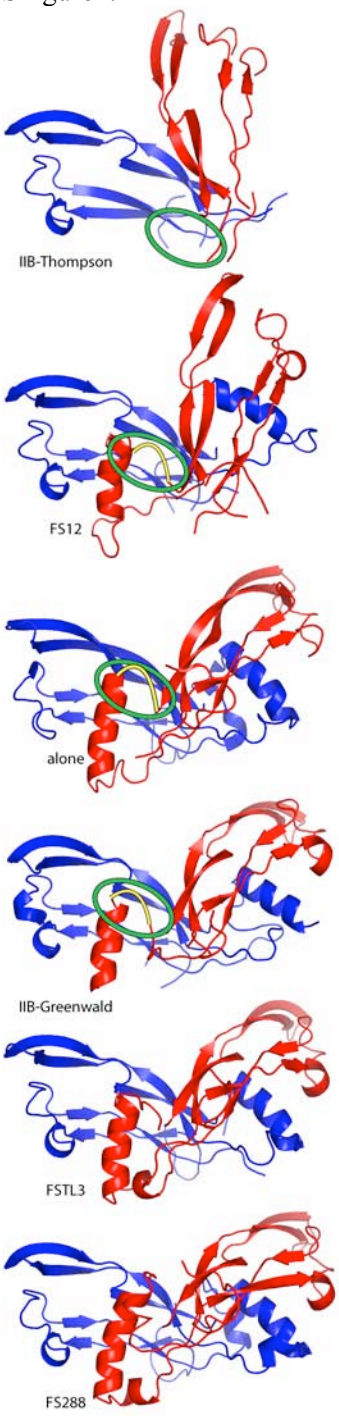
Supplemental figure legend.

Figure S1. Flexibility of activin A. Blue monomers were aligned to one another. Molecules are in increasing extension from top to bottom. The pre-helix loop is missing in the top four structures (outlined with a green ellipse and the two ends joined with a yellow line). Structures shown from top to bottom have the PDB identifiers: 1NYS (37), 2ARP (21), 2ARV (21), 1S4Y (36), 3B4V (The present study), 2B0U (24).

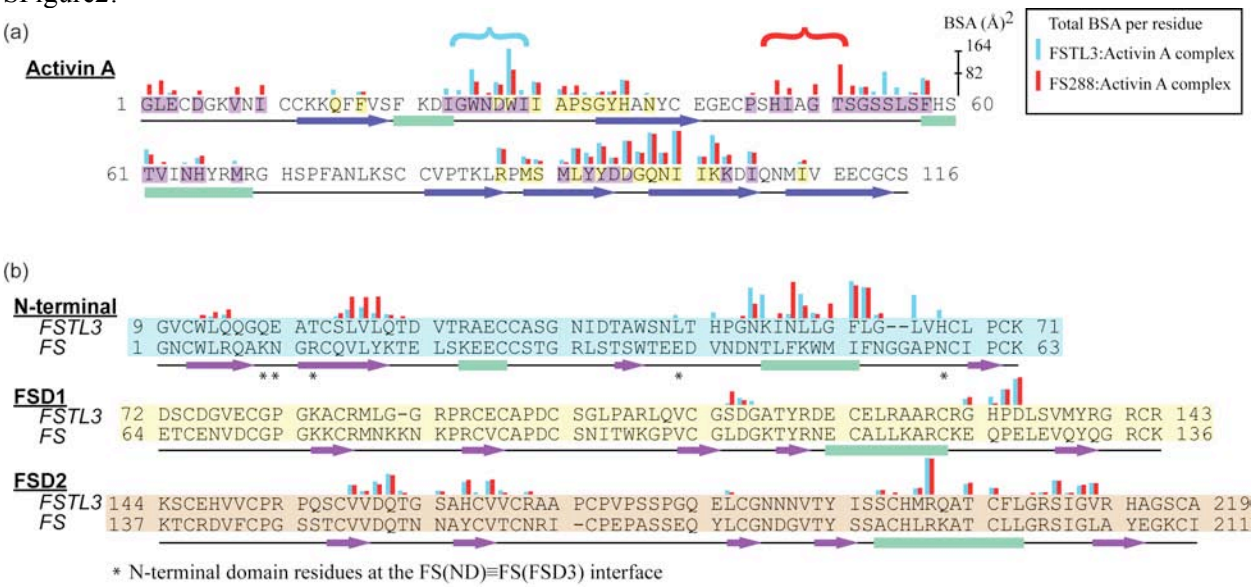
Figure S2. Primary amino acid sequence showing the distribution of buried surface residues. Contact residues in the respective proteins are shown by blue bars for FSTL3 and red for FS. (a) BSA for activin A residues in complex with FSTL3 and FS288. The blue bracket emphasizes BSA fluctuations near W25 and W28 upon interaction with each antagonist. The red bracket indicates residues in the pre-helix loop of activin A that interact with the FS, but do not interact with FSTL3. (b) Sequence alignment by domain of FSTL3 and FS. Bars indicate the total BSA for residues that interact with activin A (colored according to the legend). Significant differences in the BSA for N-terminal domain residues are observed, whereas residues in both FSD1 and FSD2 of each complex that interact with activin A are similar.

Figure S3. Binding footprints of type II receptors and FS-type antagonist on activin A. Buried surface area depicted for one monomer of activin A from complexes with activin type II receptors or FS-type antagonists (ActRIIB (pink) (37), ActRIIB (red) (36), FSTL3 (light blue) and FS288 (blue) (24)). Ellipses indicate surfaces unique to either FSTL3/FS or the type II receptors. Surfaces for receptors are colored with reds and antagonists with blues.

SFigure1.

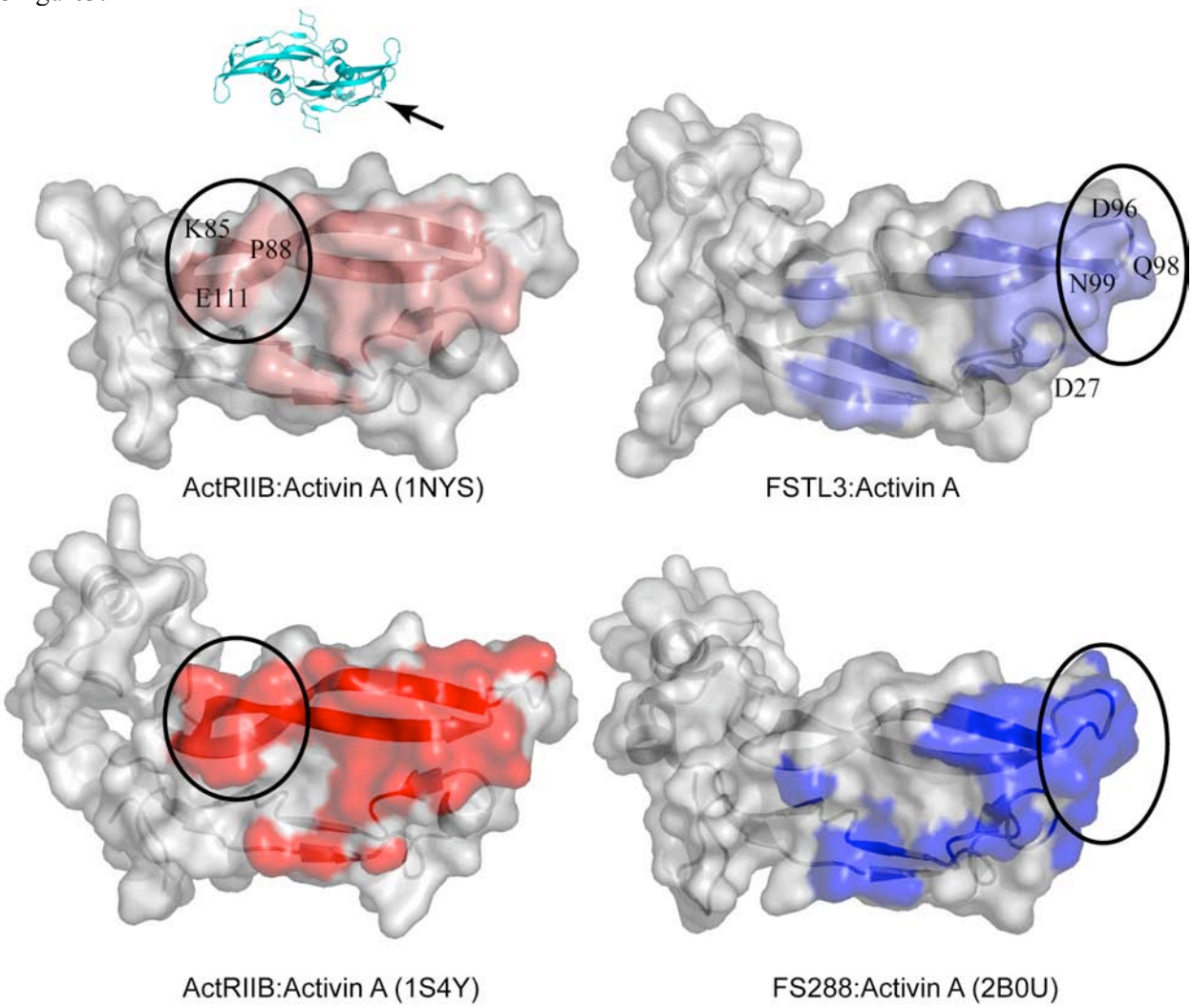


SFigure2.



* N-terminal domain residues at the FS(ND)≡FS(FSD3) interface

SFigure3.


K85
P88
E111
ActRIIB:Activin A (1NYS)
D96
Q98
N99
D27
FSTL3:Activin A
ActRIIB:Activin A (1S4Y)
FS288:Activin A (2B0U)