Correlating CFTR function with clinical features to inform precision treatment of cystic fibrosis

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ONLINE DATA SUPPLEMENT

Figure E1

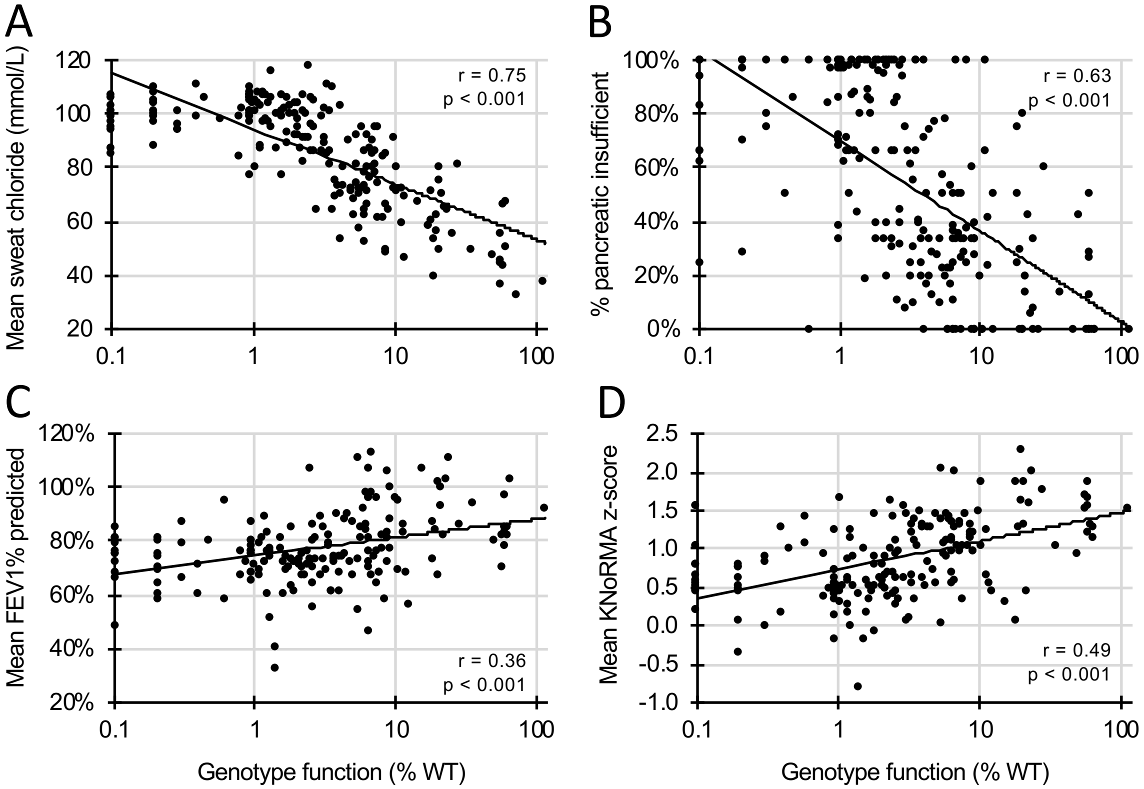

Figure E1. Genotype function has a non-linear relationship with CF clinical traits across the range of CFTR function. Correlations between CFTR genotype function and each CF clinical trait (sweat chloride **[A]**, pancreatic insufficiency **[B]**, FEV1% predicted **[C]**, and KNoRMA **[D]**) were determined as in **Figure 2 right-hand panels**, but without restricting to between 0.85 and 50% total CFTR genotype function. All slopes remain significantly different than zero ($p<0.001$) with r-values ranging from 0.36 to 0.75; these are similar to those reported in **Figure 2**.

Figure E2

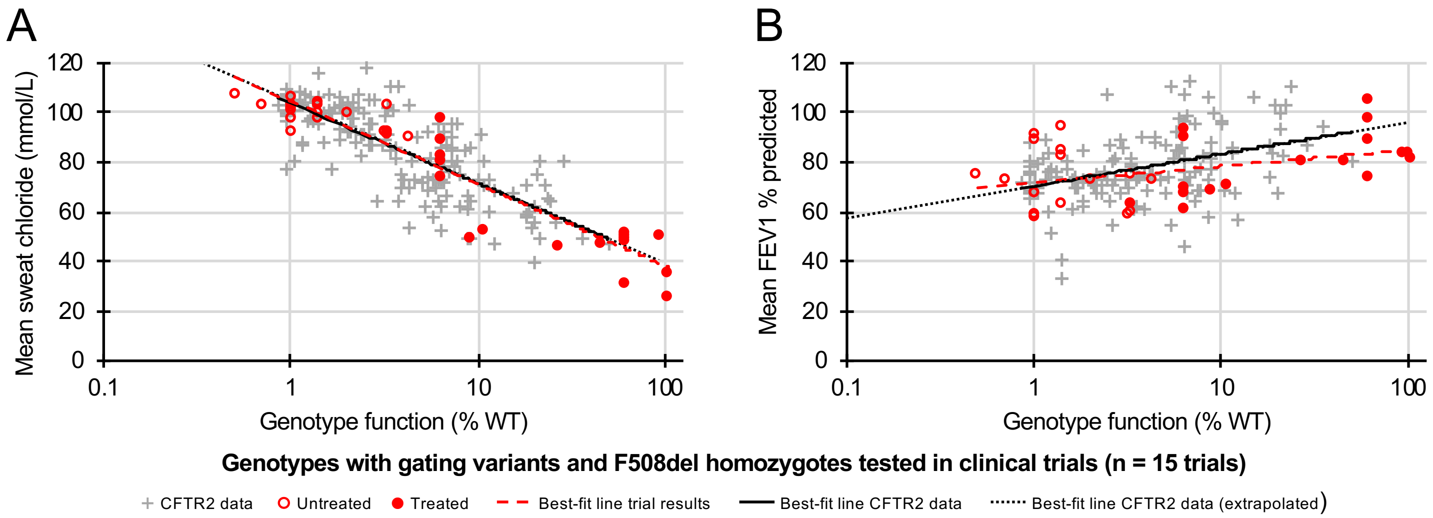

Figure E2. Treatment effect mirrors the relationship between genotype function and phenotype determined using CFTR2 data across all genotypes tested in clinical trials. Genotype function vs. sweat [Cl^{-}] (**A**) or FEV1 % predicted (**B**) on a semi-log plot indicates that the treatment effect of CFTR modulators on individuals with genotypes including gating variants or F508del homozygotes does not differ from the relationship shown between these variables using CFTR2 data (solid line determined from genotypes with 0.85% to 50% function; dotted line extrapolates this relationship below 0.85% or above 50% function). Genotype function and baseline sweat [Cl^{-}] or FEV1% predicted of individuals tested in clinical trials of duration 4 to 144 weeks, and by multiple CFTR modulators, are represented by open red circles; following treatment, genotype function (determined by *in vitro* CFBE or FRT cell testing or *ex vivo* primary cell testing) and resulting sweat [Cl^{-}] or FEV1 % predicted are represented by filled red circles. Clinical trials included in these plots are referenced in **Table E4** and shown in **Figures 4 and 5**, parsed by genotype and age cohort. Comparisons were performed using an interaction term between CFTR2 data and data from clinical trials and indicated no significant difference between the regressions for each data set.