Supplementary Information

Figure S1: γ-secretase inhibitors induce generation of Met-CTF

MDCK epithelial cells were treated or not overnight with 1 μM E Compound, 10 μM DAPT or 100 mM L-685 458. The following day the cells were treated or not 5 h with 10 μM lactacystin. For each condition, the same amount of protein was resolved by 10% SDS-PAGE and analysed by western blotting with an antibody directed against the kinase domain of Met (WB Met). Arrows indicate the positions of precursor and mature full length Met, Met-CTF and Met-ICD.

Figure S2: Metalloprotease inhibitor prevents Met-CTF generation in MCF10A cells

MCF10A cells were treated or not overnight with 1 μM E Compound and 50 μM TAPI-1. The cells were then treated for 5 h with 10 μM lactacystin. Proteins were resolved by 10% SDS-PAGE and analysed by western blotting with antibodies directed against the kinase domain of Met (WB Met). Arrow indicates the position of Met-CTF.

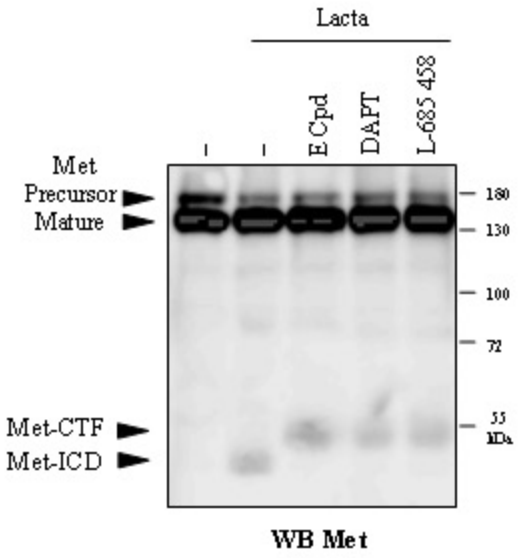
Figure S6: Ligand-independent migration of MDCK cells expressing TRK-Met chimeras

(A) MDCK cells stably expressing TRK-Met (Clones 1 and 4) or TRK-Met-juxta (clones 7) were lysed. Proteins were resolved by 10% SDS-PAGE and analysed by western blotting with antibodies directed against the C-terminal domain of mouse Met (WB moMet). Arrows indicate the positions of the mature and immature forms of TRK-Met and TRK-Met-juxta. (B) The MDCK stably expressing TRK-Met and TRK-Met-juxta were cultured two days in invasion chambers. The relative number of infiltrated cells was determined after staining of nuclei with Hoechst (n=3, -/+ SD).

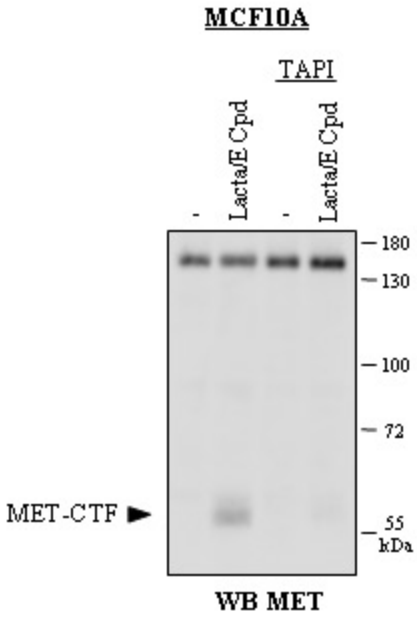
Figure S7: Induction of the Met PS-RIP by the Met inhibitory antibody DN30 in GTL16 cell line

GTL16 cells were treated 2 h with 1 μM of DAPT, 100 μM of γ-secretase inhibitor VI or 10 μM of lactacystin. The cells were then treated 4h with 40 μg/ml of DN30 antibody or control IgG. Proteins were resolved by 10% SDS-PAGE and analysed by western blotting with antibodies directed against the kinase domain of Met (WB Met). Lower exposure is shown to visualise the downregulation of Met induced by DN30 treatment. The filter was

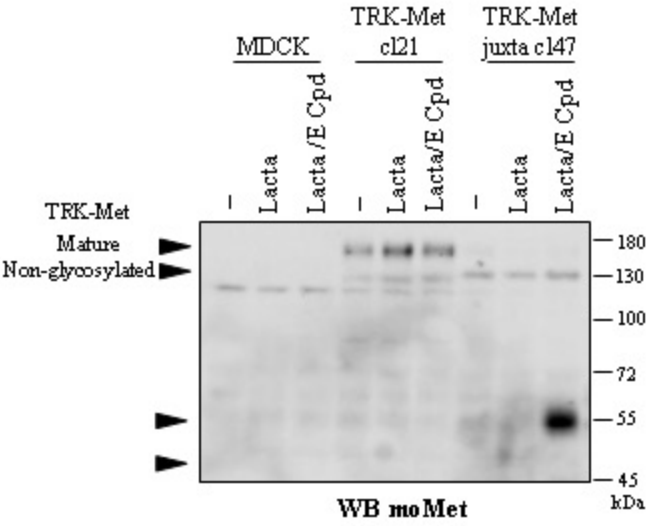
stripped and reprobed with an antibody directed against β-actin to assess the loading. Arrows indicate the positions of precursor and mature full length Met, Met-CTF and Met ICD.



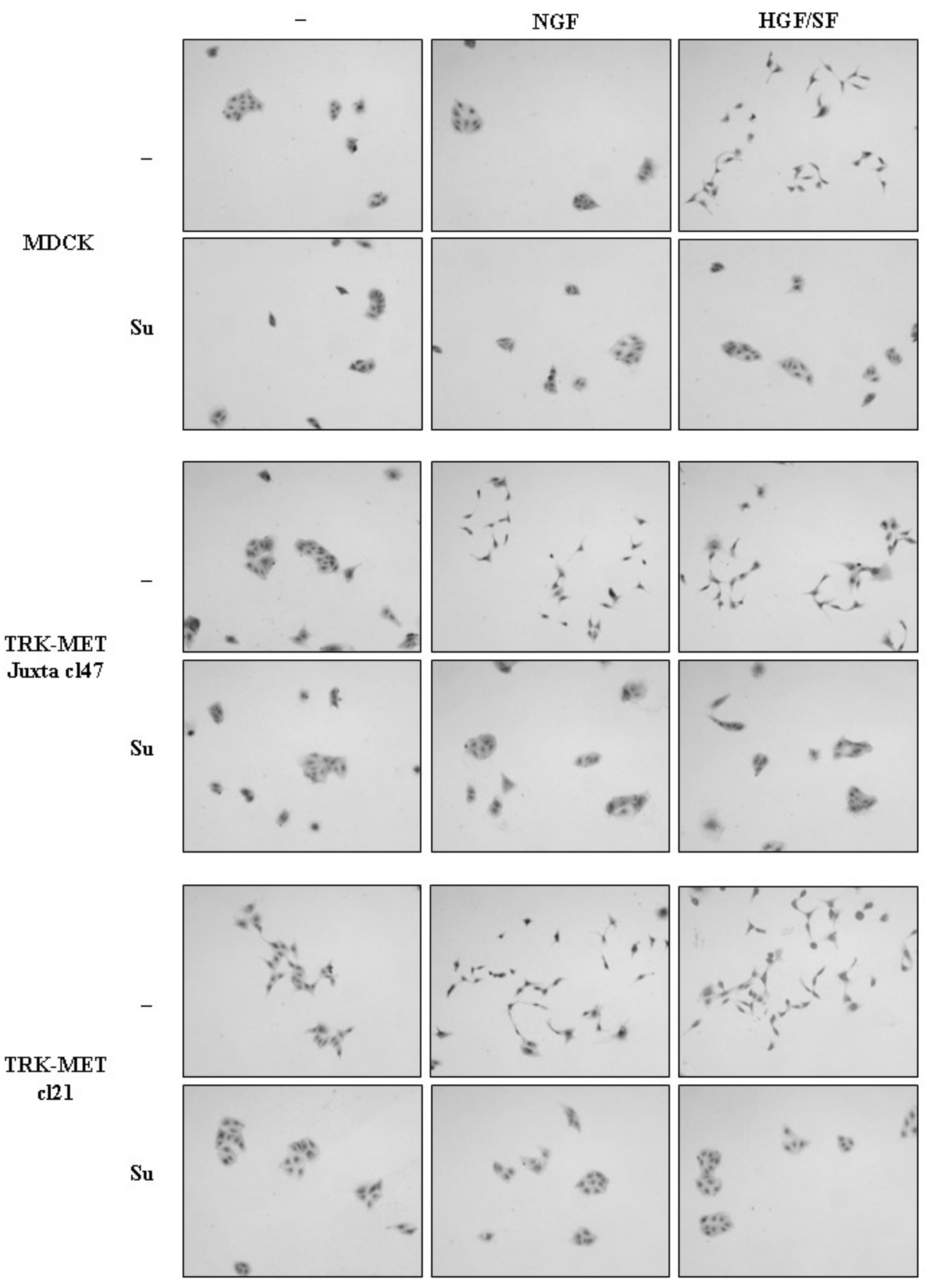
Supplementary Data Figure S1



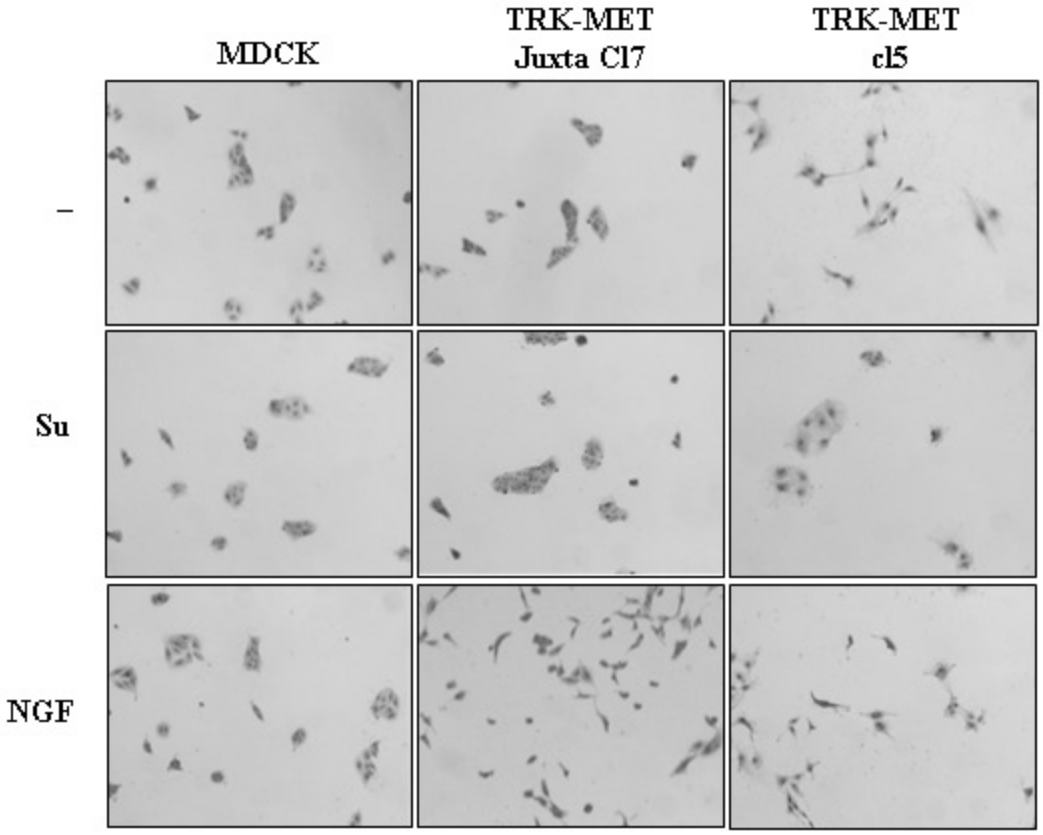
Supplementary Data Figure S2



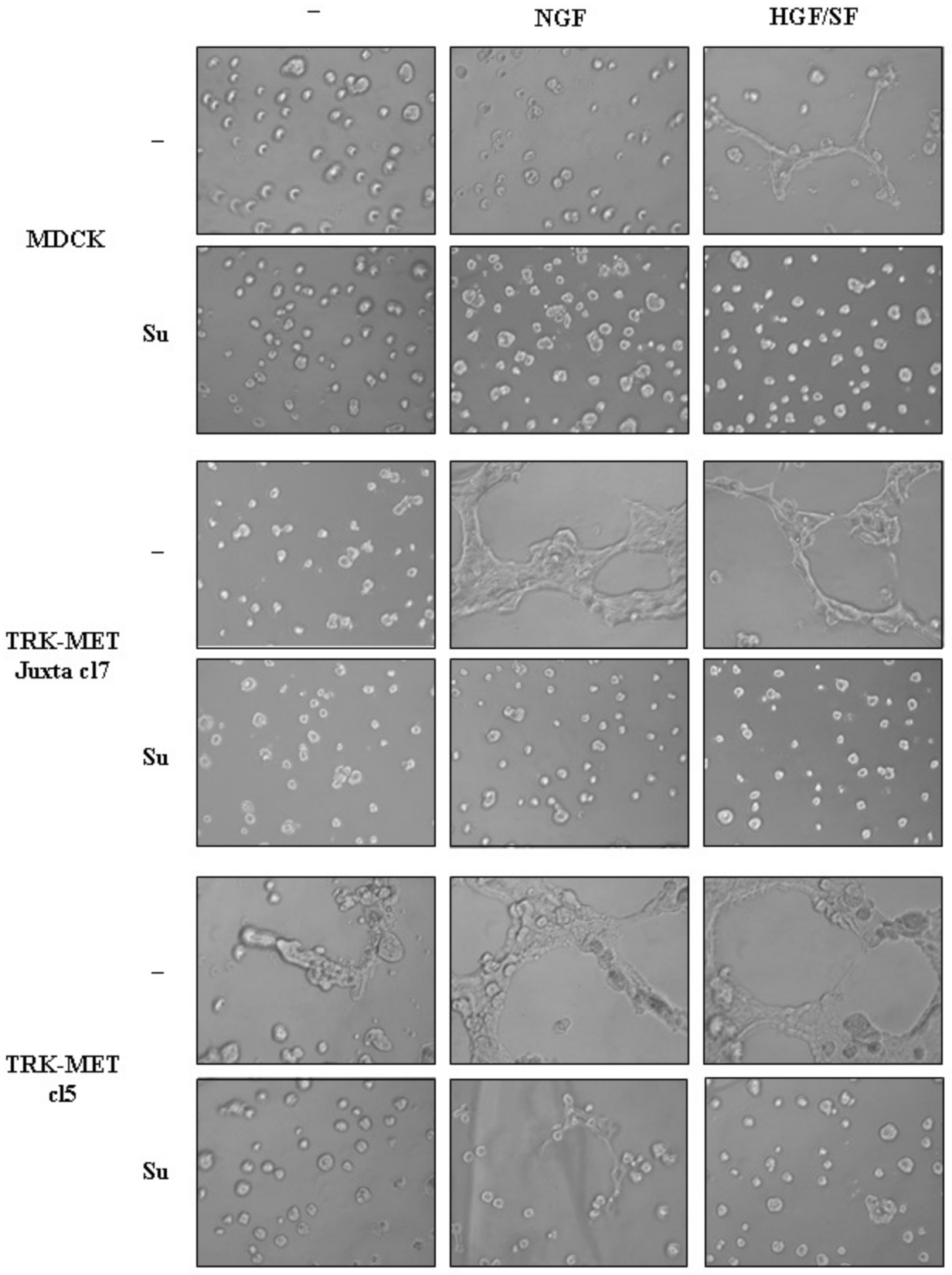
Supplementary Data Figure S3



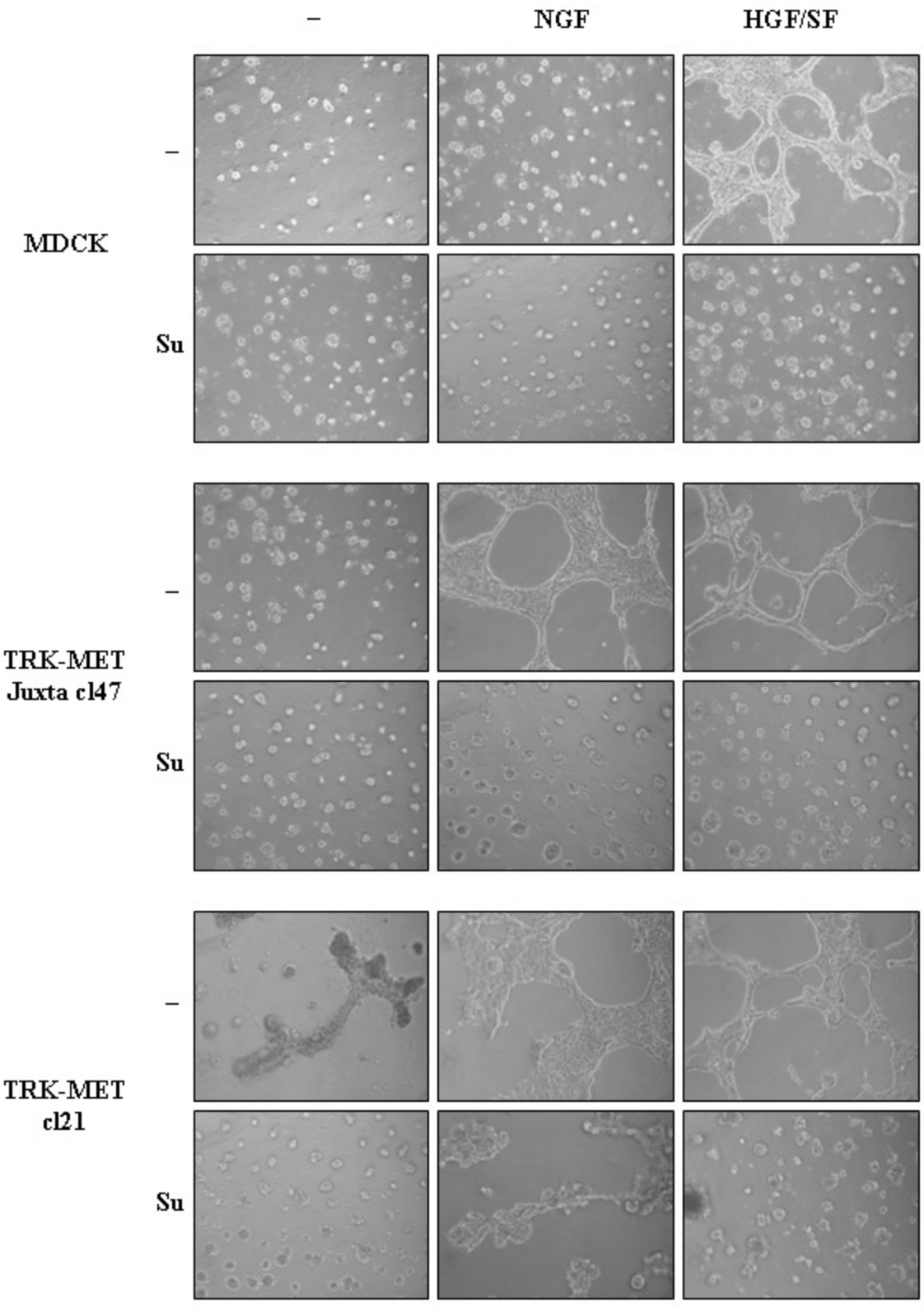
Supplementary Data Figure S4A



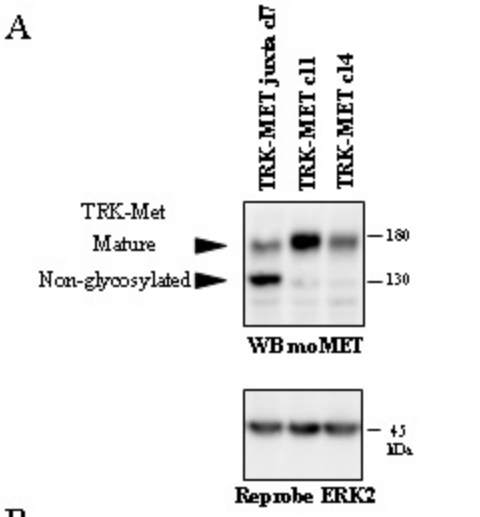
Supplementary Data Figure S4B

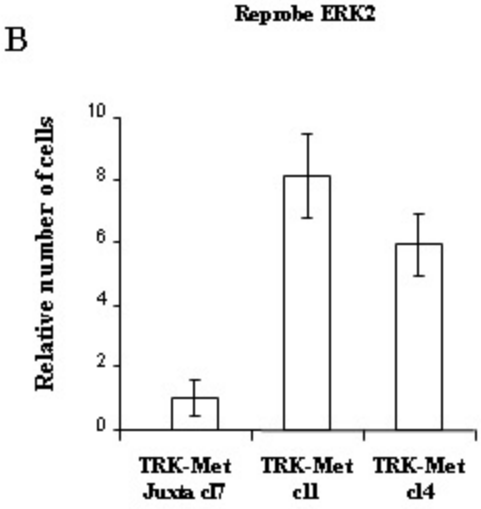


Supplementary Data Figure S5A

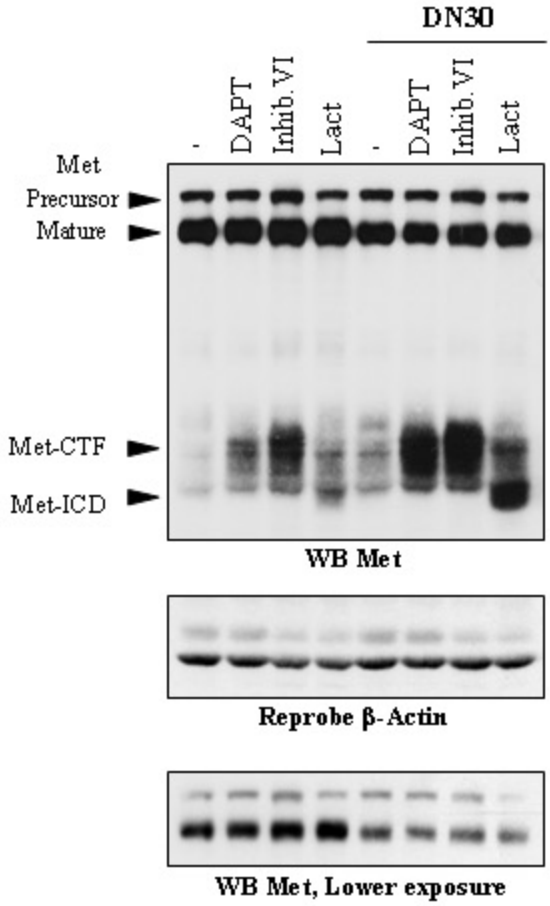


Supplementary Data Figure S5B





Supplementary Data Figure S6



Supplementary Data Figure S7