## LIGER

Adapter proteins:

- CUL3 - BTB

- CUL1 - SKP1 - FBOX

- CUL4A/B - DDB1 - DCAF

- CUL2/5 - Elongin - VHL/SOCS

Protein degradation via the proteasome-ubiquitin system (UPS) plays a crucial role in cellular homeostasis. Defects in this system are often associated with pathologic states like cancer or developmental abnormalities. E3-ubiquitin ligases are responsible for substrate recognition and subsequent degradation. Despite this fact, many of the ubiquitin ligases have not been paired with any specific substrate yet. In LIGAR project supported by MSCA, we focused on "orphan" ubiquitin ligases with unknown functions and substrates. The objectives of the project were based on systematic and functional analysis of these ubiquitin ligases. We aspired to select several of them potentially involved in processes underlying above mentioned pathological states. The main motto and relevance of this approach were centered on the idea that novel biological therapies in the future will require a deep understanding of cellular mechanisms required for cellular growth and survival and that only basic research and detailed biochemical analysis could provide these facts.

Cullin

Substrate

NEDD8

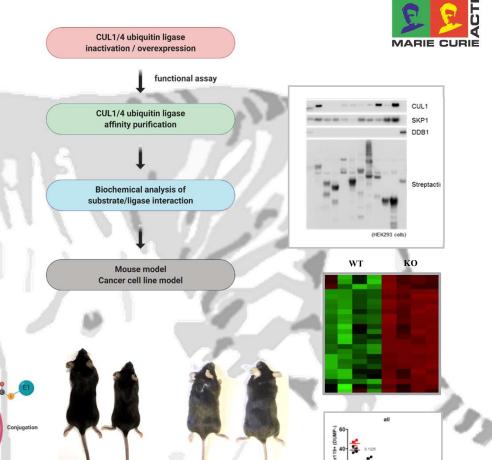
Activation

ATP -+ AMP + PP

rotoohei

Unfolding

(ATP dep.)



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KOď

WTo

KO O