

Figure 1: Dose response of Semagacestat in HNECs

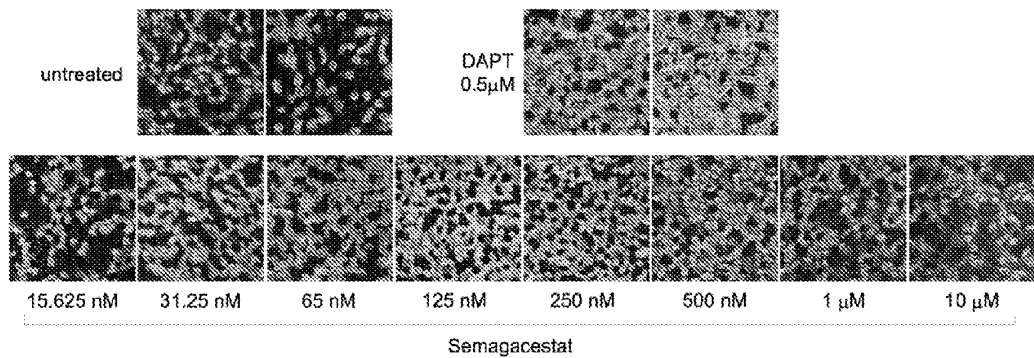


Figure 2: Ratio of MCCs to total luminal cells in HNECs treated with DAPT and various doses of semagacestat

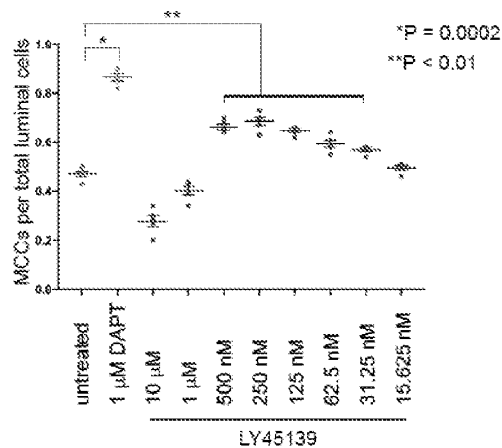


Figure 3: Mouse epithelial cells after 3-day systemic (IP) dosing

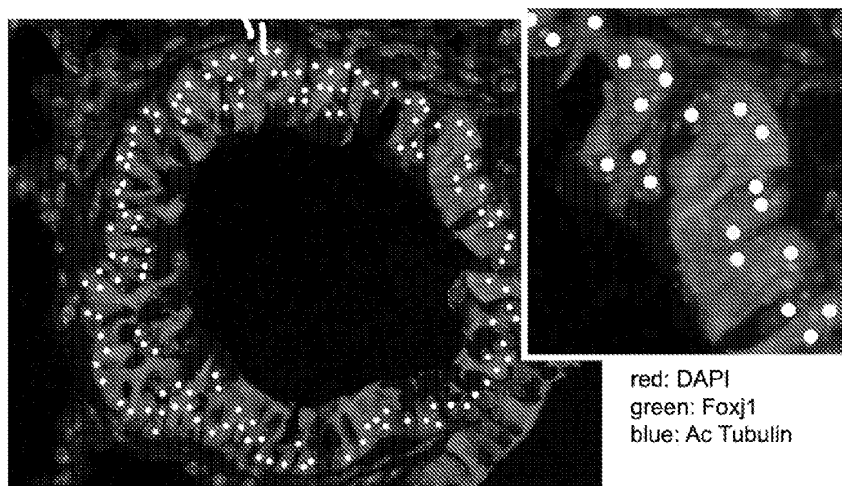


Figure 4: Body Weight at Days 9, 24 and 30 with daily systemic (IP) administration of semagacestat and vehicle control

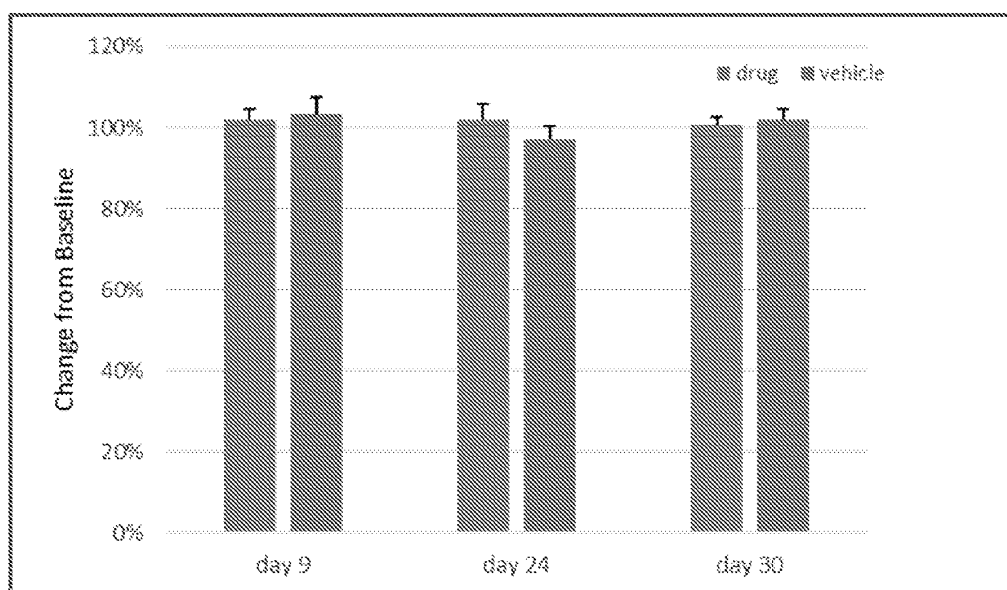


Figure 5: Ratio of MCCs to total cells at day 3 following treatment with DAPT and low and high doses of semagacestat

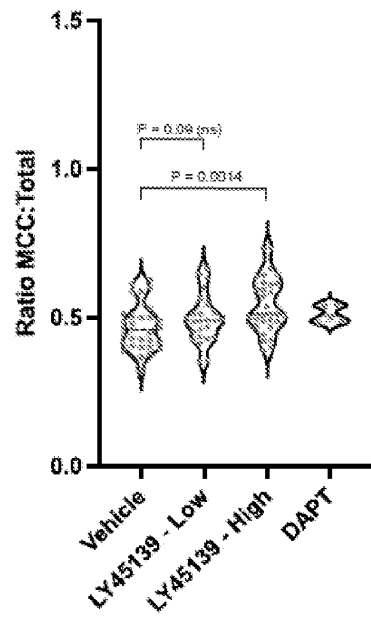


Figure 6: Ratio of MCCs to total cells at day 31 following treatment with semagacestat

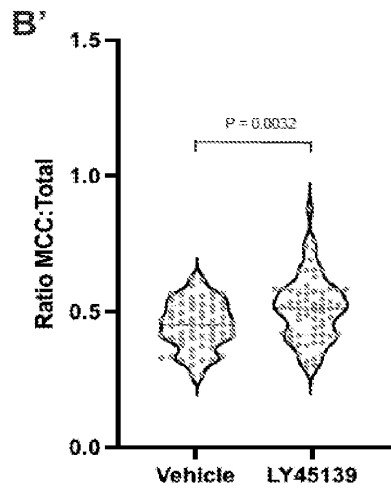


Figure 7: GSI Treatment Effects During Proliferation and Differentiation

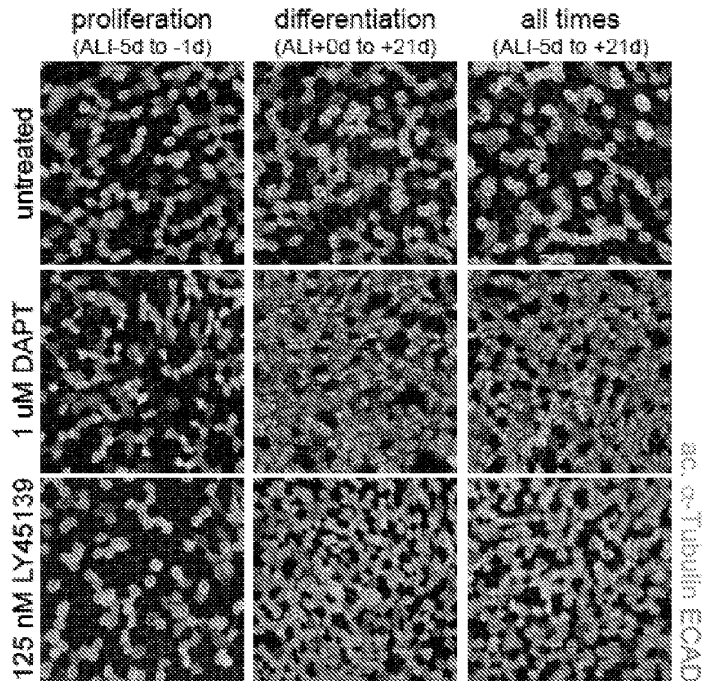


Figure 8: MCCs per total luminal cells for treatments in Figure 7

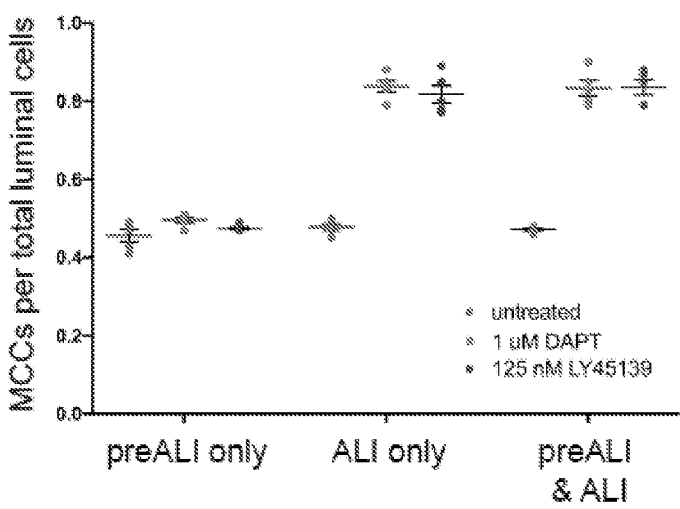


Figure 9: Effects of GSI treatment times on mature primary human airway epithelial cells

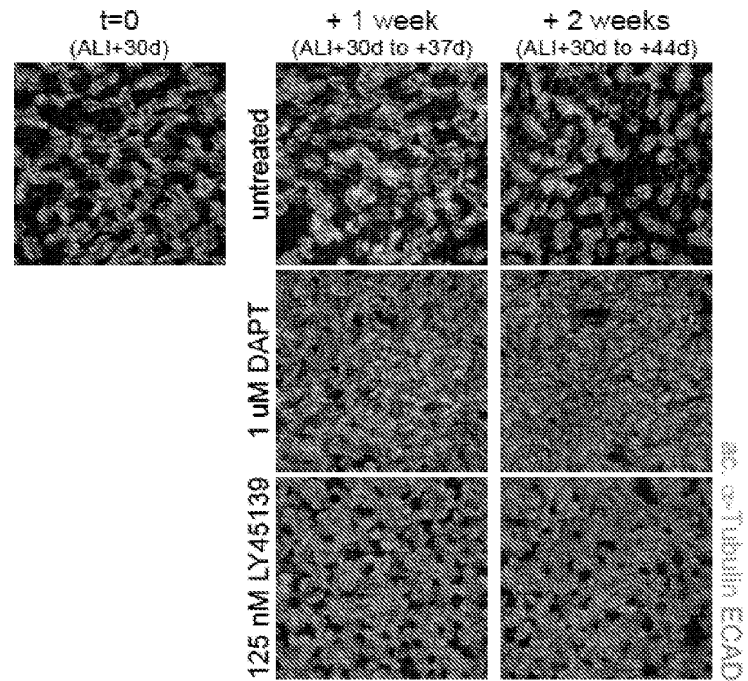


Figure 10: MCCs per total luminal cells for treatments in Figure 9

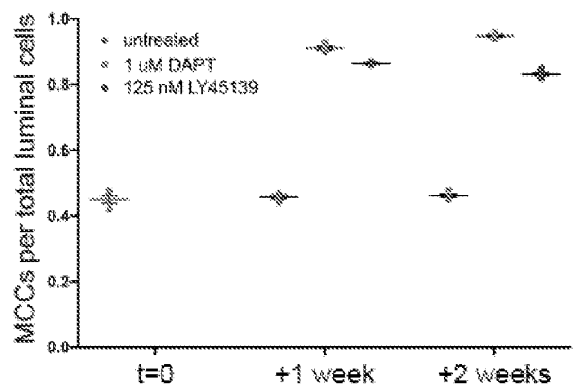


Figure 11: GSI Treatment Application from apical or basal surface

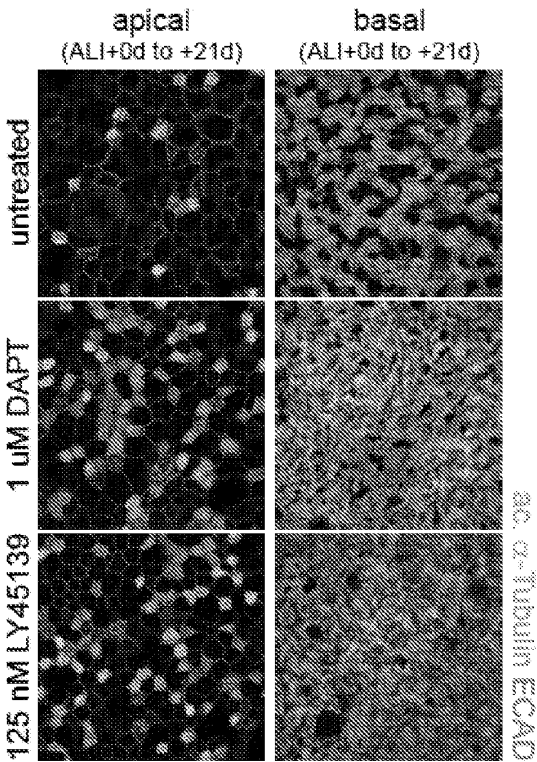


Figure 12: MCCs per total luminal cells for treatments in Figure 11

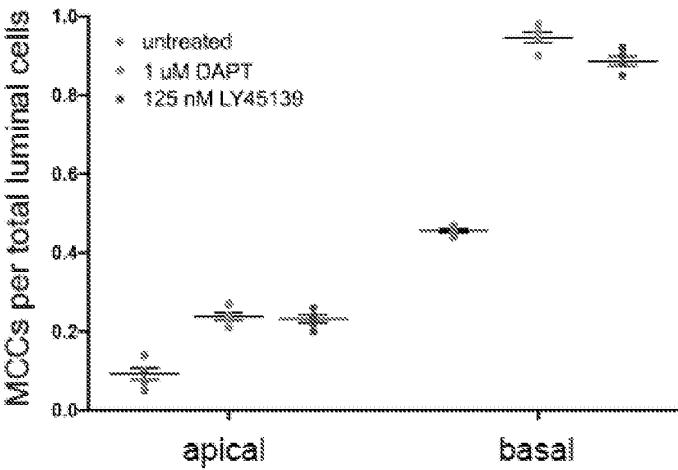


Figure 13: GSI treatment in IL-13 Chronic Inflammation model

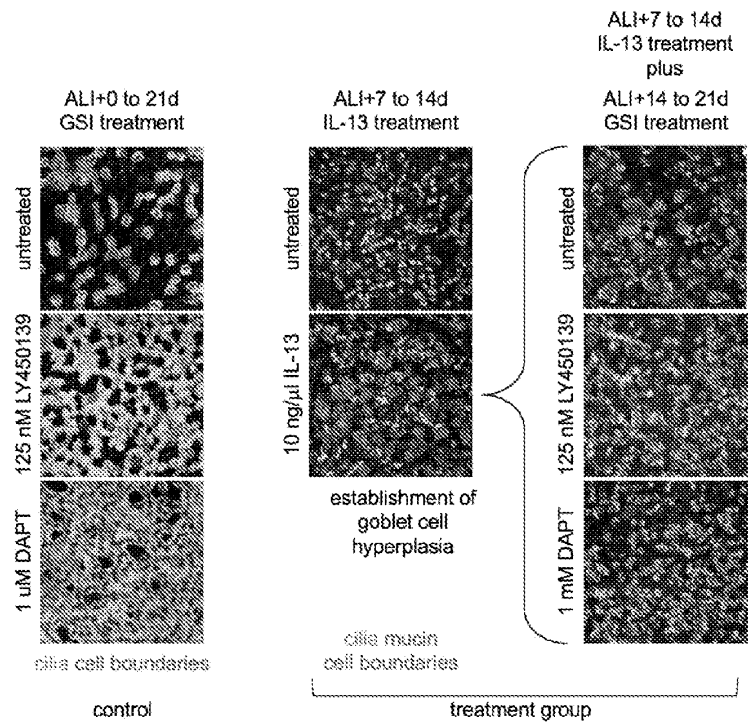


Figure 14: Ratio of MCCs per total luminal cells for treatments in Figure 13

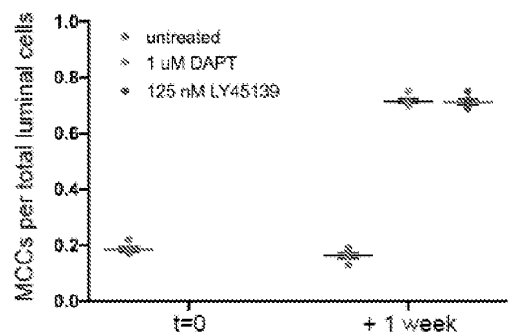


Figure 15: Representative Ussing Chamber Tracings of epithelial cell cultures treated with vehicle control, the CFTR modulator combination Elexacaftor-Tezacaftor-Ivacaftor (ETI), semagacestat (LY), or both (ETI+LY)

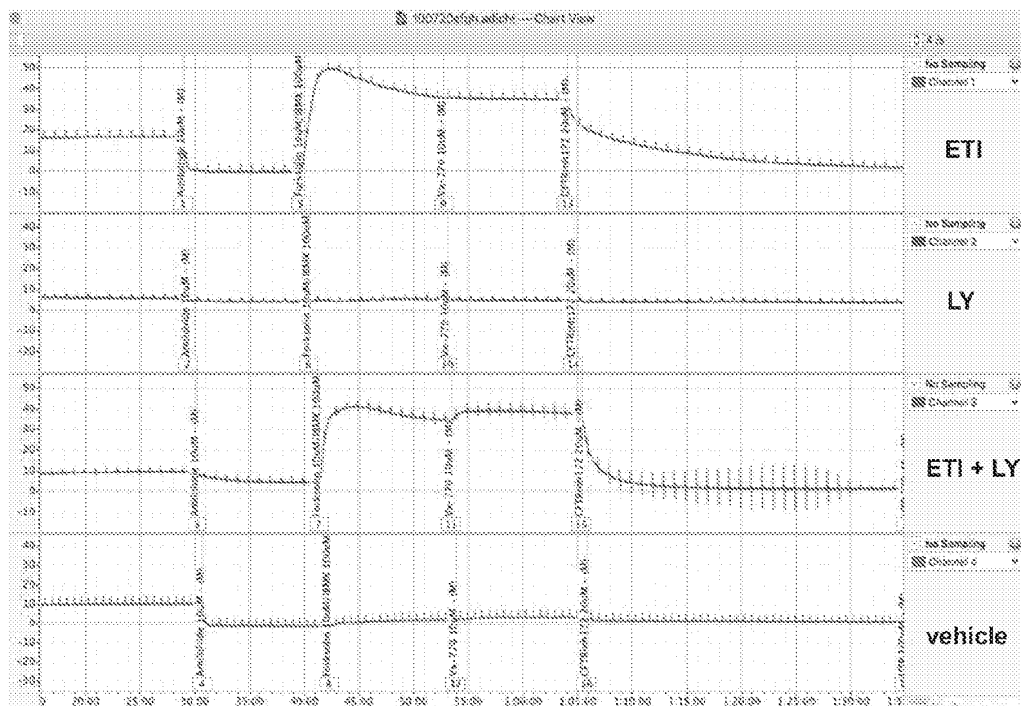


Figure 16: Ussing Short Circuit Currents, Representative Tracings

Healthy Subject



CF Subject



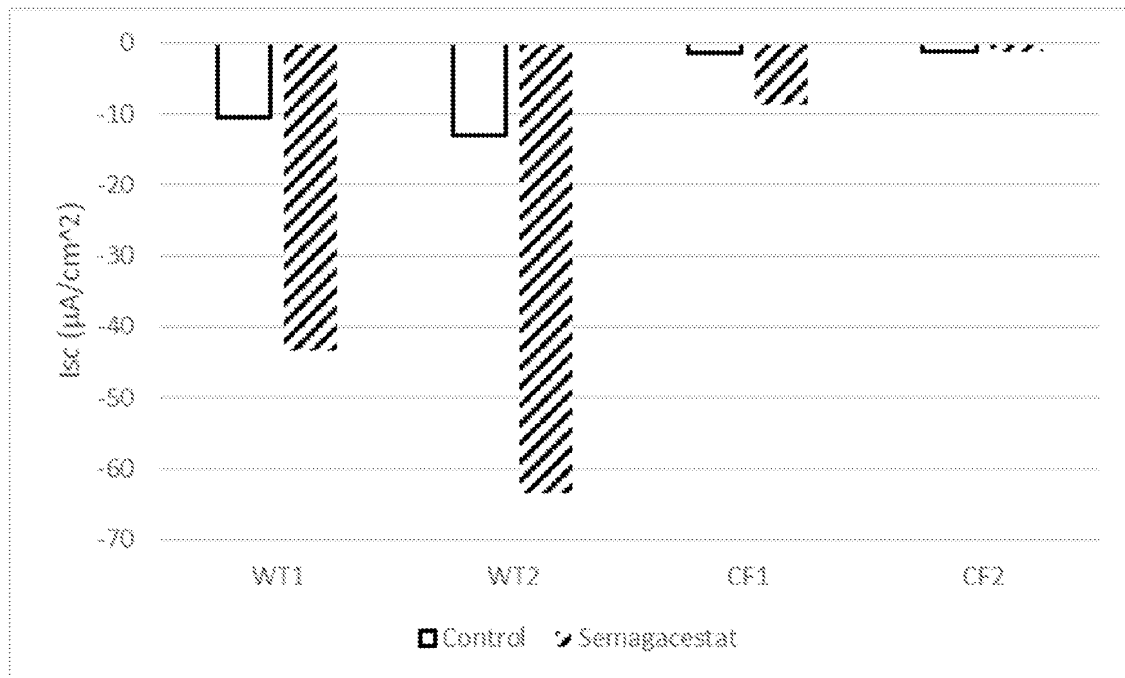
Figure 17: CFTR_{inh}-172 Isc Responses

Figure 18: Decreased Mucus Production in Human CF samples treated with semagacestat

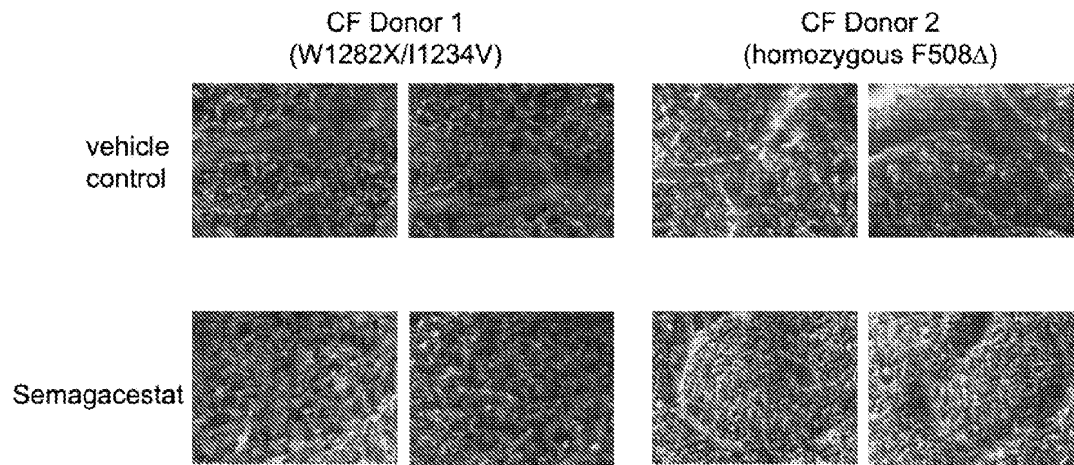


Figure 19: CF Samples following treatment with Semagacestat, Lumacaftor and combinations

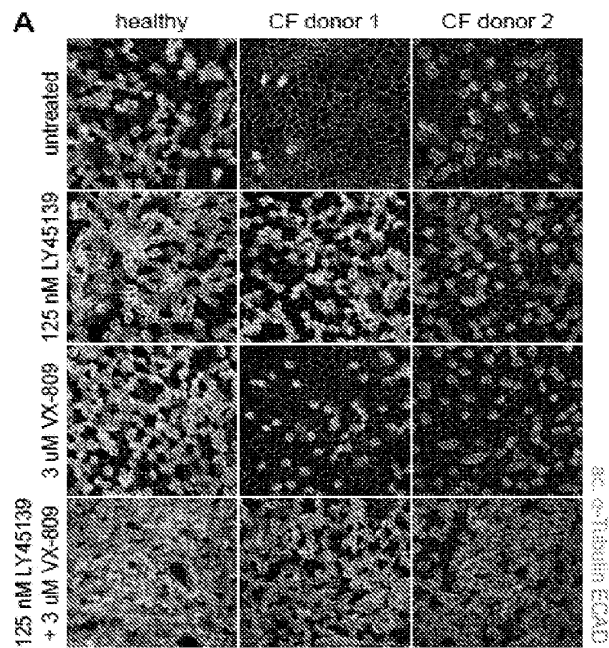


Figure 20: Ratio of MCCs to total luminal cells for treatments shown in Figure 19 for healthy and CF donor 1

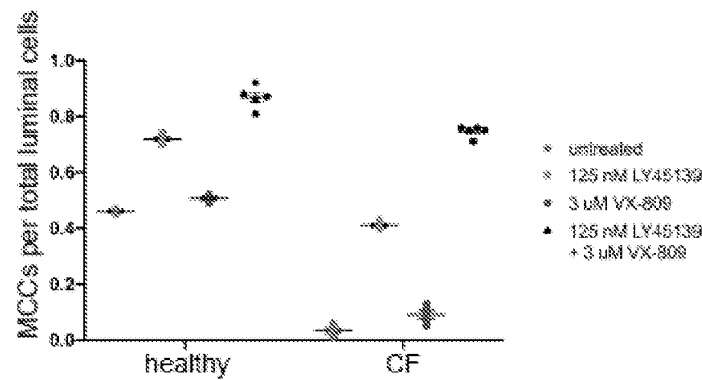


Figure 21: Effects on primary healthy and cystic fibrosis airway epithelial cells treated with semagacestat during differentiation

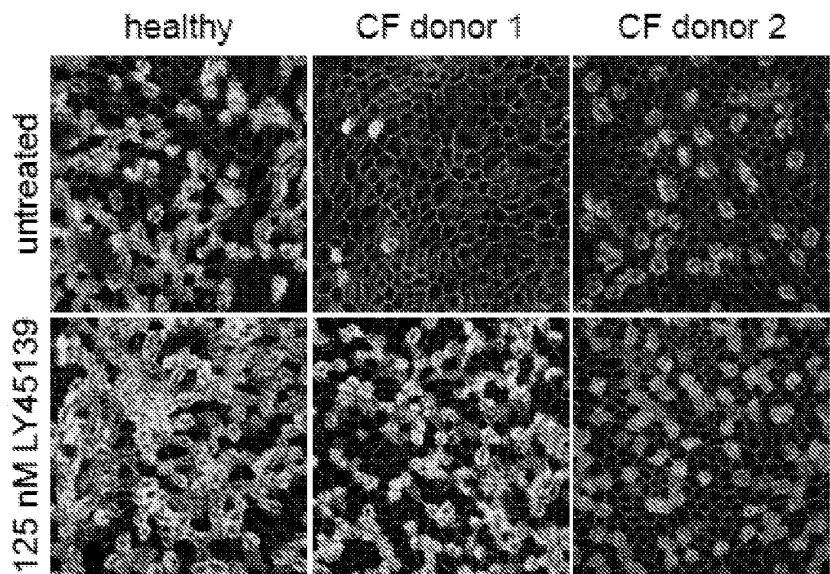


Figure 22: SEM of healthy and CF primary human airway epithelial cultures

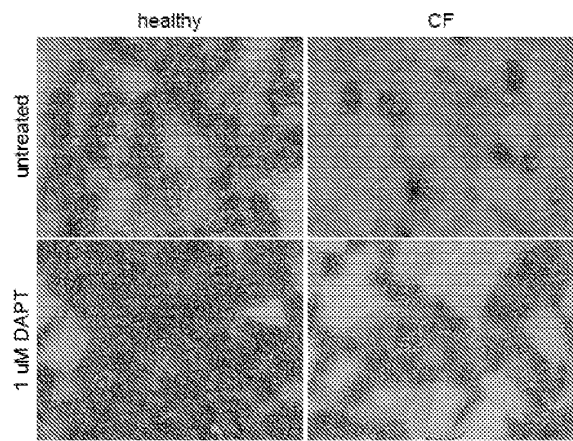


Figure 23: GSI treatment induces the formation of additional multiciliated cells in mature cystic fibrosis cultures

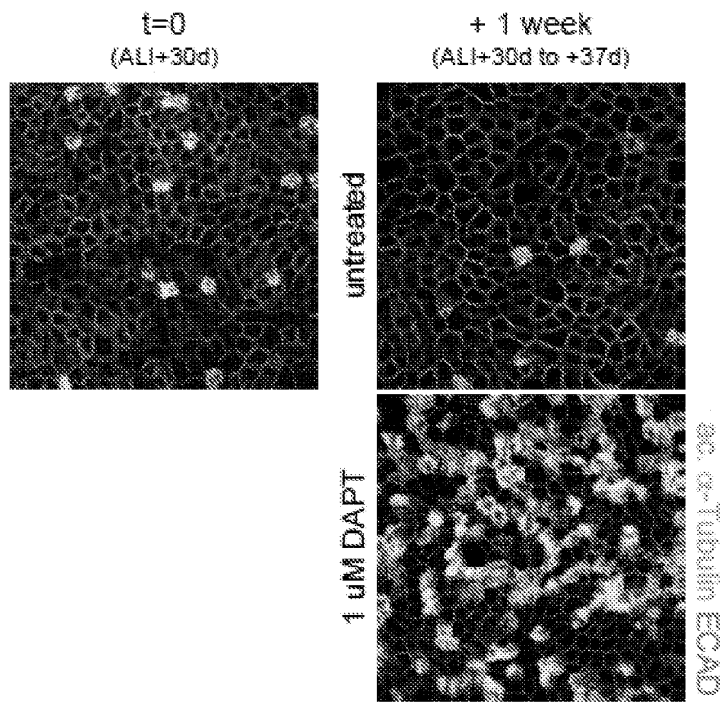


Figure 24: Primary human airway epithelial cells treated during differentiation with DAPT and high and low concentrations of various GSIs

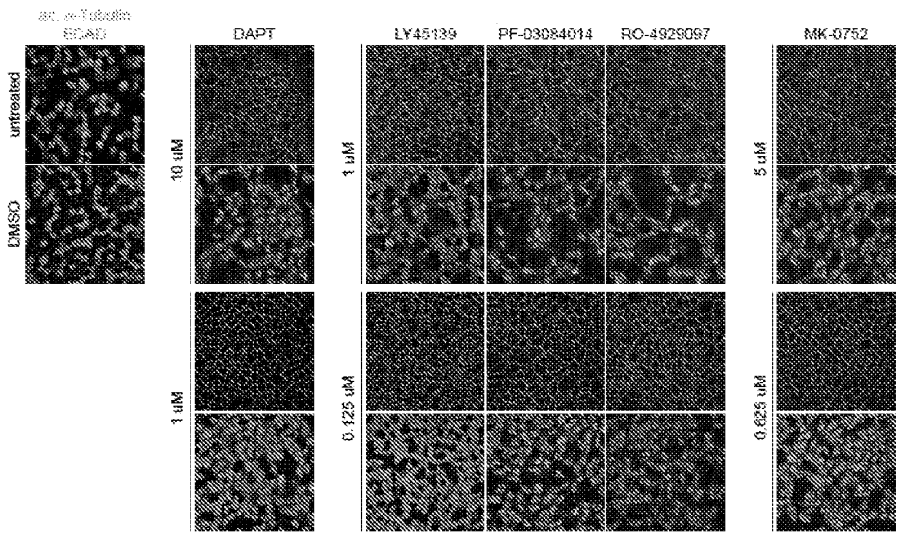


Figure 25: Ratio of MCCs to total luminal cells for treatments shown in Figure 24

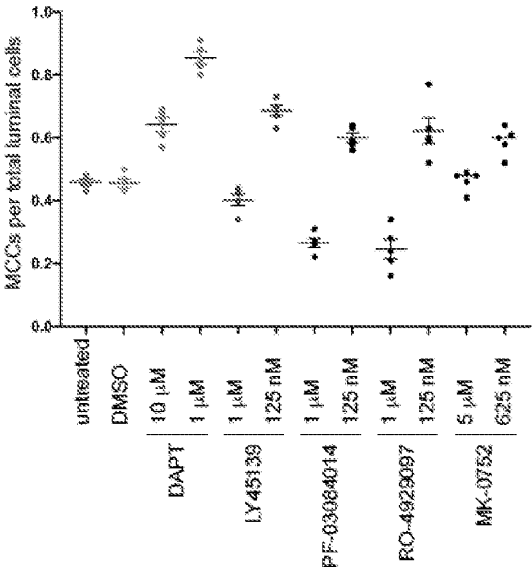


Figure 26: CFTR activity using Ussing chambers in cultures from CF patients treated with LY45139, ETI, or both.

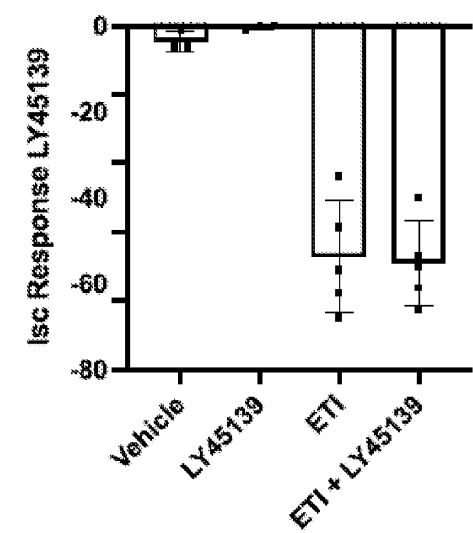


Figure 27: CFTR activity using Ussing chambers in cultures from CF patients treated with MK04752, ETI, or both

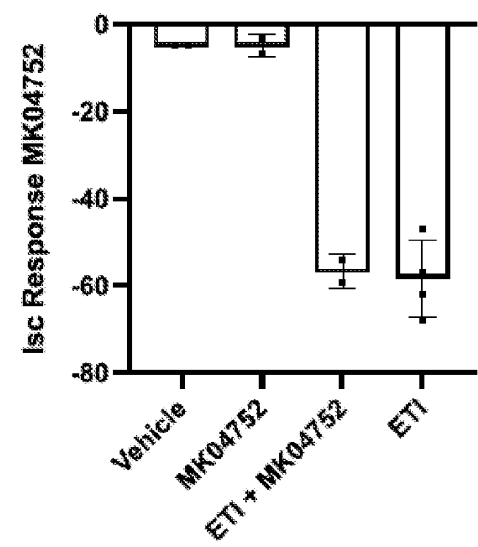


Figure 28: CFTR activity using Ussing chambers in cultures from CF patients treated with MK04752, ETI, or combinations with reduced doses of ETI

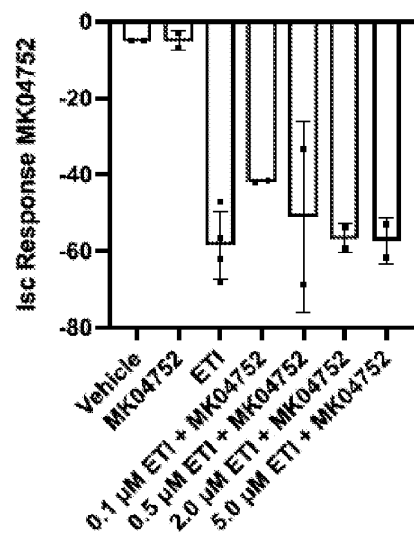


Figure 29: GSI Treatment has no Impact on Ionocyte Formation

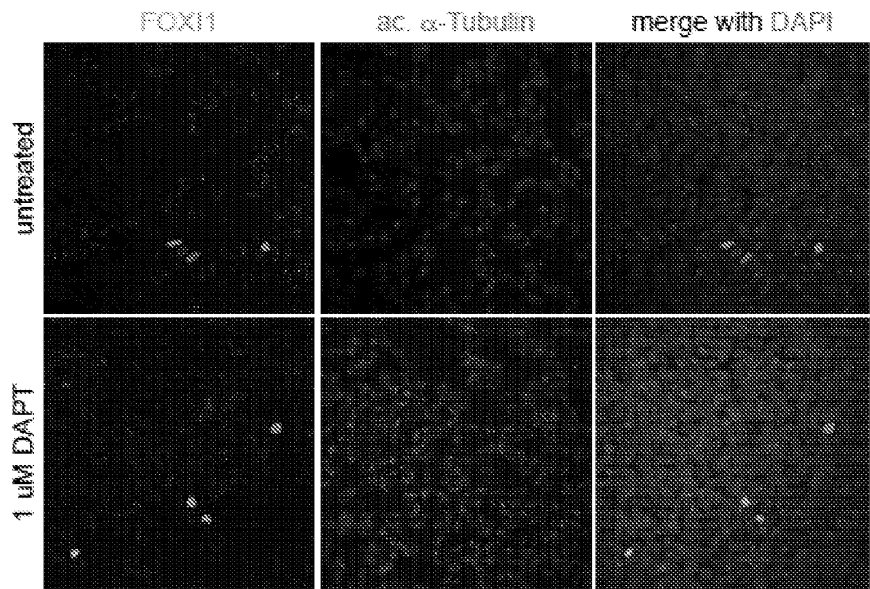


Figure 30: Effect of the GSI MK-0752, Elexacaftor and their combination at low doses on ciliary beat frequency (CBF) of CF cells. Results are presented as the mean (95% UCL) relative increase in CBF compared to control untreated cells.

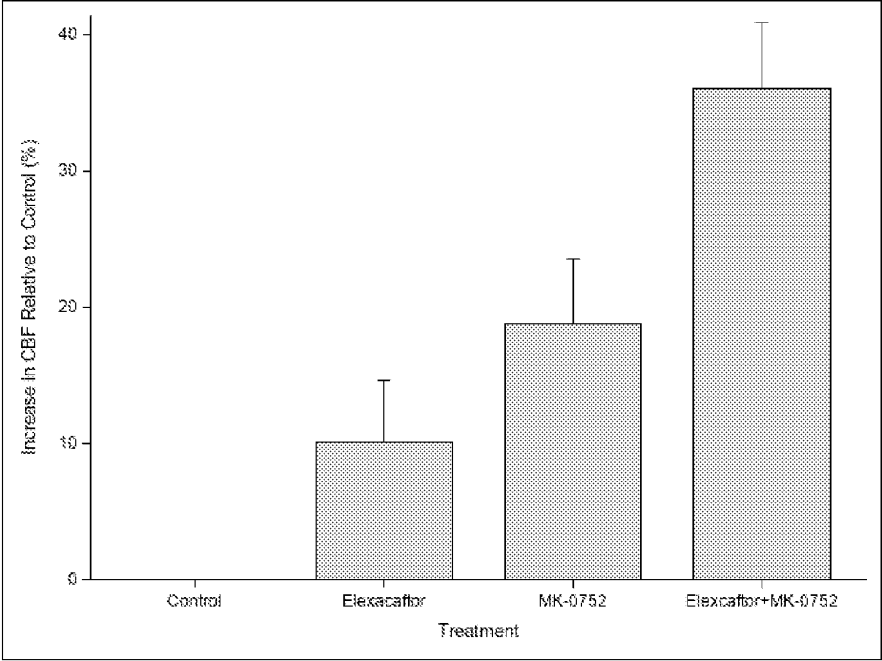


Figure 31: Ciliary beat frequency (CBF) and cilium length of primary human epithelial cells treated with DAPT

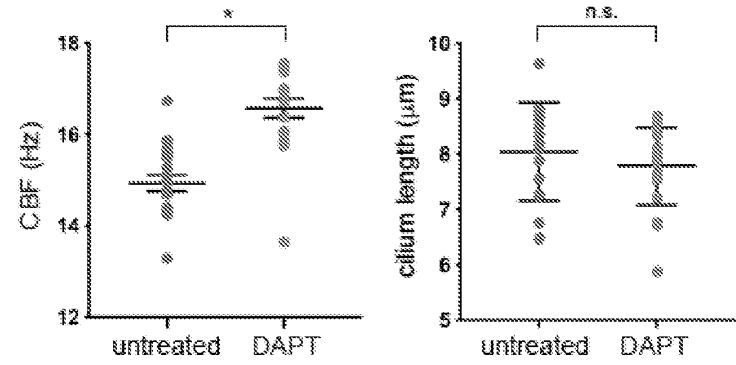


Figure 32: Airway surface liquid (ASL) reabsorption characteristic of CF cultures treated with ETI, semagacestat, or both.

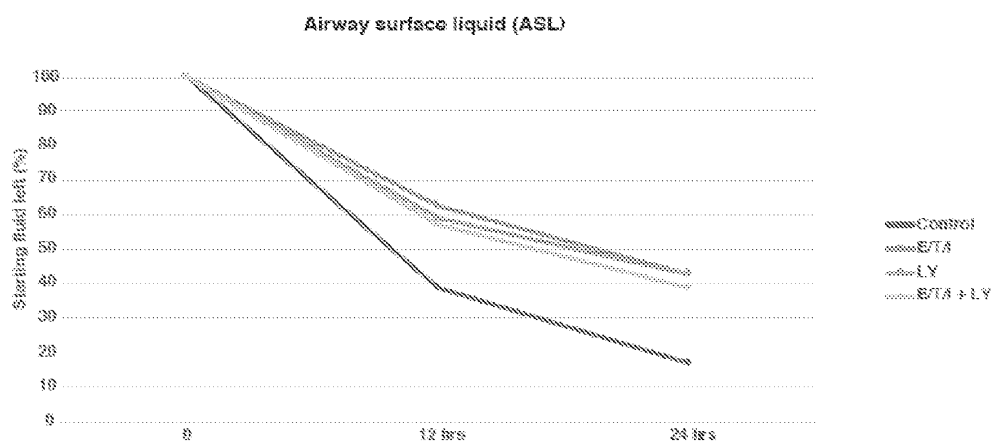


Figure 33: Images of mucociliary transport by the ciliated surface of cell cultures treated with vehicle control, ETI, LY-45139 or both.

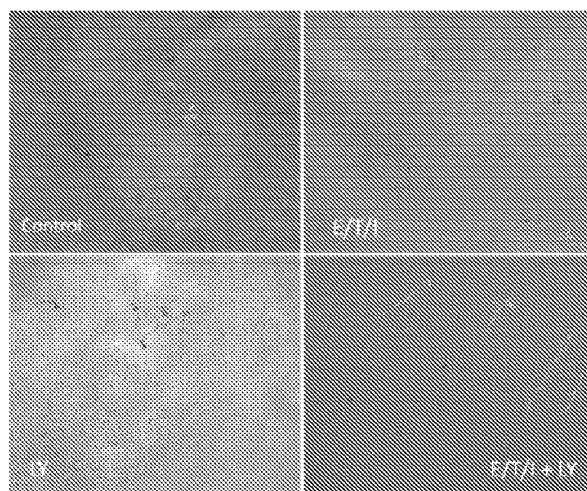


Figure 34: Mucociliary transport in cultures treated with ETI, LY-45139 or both shown in Figure 33

