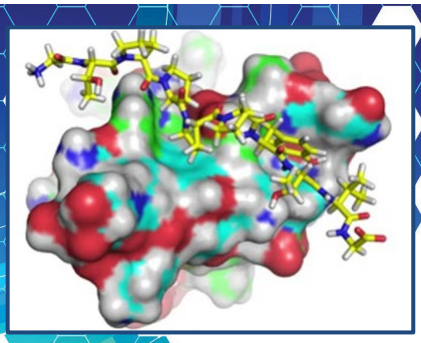
LICENSING OPPORTUNITY

Small Molecule Inhibitors that Target Stemness to Overcome Resistance in Lung Cancer



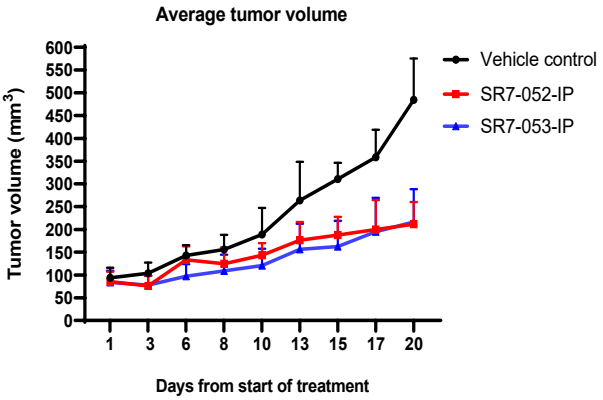
Disruption of the OCT4-YAP1 interaction inhibits the self-renewal of stem-like cells thus preventing tumor initiation, progression, drug resistance and metastasis. Here we present highly potent and selective disruptors of the Oct4-YAP1 interaction that **target the stemness to overcome drug resistance in lung cancer**. Drug-like and selective YAP1-OCT4 inhibitors have been developed with an IC_{50}as low as 0.4 uM. These compounds can be developed into anti-cancer therapies for lung cancer and possibly other malignancies

COMMERCIAL OPPORTUNITY

- The American Cancer Society's estimates about 236,740 new cases of lung cancer in 2022. Lung cancer is the leading cause of cancer mortality, accounting for almost a quarter of all cancer deaths. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer with up to 90% of all lung carcinomas falling into the non-small cell category.
- There are several FDA approved targeted agents for advanced NSCLC. More recently, FDA has approved four novel drugs for the treatment of lung cancer, in addition to eight expansions for the use of therapeutics previously approved for other indications: (1) Lumakras (sotorasib), (2) Capmatinib (Tabrecta), (3) Targeted therapeutic pralsetinib (Gavreto; previously called BLU-667), and (4) Lurbinectedin (Zepzelca) for patients with metastatic SCLC.
- Non-small cell lung cancer (NSCLC) is highly correlated with smoking and has very low survival rates. Multiple studies have shown that stem-like cells contribute to the genesis and progression of NSCLC. Drug resistance is a major cause for therapeutic failure in NSCLC leading to tumor recurrence and disease progression. The most frequent form of acquired resistance in NSCLC is secondary mutations in EGFR occurring in 60% of patients treated with second generation TKIs. **Moffitt's highly potent and selective disruptors of the YAP1-OCT4 interaction may offer an effective strategy to the treatment of NSCLC by targeting the stemness to overcome drug resistance.**

TECHNOLOGY

Preliminary mouse xenograft studies shows a significant decrease in tumor volume (55%) when treated with small molecule YAP1-OCT4 disruptors (**see figure below**).



PUBLICATION/PATENT

Provisional application was filed for Drs. Chellappan & Lawrence, *et al.* 2021

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