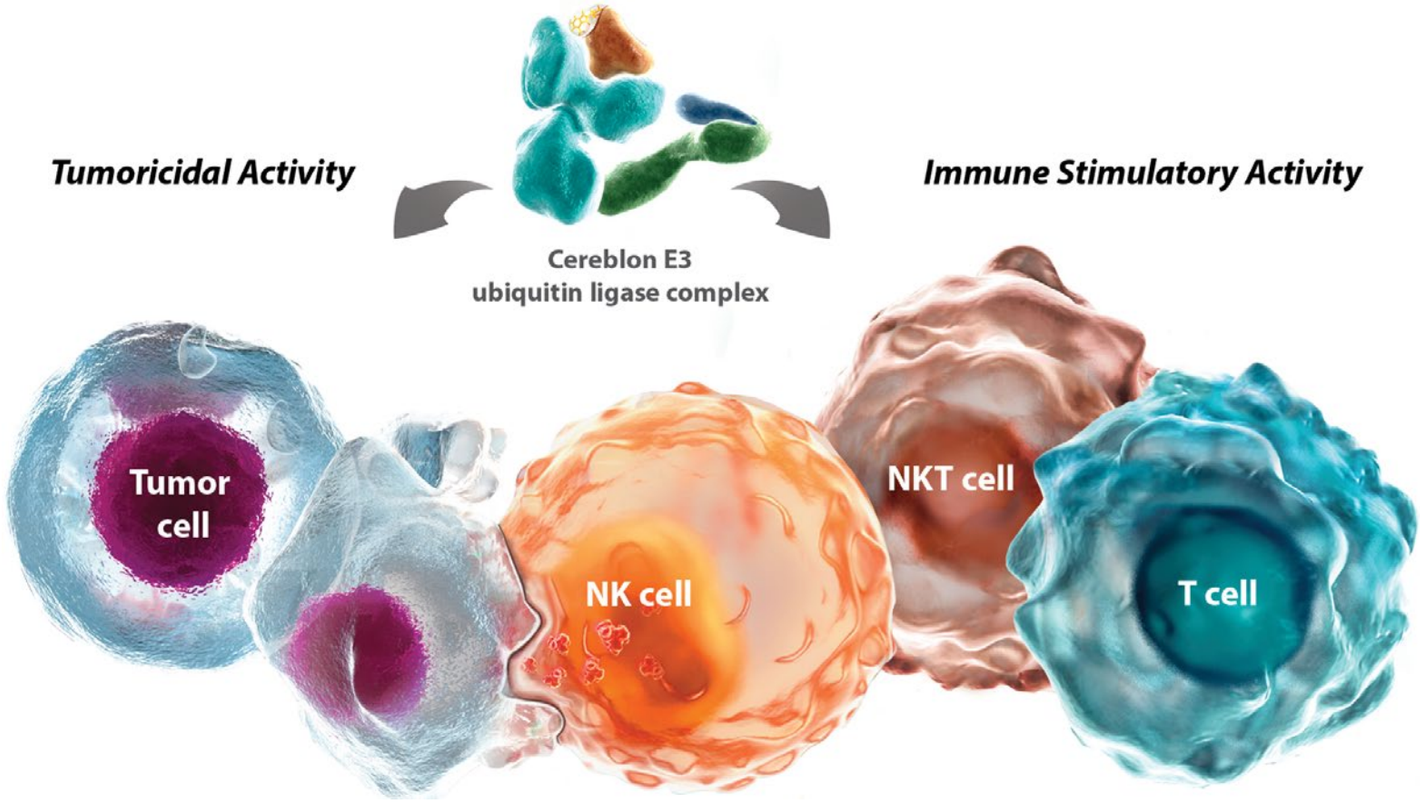
Co-opting cereblon to mediate protein degradation

Role in normal cell

Maintenance of protein homeostasis is a critical function of the cell, and disruptions of this process contribute to the development of numerous diseases, including cancer.[1-3] Cereblon (CRBN) mediates protein degradation through the ubiquitin-proteasome pathway.[4]

- CRBN is expressed in a variety of tissues, with the highest levels detected in T and B cells among other immune cells[5,6]

Modulation of CRBN specificity alters target protein degradation and may lead to immune stimulatory and tumoricidal activity.[7]



Preclinical evidence

Preclinical studies suggest that co-opting CRBN to mediate the ubiquitination and proteasomal degradation of substrate proteins may lead to anti-proliferative and immunomodulatory activities.[8-13]

The safety and efficacy of the agents and/or uses under investigation have not been established. There is no guarantee that the agents will receive health authority approval or become commercially available in any country for the uses being investigated.

NK=natural killer; NKT=natural killer T.

1. Sontag EM et al. *Curr Opin Cell Biol*. 2014;26:139-146. **2.** García-Santisteban I et al. *Mol Cancer*. 2013;12:91. **3.** Sévère N et al. *Cell Death Dis*. 2013;4:e463. **4.** Ito T et al. *Science*. 2010;327:1345-1350. **5.** https://www.proteinatlas.org/ENSG00000113851-CRBN/tissue **6.** http://www.immgen.org/databrowser/index.html. Search term: CRBN. **7.** Collins I et al. *Biochem J*. 2017;474:1127-1147. **8.** Lopez-Girona A et al. *Leukemia*. 2012;26:2326-2335. **9.** Gandhi AK et al. *Br J Haematol*. 2014;164:811-821. **10.** Xu Y et al. *Blood*. 2009;114:338-345. **11.** Krönke J et al. *Science*. 2014;343:301-305. **12.** Lu G et al. *Science*. 2014;343:305-309. **13.** Zhang LH et al. *Br J Haematol*. 2013;160:487-502.