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

World Cancer Fund, American Cancer Society
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

Surface representation of the binding pocket on CBFβ (grey) with AI-4-57 (blue) bound

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

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 and oral administration results in similar plasma levels of inhibitors as intraperitoneal injection.

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

○: Concentration from oral gavage dosing

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

• UVA Tech ID: Bushwellner-126mono
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