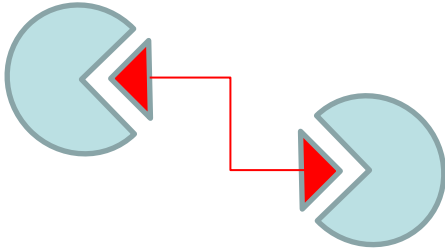


Cereblon Degrading Molecules for the Treatment of SCLC and Melanoma



Cereblon knockout mice have been shown to reduce xenograft tumor growth—see figure below. Novel Cereblon Degrading Molecules (CDMs) which mimic PROTACs were developed to decrease cereblon protein levels. This new class of molecules seems to have advantages over currently approved immunomodulatory drugs (IMiDs) including thalidomide, lenalidomide, and pomalidomide.

Cereblon loss by CDMs increases T-Effector cell function and reverts the suppression of the DNA damage response caused by cereblon. In addition, they may also improve the efficacy of checkpoint inhibitors, as well as the efficacy of chemotherapy. The lead compound has a degradation constant (DC_{50}) of 0.01 nM and has demonstrated dose dependent degradation of cereblon target protein in vitro. It also shows a superior pharmacokinetics profile and has a validated four step synthetic route. In vivo, the lead compound was orally administered and resulted in significant degradation of cereblon target protein at lower doses.

COMMERCIAL OPPORTUNITY

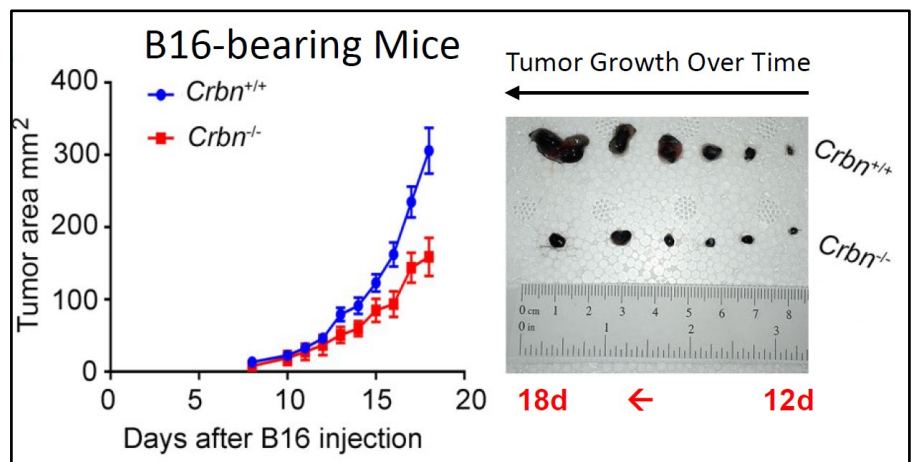
- In U.S., 15% of all lung cancers is small cell lung cancer with 35,000 new cases each year. There are over 20,000 deaths each year and the 5-year overall survival is 3-6%. SCLC numbers and treatment options have not improved in 40 years. For melanoma, there were about 100k new diagnoses in 2020, and almost 7,000 deaths. Data suggest cereblon may be a good target in these cancers.
- BMS' IMiDs, Pomalidomide, sold under the brand name Pomalyst, and Lenalidomide, sold under the brand name Revlimid was approved in 2013 and 2017, respectively. While Pomalyst has resulted in \$3.3 billion in revenue in 2021 worldwide, Revlimid has generated \$12.8 billion in revenue in the same year worldwide and was BMS' top selling drug in 2021.
- In recent years, cereblon has been extensively studied because it is involved in many biological processes and is responsible for the multiple effects of immunomodulatory drugs (IMiDs). Cereblon performs these functions generally under two circumstances: with and without IMiDs. Cereblon expression in the cells can affect cell metabolism and cause disease in the absence of IMiDs. Cereblon is also the target protein of IMiDs and enhances their effects when present.

TECHNOLOGY

B16 tumor growth (s.c.) over time in *Crbn*^{+/+} and *Crbn*^{-/-} recipient mice, with representative images of isolated tumors.

PUBLICATION/PATENT

- Provisional application was filed in June of 2022 for Drs. Nicholas Lawrence, Harshani Lawrence, and Mark Alexandrow.



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LICENSING OPPORTUNITY

