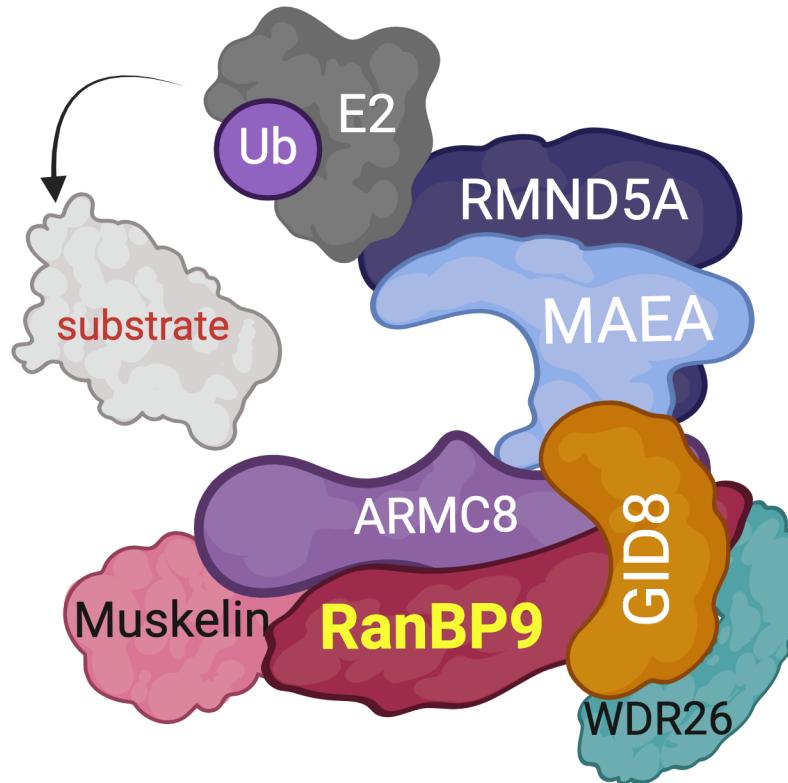
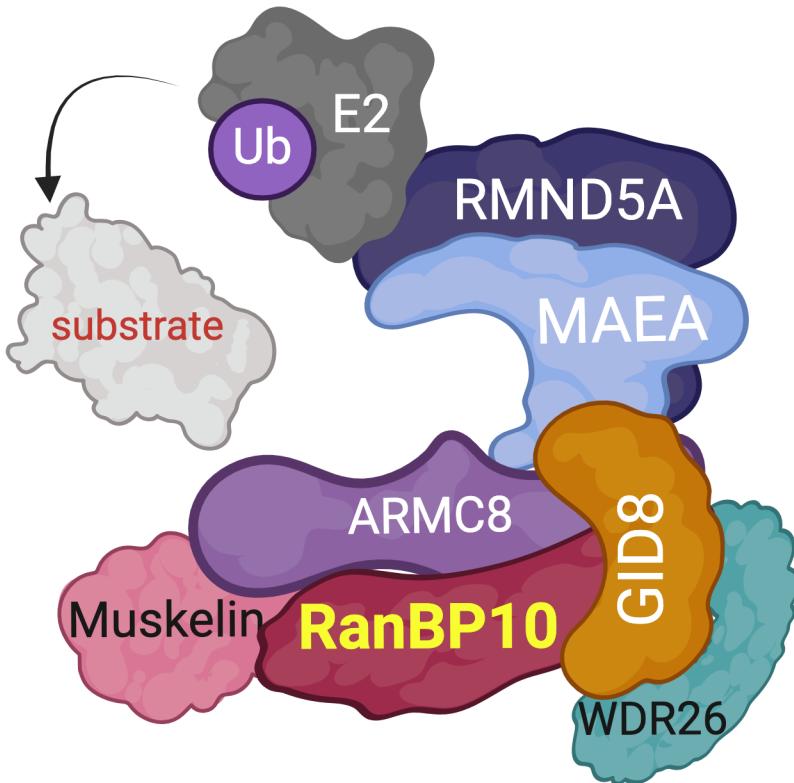


Normal lung

CTLH^{BP9} COMPLEX

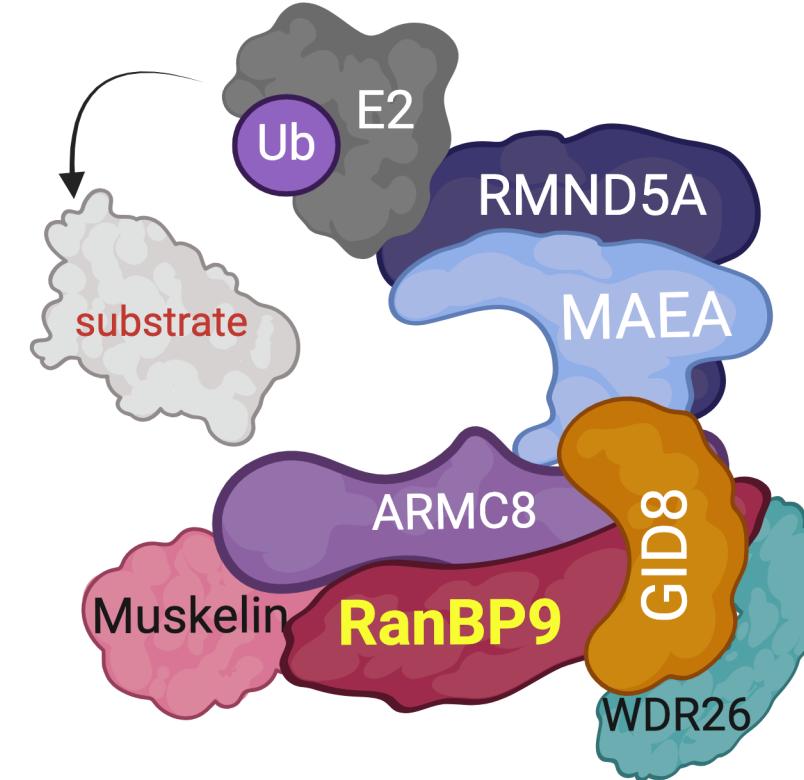


CTLH^{BP10} COMPLEX

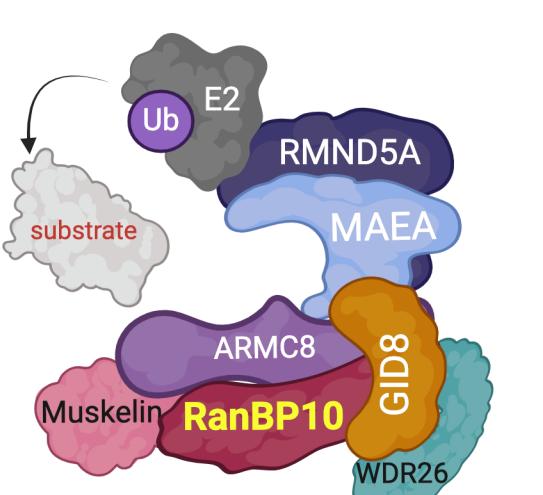


NSCLC

CTLH^{BP9} COMPLEX



CTLH^{BP10} COMPLEX



Pro-tumorigenic
Pro-proliferative

In normal lung cells, the CTLH E3 ligase can be built on the scaffold provided by RANBP9 (CTLH^{BP9}) and RANBP10 (CTLH^{BP10}).

In NSCLC, the expression of RANBP10 is downregulated while the expression of RANBP9 increases, but both proteins are still present, and both protect their binding partner GID8 from degradation. The CTLH^{BP9} and CTLH^{BP10} complexes cross-regulate each other at protein level.

The combined increase of CTLH^{BP9} and decrease of CTLH^{BP10} is pro-tumorigenic: it causes ubiquitylation and amount changes of proteins involved in cell proliferation, and other pathways critical to NSCLC pathogenesis.