**Figure 1A. CFBE iCFTR cells exposed to air-liquid interface culture (ALC) show enhanced AREG shedding compared to submerged culture on permeable inserts. AREG shedding is significantly higher in CFTR deficient cells (CFTR-) compared to CFTR induced cells CFTR+)**

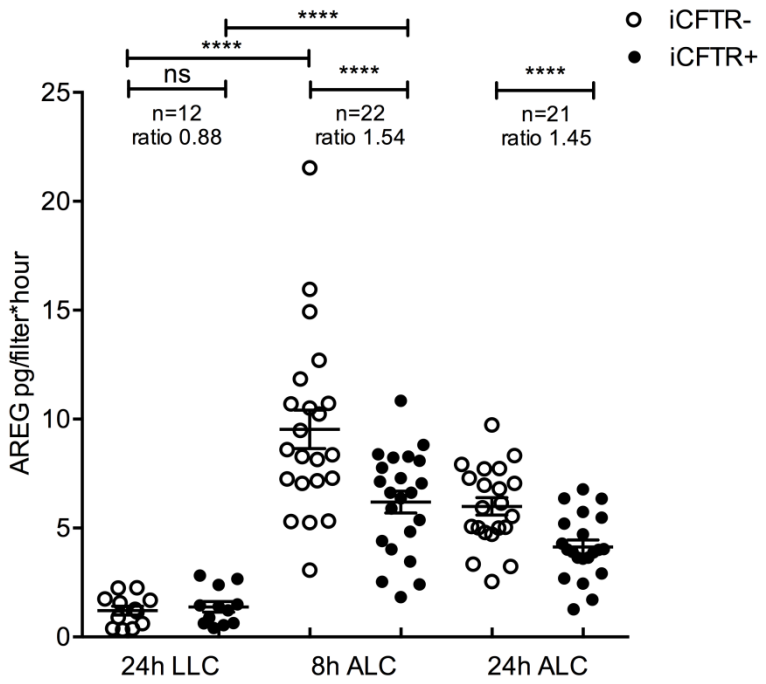


**Figure 1B. AREG shedding from CFTR iCFTR under air-liquid interface culture is inhibited by an inhibitor of EGFR ( AG1478) and of Src (PP2).**

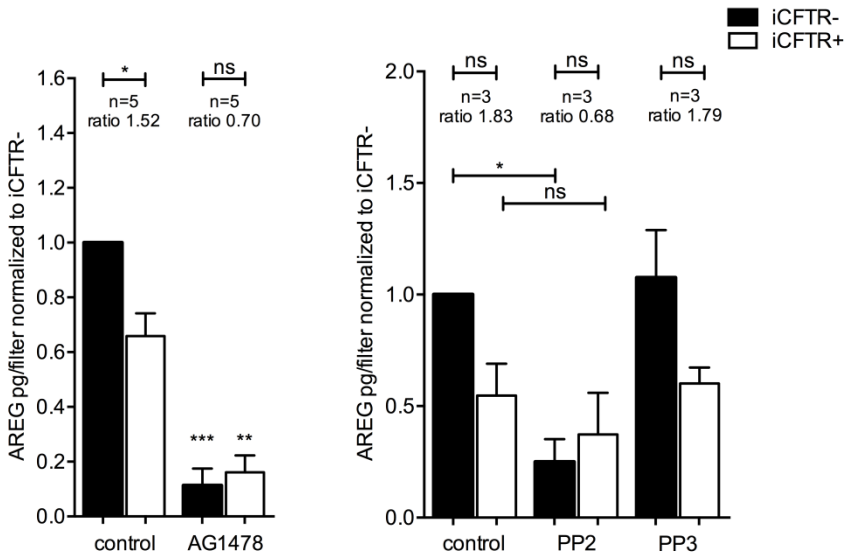

**Figure 2A. Cigarette smoke induces basolateral IL6R and AREG shedding in ALI PBEC from COPD and non COPD patients.**

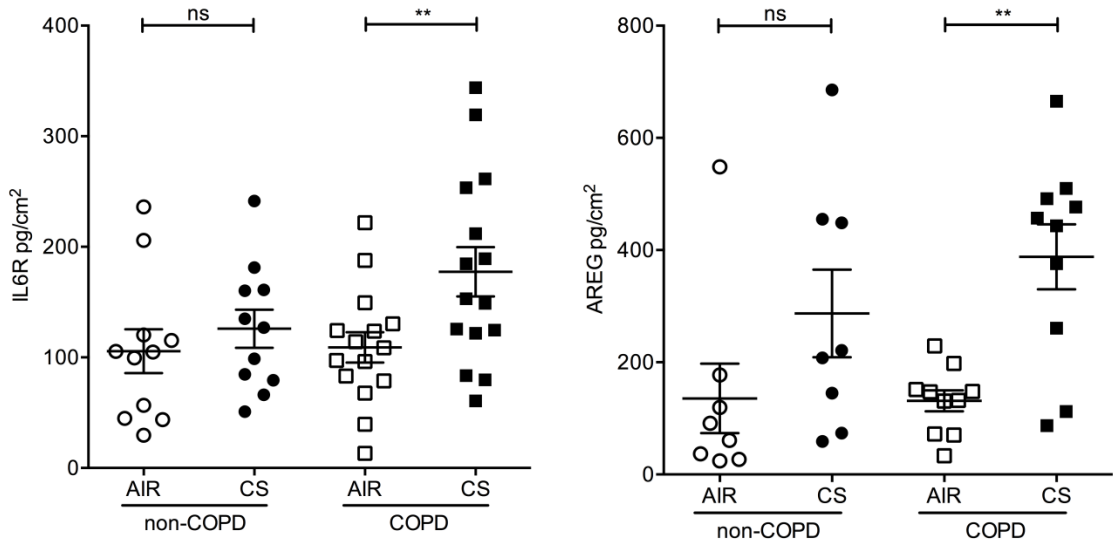


**Figure 2B Quantitative proximity ligation assay (PLA) three hours after CS exposure (Right upper red signal) compared to air exposed (left upper) shows increased interaction between ADAM17-P and its substrates AREG and IL6R in an intracellular compartment (lower panels). Red lines indicate non-specific signal levels in control experiments.**

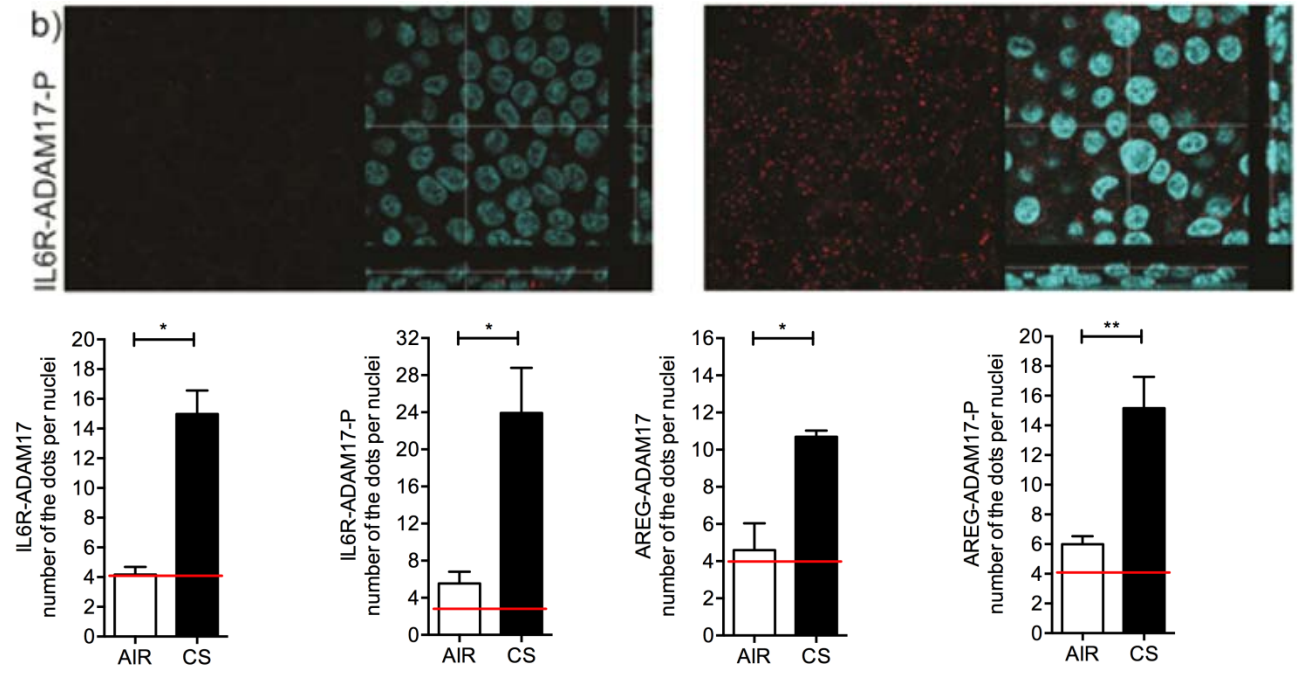

**Figure 2C Cigarette smoke treatment results in a transient increase of full length IL6R mRNA (a), and AREG (c) mRNA but not alternatively spliced IL6R mRNA (b). In COPD cells the increase of IL6R (d) and AREG (f) mRNA is significantly lower than in non-COPD cells.**

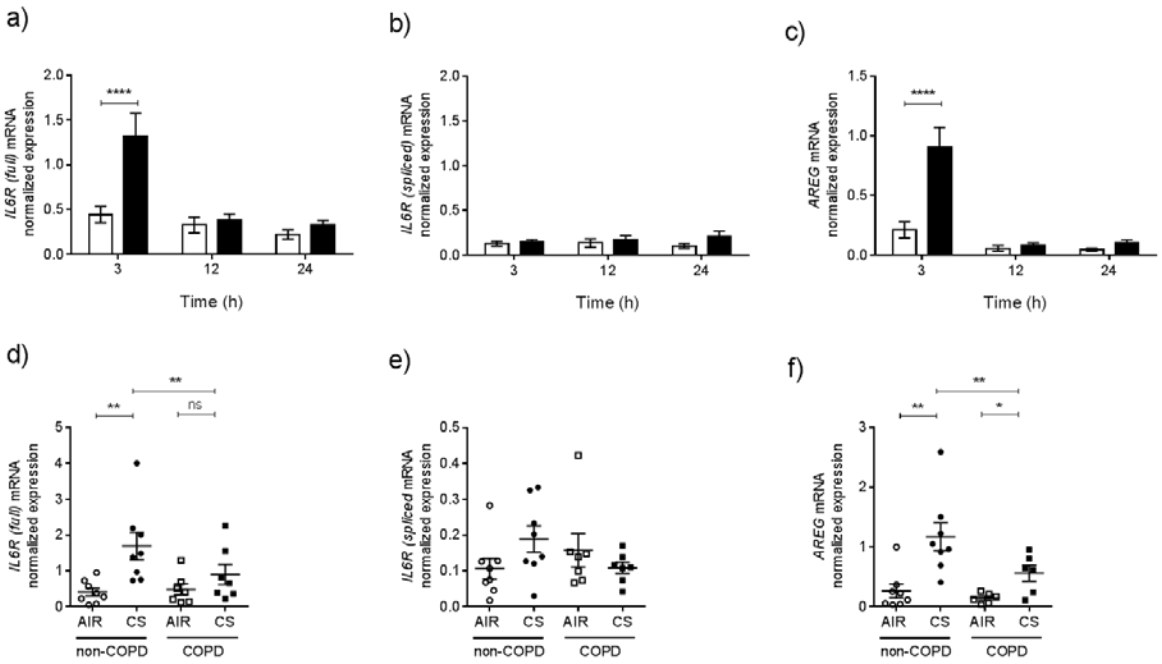


**Figure 2D. CS induced ADAM17 related AREG and IL6R shedding is inhibited by a specific ADAM17 inhibitor TMI-2 and by an EGFR inhibitor AG1478.**

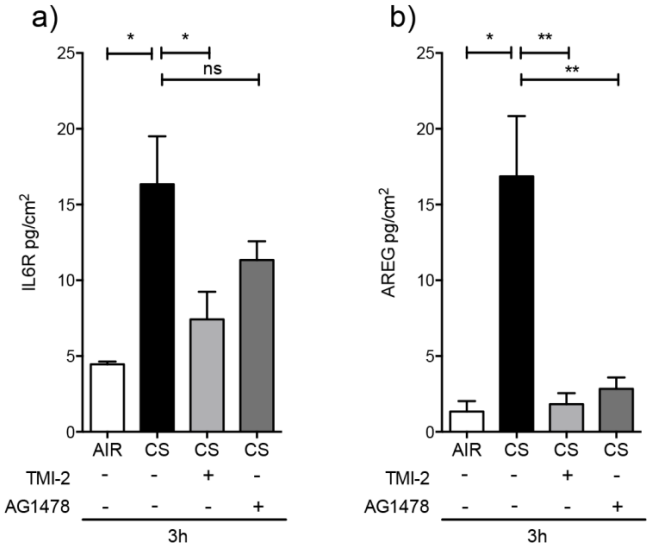

**Figure 2E CS induced full length IL6R (a), AREG (c) and IL8 (d) mRNA is inhibited by both a specific ADAM17 inhibitor TMI-2 and a EGFR inhibitor AG1478.**

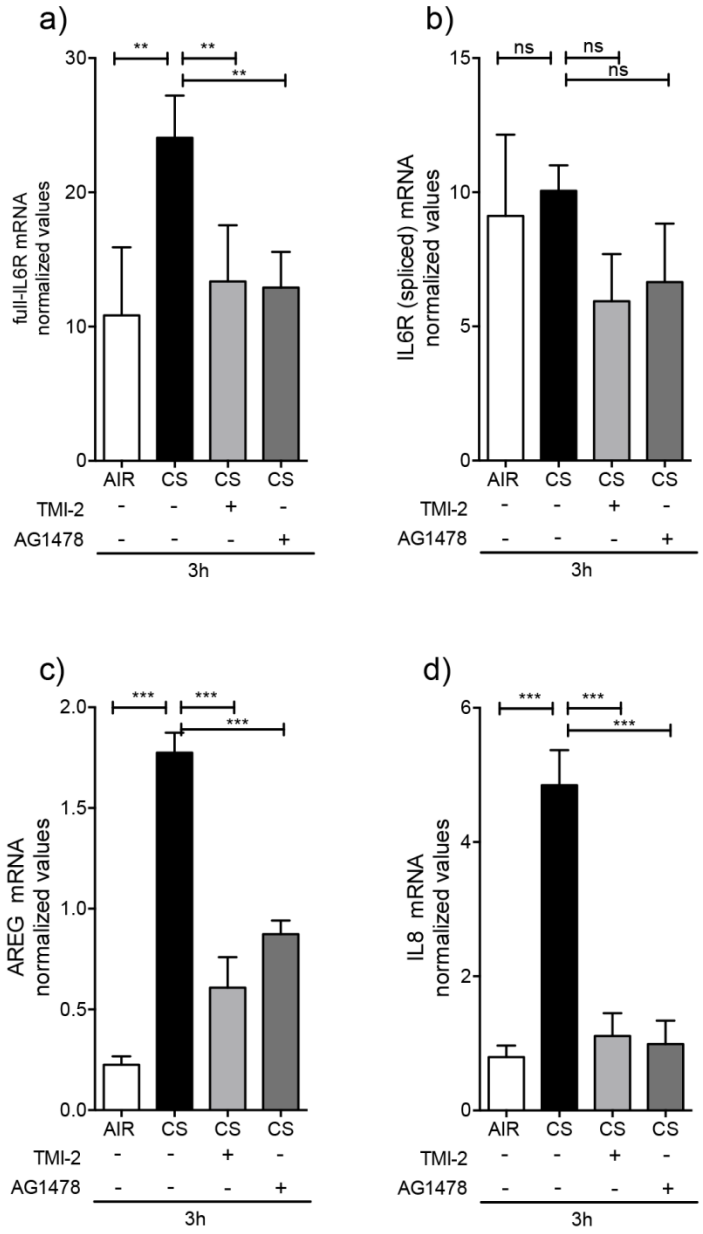

**Figure 3A Mass spectrocopy analysis of Broncho-Alveolar Lavage Fluid from CF infants (1-5 yr), can distinquish patients with high ● or low ● lung disease scores (CT scan, PRAGMA scores) in the oxidative stress lipid panel. Left: total disease score, middle: bronchiectasis, right: airtrapping.**

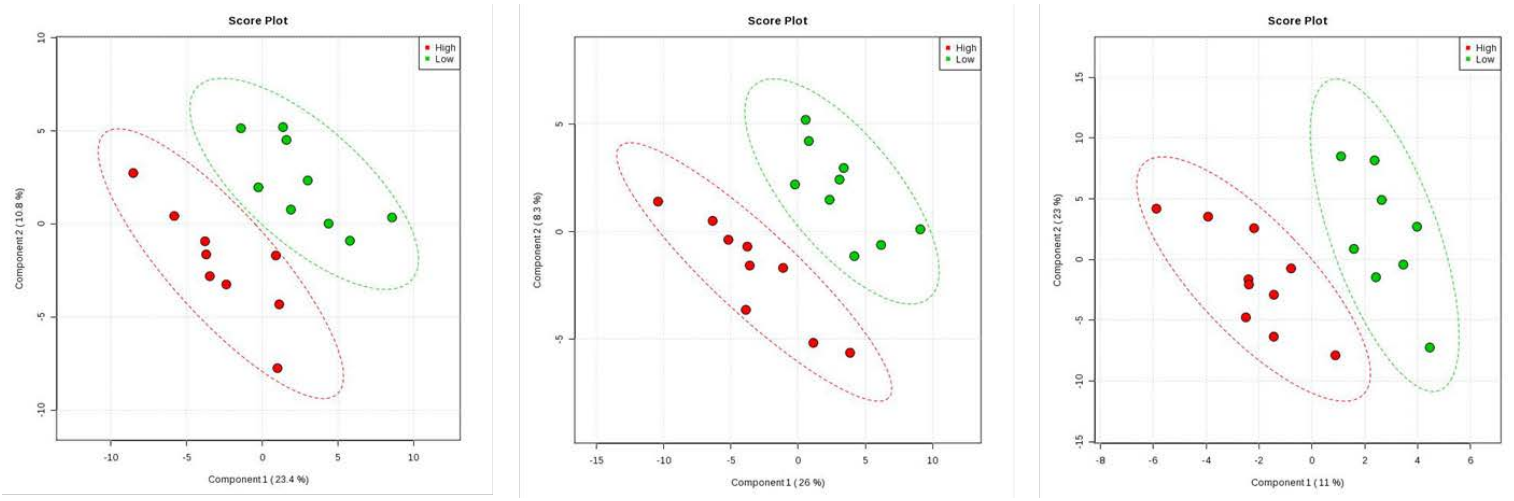


**Figure 3B Lysolipids including Lysolecithins and their derivative Lyso Phosphatidic Acids (LPA) correlate positively with PRAGMA CT scores in two independent series of 20 Infant CF BALF samples (Fisher correlation P<0.05, Rho 0.6). The LPA receptor is known to be involved in chronic lung disease, in particular IPF.**