

# Novel Transcription Factor Inhibitor as Treatment for Epithelial Cell Cancers

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# Lung, breast and ovarian cancer

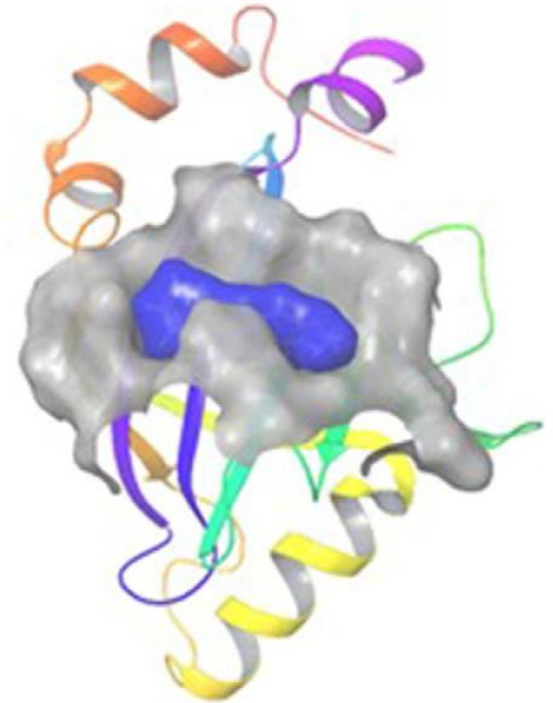
- Lung, breast and ovarian cancer represent over 25% of all globally diagnosed cancers (excluding non-melanoma skin cancer), with an estimated 522,390 new cases in the United States in 2018.
- The global cancer drug market was estimated at \$110 billion in 2015 and expect to grow to over \$150 billion 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

# CBF $\beta$ 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

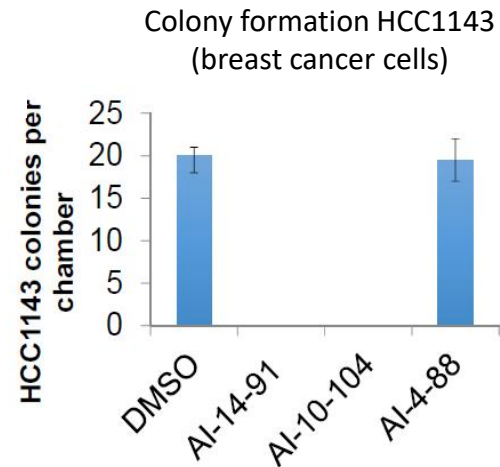
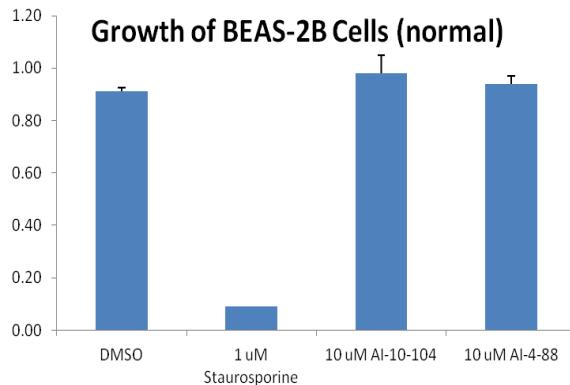
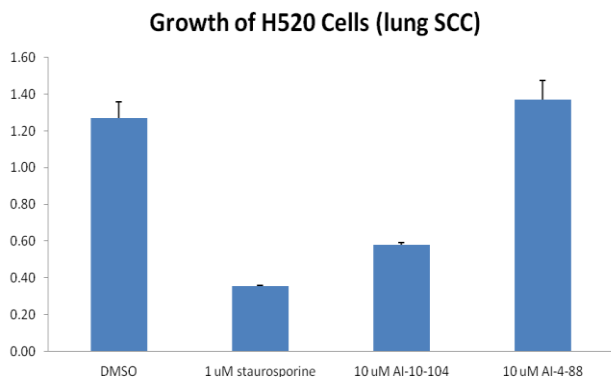
- Novel CBF $\beta$  Inhibitors potently and specifically ablate cancer cells and not normal cells *in vitro*
- CBF $\beta$  Inhibitors are orally bioavailable



Surface representation of the binding pocket on CBF $\beta$  (grey) with AI-4-57 (blue) bound

Illendula A et al., EBioMedicine 2016

# CBF $\beta$ Inhibitors are effective against cancer cell lines but not normal cells

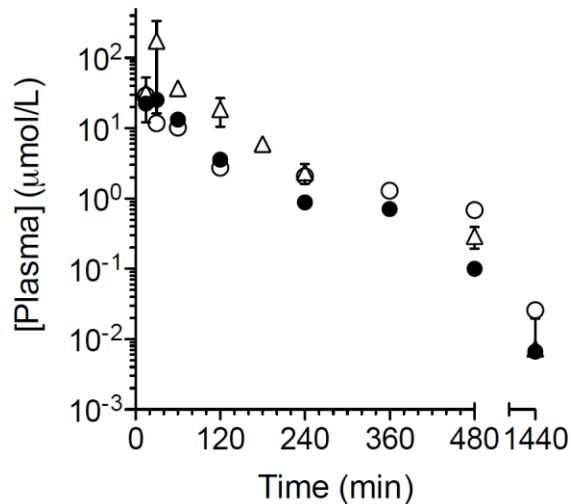


**Active inhibitor (AI-14-91, AI-10-104)**

**Inactive control (AI-4-88)**

**CBF $\beta$  Inhibitors reduce cancer cell line growth to a similar level as known cell death inducers, but do not effect normal cell growth**

# CBF $\beta$ Inhibitors are orally bioavailable



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

$\circ$ : concentration from oral gavage dosing

$\bullet$ : Concentration from intraperitoneal dosing (100 mg/kg) in mice.

**CBF $\beta$  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.

# Intellectual Property

- UVA Tech ID: Bushweller-126mono
  - Title: INHIBITORS OF INV(16) LEUKEMIA
  - Issued U.S. Patent 8,748,618 B2 Jun. 10, 2014