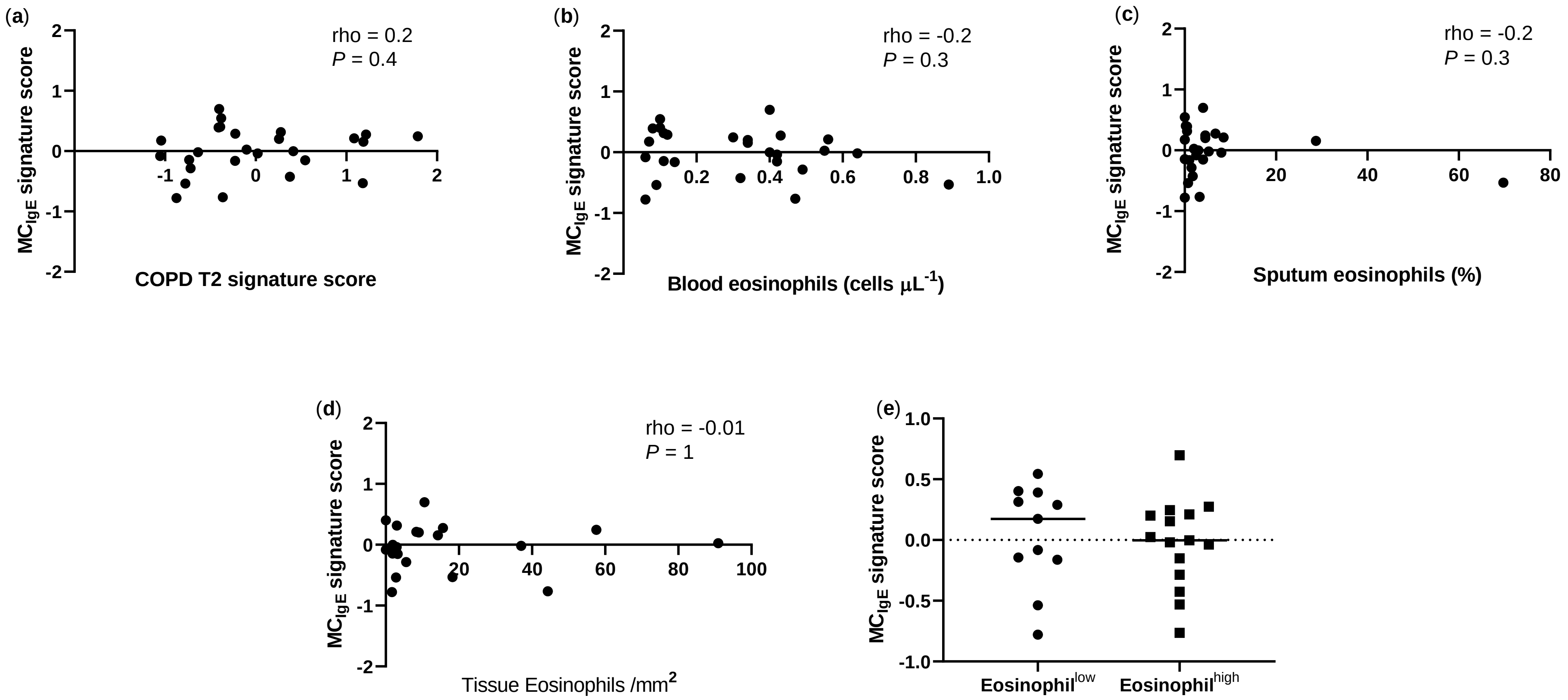
Supplementary figure 9. Sputum mast cell gene expression in eosinophil^{low} and eosinophil^{high} COPD patients. RNA sequencing was used to examine the expression of (**a**) *TPSAB1*, (**b**) *CPA3*, (**c**) *CMA1*, (**d**) correlations between the MC$_{bb}$ signature and bronchial biopsy eosinophils and (**e**) MC$_{IgE}$ signature in n = 11 eosinophil^{low} and n = 15 eosinophil^{high} COPD patients.



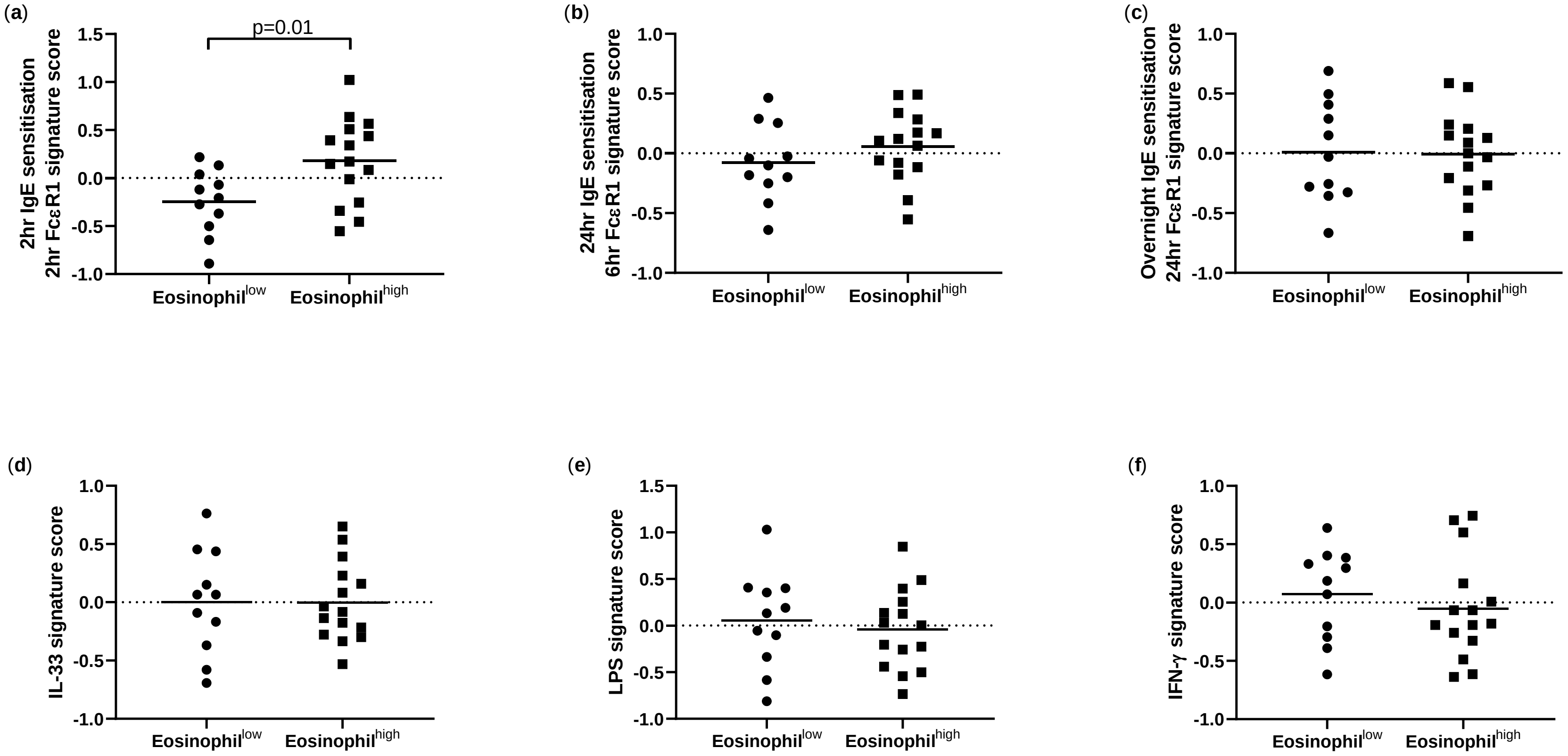
Supplementary figure 10. Correlations between sputum mast cell gene expression and T2 biomarkers. RNA sequencing was used to examine correlations between the MC$_{bb}$ signature and (**a**) *IL13*, (**b**) *CLCA1*, (**c**) *CST1*, and (**d**) *CCL26*. Data analysed by Spearman correlation.



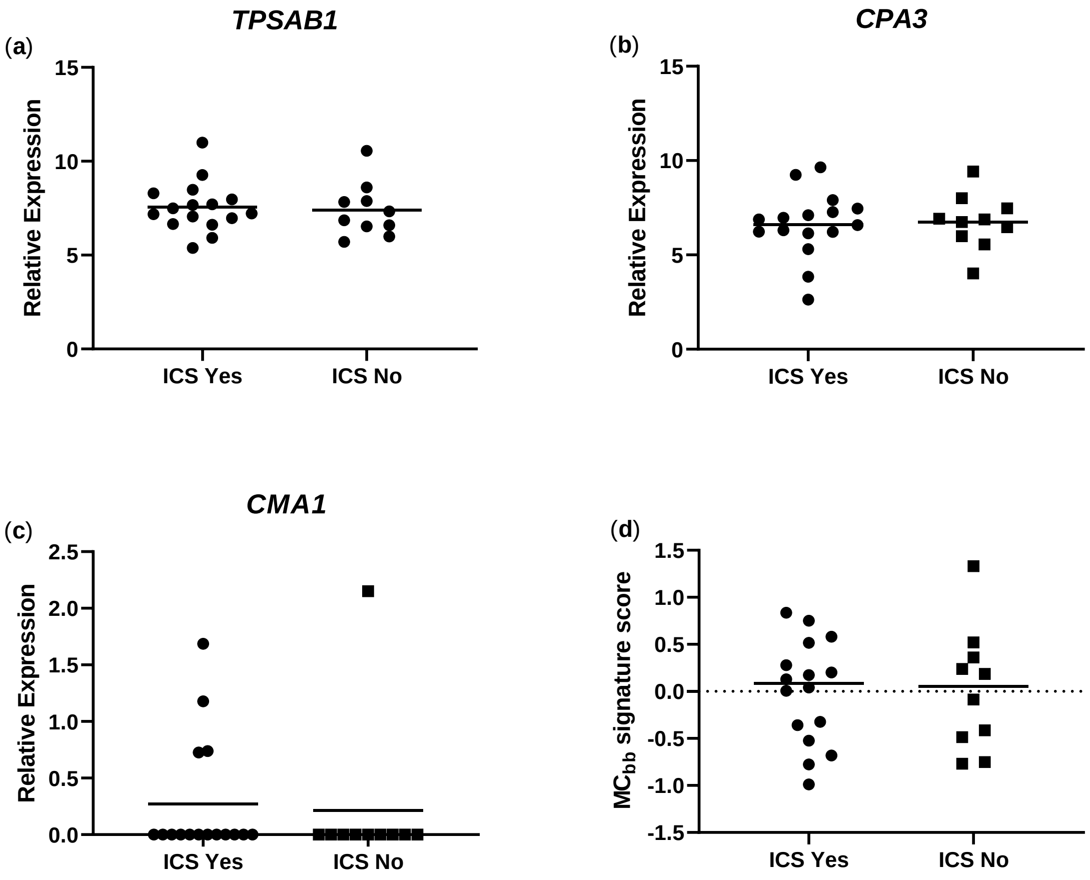
Supplementary figure 11. Correlations between sputum mast cell gene expression and T2 biomarkers. RNA sequencing was used to examine correlations between the MC_{bb} signature and (**a**) *IL5*, (**b**) FeNO **(c)** bronchial brushing mast cell signature**.** Data analysed by Spearman correlation.



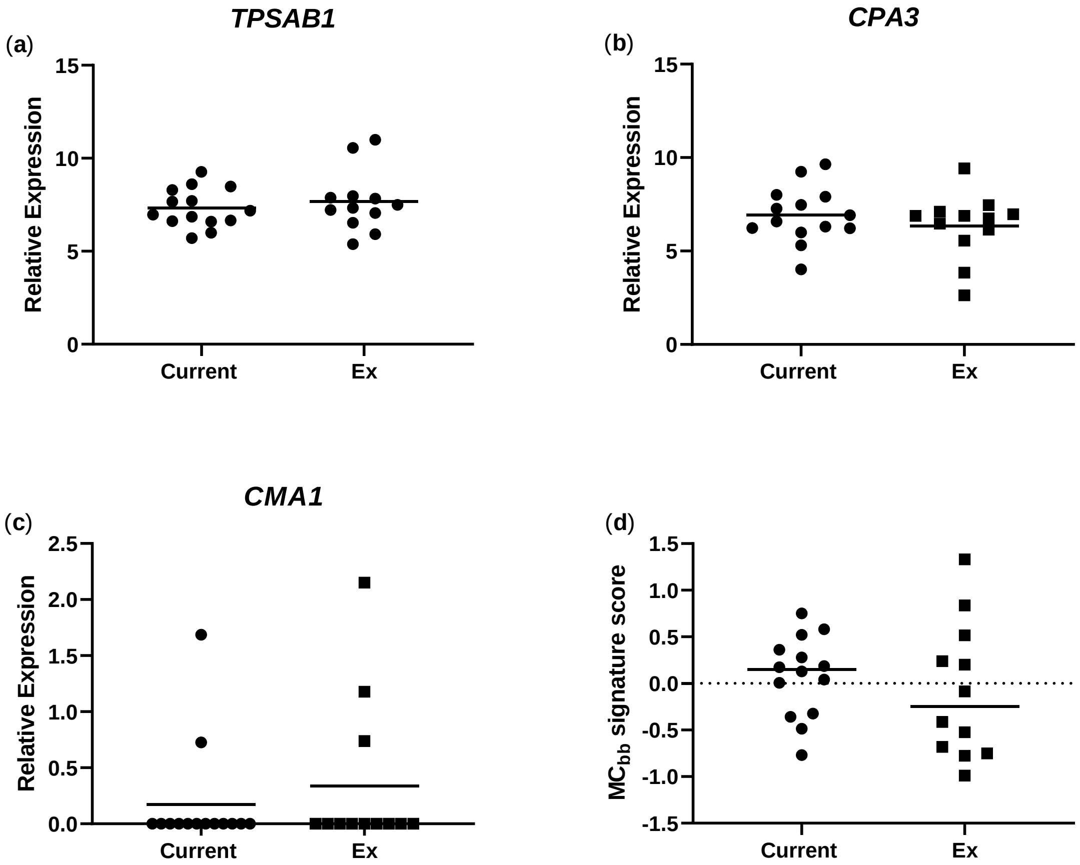
Supplementary figure 12. Sputum MC$_{IgE}$ gene expression and T2 biomarkers. RNA sequencing was used to examine correlations between the MC$_{IgE}$ signature and (**a**) COPD T2 signature, (**b**) blood eosinophils, (**c**) sputum eosinophils, and (**d**) bronchial biopsy eosinophils and compare MC$_{IgE}$ expression between eosinophil^{high} and eosinophil^{low} groups **(e).** Data analysed by Spearman correlation.



Supplementary figure 13. Sputum mast cell gene expression in eosinophil^{low} and eosinophil^{high} COPD patients. RNA sequencing was used to examine the expression of (a - c) acute IgE signatures, (d) IL-33 signature, (e) LPS signature, and (f) IFN-γ signature in n = 11 eosinophil^{low} and n = 15 eosinophil^{high} COPD patients. Data presented as individual values where the black horizontal line represents the median.



Supplementary figure 14. Sputum mast cell gene expression in ICS users and non-users. RNA sequencing was used to examine the expression of (**a**) *TPSAB1*, (**b**) *CPA3*, (**c**) *CMA1*, and (**d**) MC$_{bb}$ signature in ICS users (ICS yes; n=16) vs non-users (ICS no; n=10). Data presented as individual values where the black horizontal line represents the mean (**a** – **c**) or median (**d**).



Supplementary figure 15. Sputum mast cell gene expression in current vs ex-smokers. RNA sequencing was used to examine the expression of (**a**) *TPSAB1*, (**b**) *CPA3*, (**c**) *CMA1*, (**d**) MC_{bb} signature in current smokers (n=14) vs ex-smokers (n=12). Data presented as individual values where the black horizontal line represents the mean (**a** – **c**) or median (**d**).