Novel Transcription Factor Inhibitor as Treatment for Epithelial Cell Cancers

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Lung, breast and ovarian cancer

- Lung, breast and ovarian cancer represent over 25% of all globally diagnosed cancers (excluding non-melanoma skin cancer), with an estimated 522,390 new cases in the United States in 2018.
- The global cancer drug market was estimated at $110 billion in 2015 and expect to grow to over $150 billion by 2021.
- Current treatments utilize monoclonal antibodies or small molecule inhibitors
  - Moderately effective with off target effects
  - Toxicity
  - Most converge on small number of biological pathways and downstream effectors, e.g. EGFR, Ras
CBFβ Inhibitors

**Solution:** Researchers at University of Virginia have developed novel small molecule inhibitors that are potent against breast, ovarian, and lung epithelial cancer cell lines and use a less exploited mechanism by targeting a transcription factor involved in cancer pathways

- Novel CBFβ Inhibitors potently and specifically ablate cancer cells and not normal cells *in vitro*
- CBFβ Inhibitors are orally bioavailable

Illendula A et al., EBioMedicine 2016
CBFβ Inhibitors are effective against cancer cell lines but not normal cells

Active inhibitor (AI-14-91, AI-10-104) Inactive control (AI-4-88)

CBFβ Inhibitors reduce cancer cell line growth to a similar level as known cell death inducers, but do not effect normal cell growth
CBFβ Inhibitors are orally bioavailable

△: Plasma concentration as a function of time for active inhibitors Al-12-126 or Al-14-91

○: Concentration from oral gavage dosing

●: Concentration from intraperitoneal dosing (100 mg/kg) in mice.

CBFβ Inhibitors are orally bioavailable and oral administration results in similar plasma levels of inhibitors as intraperitoneal injection.
Relevant Publications

• Carlton AL, et al., 2018, Gynecologic Oncology. 10.1016/j.ygyno.2018.03.005.

• Illendula A et al., 2016, EBioMedicine, 8: 117-131.

• Illendula A et al., 2015 Science. 347, (6223): 779-84.
Title: INHIBITORS OF INV(16) LEUKEMIA