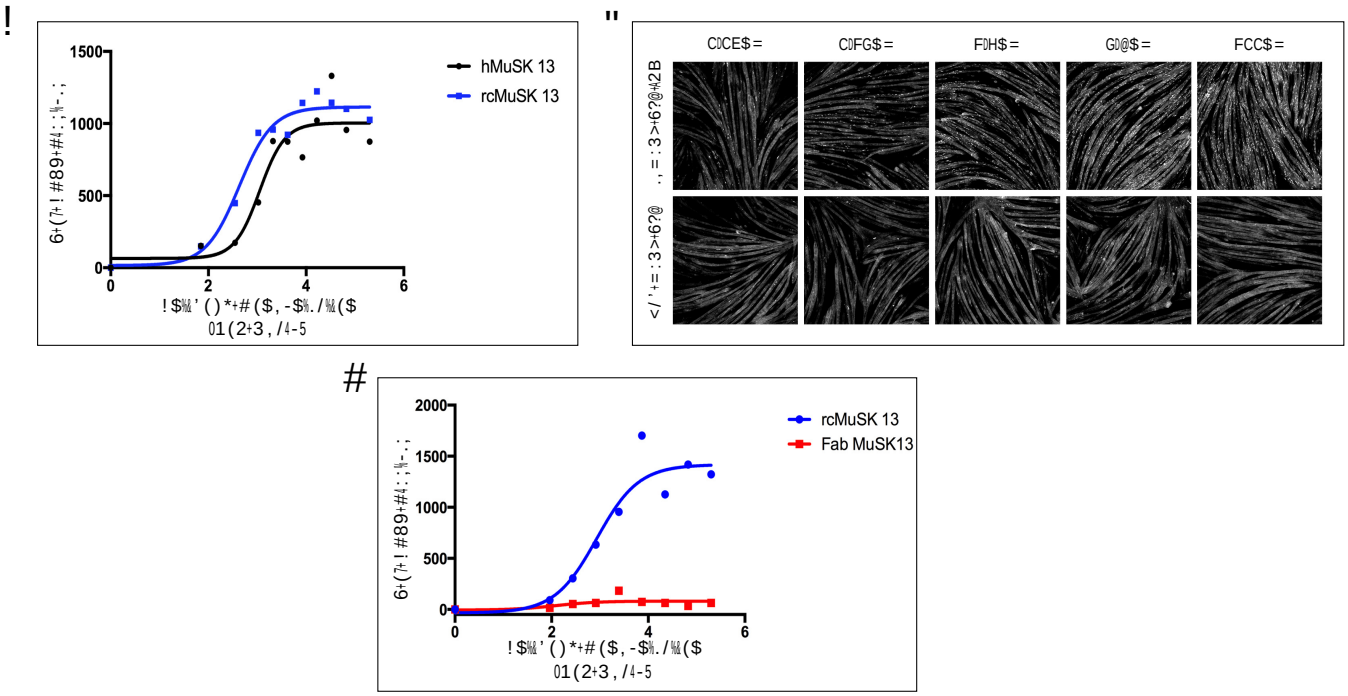
Figure 4- Figure Supplement 1



The human and reverse chimera versions of MuSK agonist antibody #13 induce acetylcholine receptor (AchR) clustering in C2C12 myotubes whereas a Fab from MuSK antibody #13 fails to stimulate AchR clustering. (A) Human (h) and reverse chimera (rc) MuSK #13 antibodies are similarly effective in stimulating AchR clustering in C2C12 myotubes (n=3). (B, C) C2C12 myotubes were treated with rc MuSK #13 or a Fab from MuSK #13 for 1 hr at the indicated concentrations and stained with α-BTX. We found that the Fab fragment from antibody #13, unlike the intact Ig or the scFv, was unable to stimulate clustering of AchRs, indicating that antibodies must be dimeric and force-dimerize MuSK and promote an orientation that is favorable for trans-phosphorylation. (D) The rc antibody #13 stimulates AchR clustering in a dose-dependent and saturable manner, whereas Fab #13 fails to stimulate AchR clustering (n= 3).