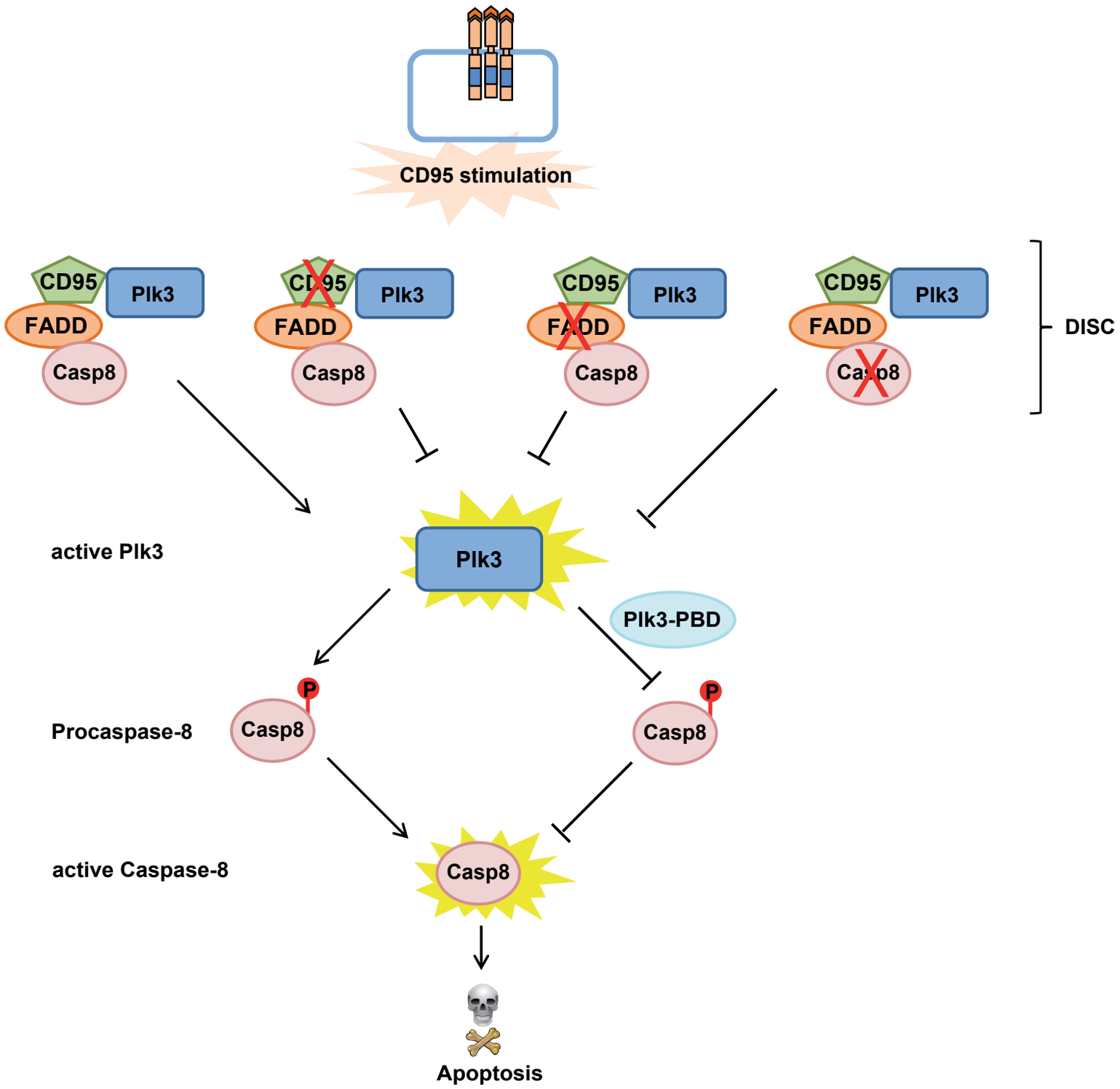
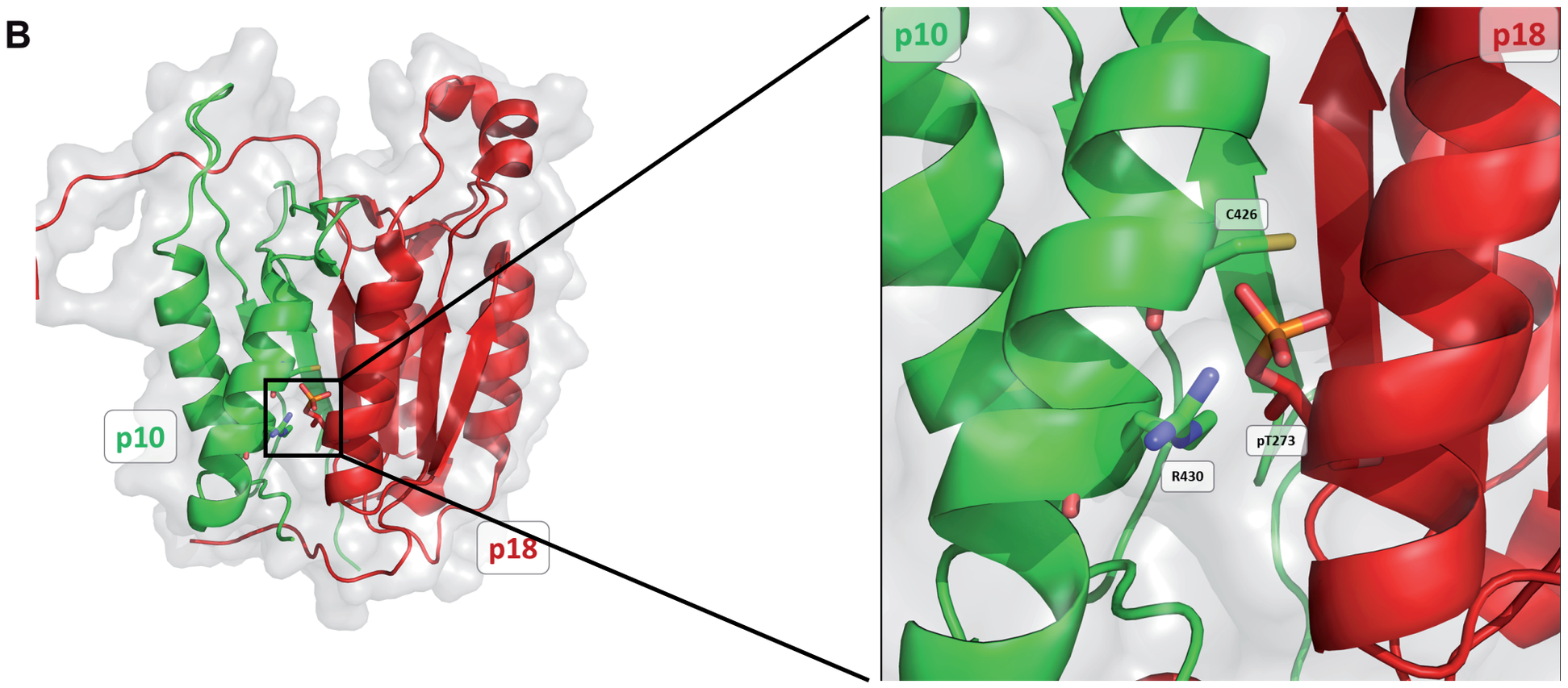
A


CD95 stimulation
CD95
Plk3
FADD
Casp8
DISC
active Plk3
Plk3
Plk3-PBD
P
Procaspase-8
Casp8
active Caspase-8
Apoptosis

B


p10
p18
C426
pT273
R430

Supplementary Information, Figure S7. Proposed model for the function of Plk3 in the extrinsic apoptotic signaling and influence of the phosphorylation of procaspase-8 at T273 on its 3D structure.

(**A**) Proposed model for the function of Plk3 in the extrinsic apoptotic signaling. Upon apoptotic ligand stimulation and DISC formation Plk3 is activated. Depletion of only one of the new identified interacting partners of Plk3 (CD95, FADD and procaspase-8), prevents Plk3 activation. Upon DISC formation Plk3 phosphorylates procaspase-8 at T273, thereby facilitating the processing of procaspase-8, its enzymatic activation and the downstream initiation of apoptotic signaling. The inhibition of Plk3 binding to its substrates through the overexpression of Plk3-PBD or knock-out of Plk3, both, reduce or prevent the phosphorylation of procaspase-8 at T273 and reduce processing and activation of procaspase-8. Our data suggest a novel mechanism of Plk3 activation. Moreover, phosphorylation of procaspase-8 by Plk3 seems to sensitize cells to extrinsic death stimuli. (**B**) 3D structure of p18 and p10 subdomains of caspase-8 including phosphorylated T273. The picture was generated using PyMOL software. The atom coordinates of the protein were obtained from the protein data base as a pdb-data (pdb ID 4JJ7).