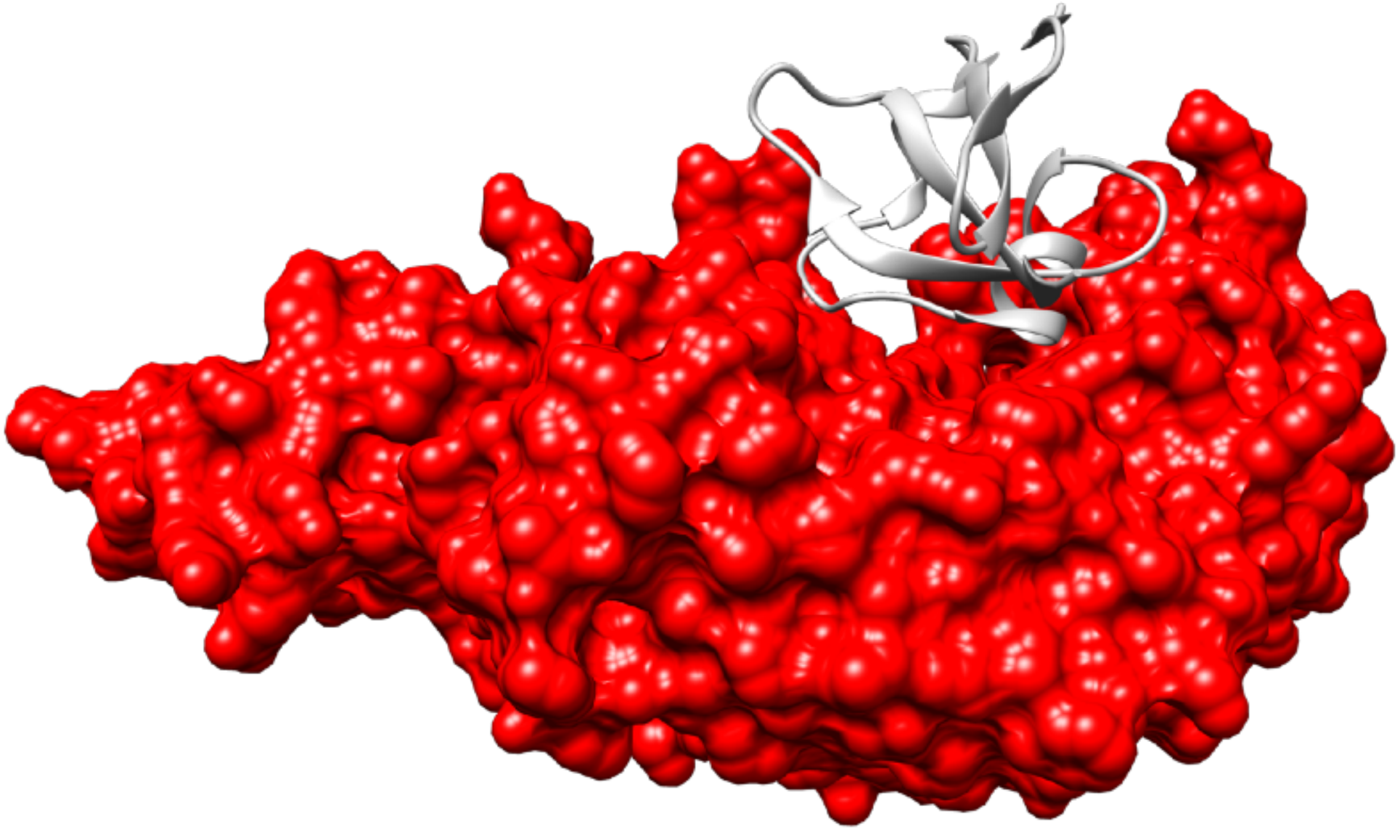
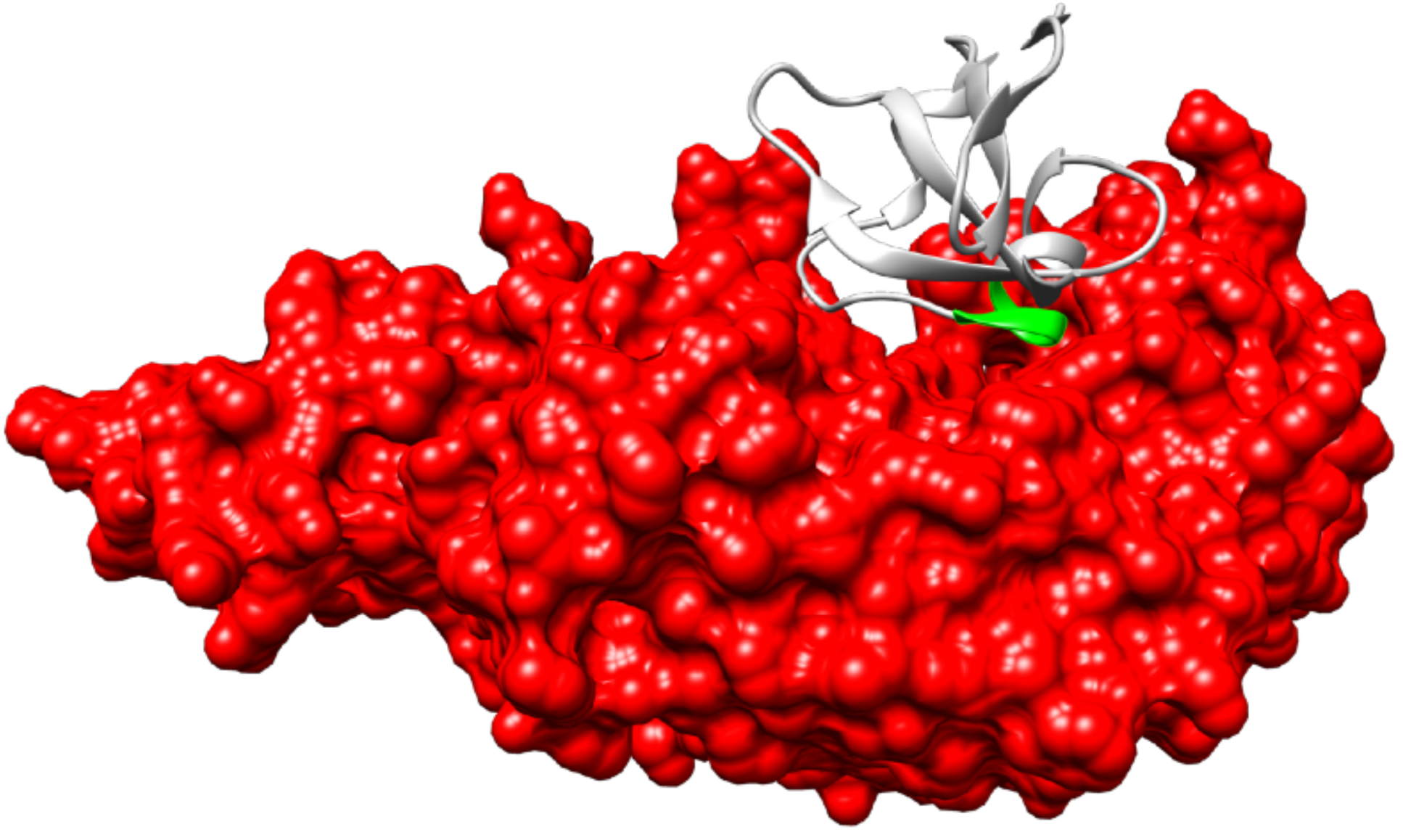
SESE is necessary, but is it sufficient?

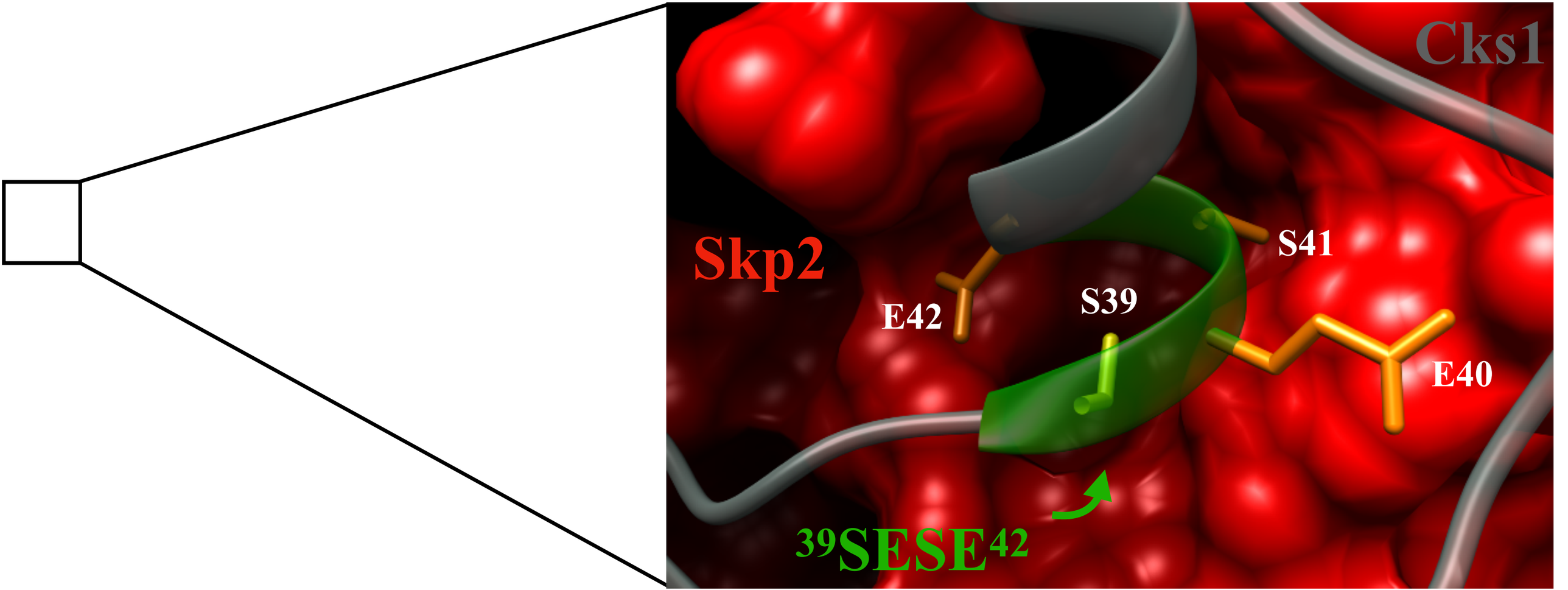


J. Gavenois et al., *Nat. Chem. Biol.* **10**, 716–722 (2014)

T. Siegert et al., *Methods Mol. Biol.* **1561**, 255-277 (2017)

B. Hal et al., *Mol. Cell* **20**, 9-19 (2005)




Cks1
Skp2
S41
E42
S39
E40
39SESE42

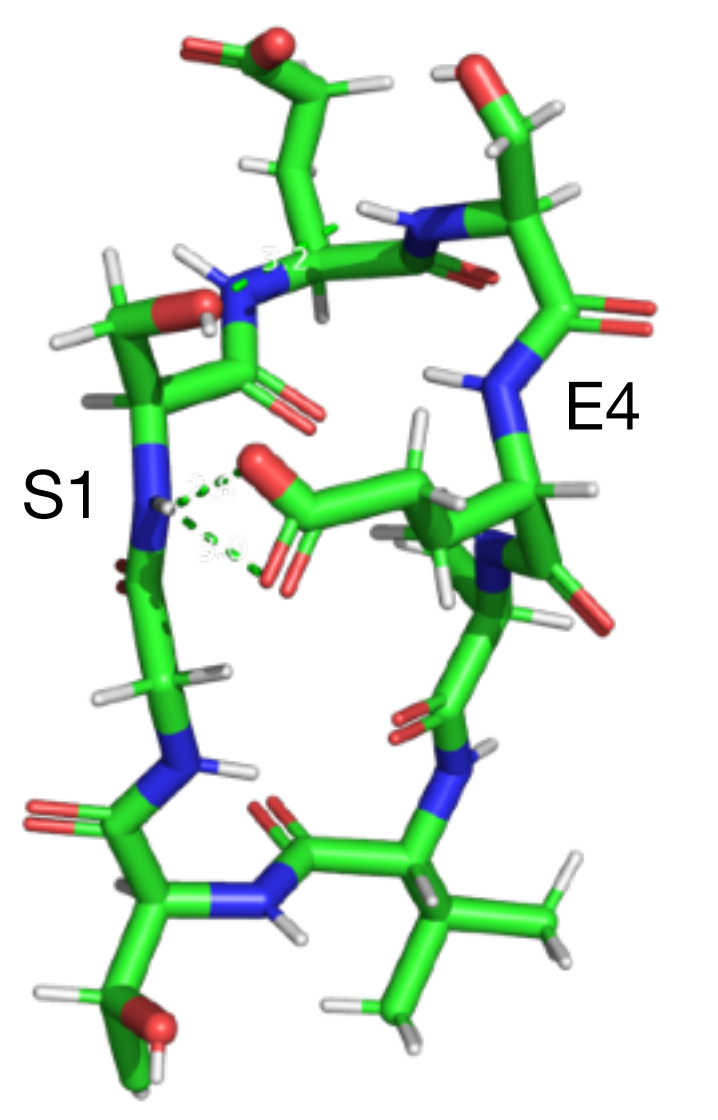
Yellow: residues contributing > 1 kcal/mol binding energy

Orange: residues contributing > 2 kcal/mol binding energy

PDB: 2ASS

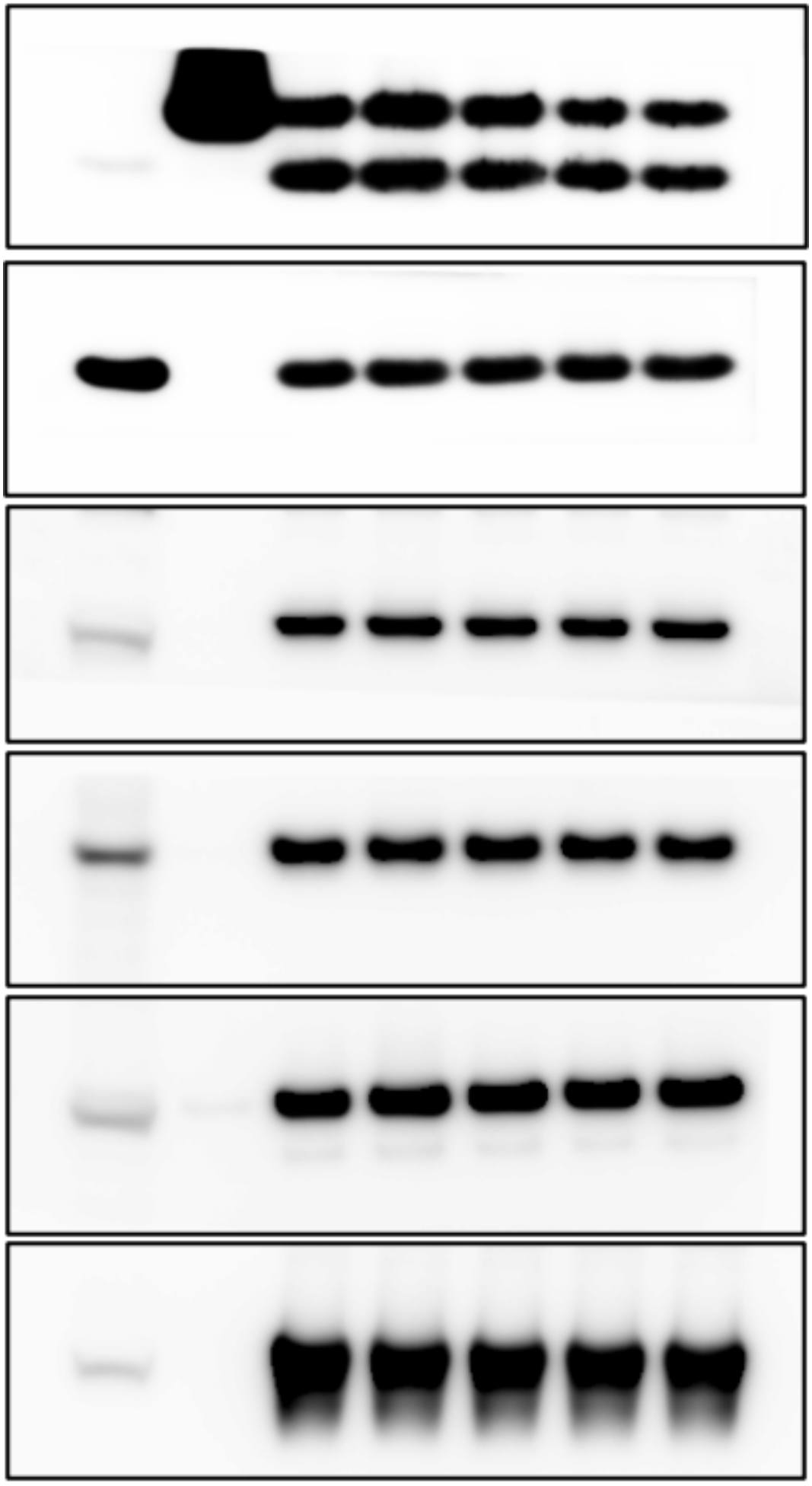

Skp2


Cks1


S1
E4

Does the *in-vitro* experiment

tell the whole story?



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His-Cks1

Endogenous Cks1


FLGA-Skp2


WCE


His-Cks1


DMSO


1 μM


10 μM


1 μM

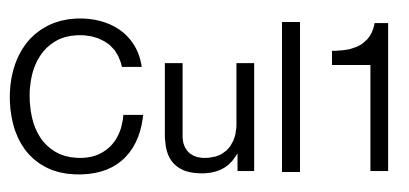

10 μM

IP: FLAG-Skp2

SESEavTG

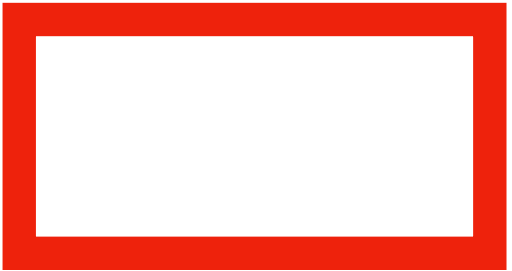
SESEGvvTG


Skp1


Cul1


CDK2

Cyclin A



- Skp2 was already pre-

already binds to Skp2?

endogenous Cks1.

occupied with

- Can the inhibitor properly

function when Cks1