Organic Synthesis Shared Resource
Director: Xiaobing Tian, Ph.D.

LEGORRETA CANCER CENTER
BROWN UNIVERSITY

Overview

The SR offers:

- ❖Assist investigators with experimental plans for drug synthesis for lead optimization.
- ❖Facilitate organic synthesis efforts through interactions with the Department of Chemistry, Industry or other collaborations.
- ❖Provide support for grant submissions.

Key Services

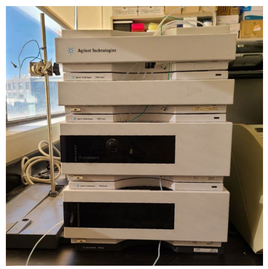
- Develop plan for organic synthesis around lead compounds
- Assist with plans for lead optimization
- Interface with Department of Chemistry (work-in-progress)

Value Added

- Support drug discovery and development
- Support interdisciplinary collaboration

Major Equipment /Technologies

- Agilent HPLC
- Chemical Hood



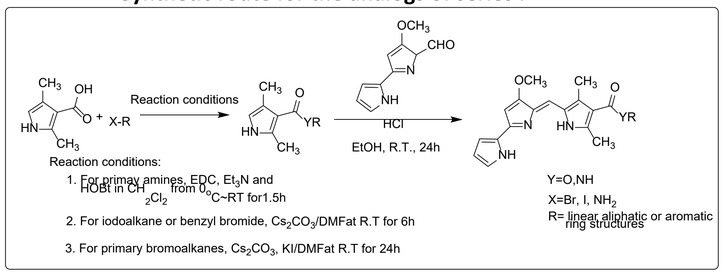
Key Personnel

- Xiaobing Tian, Ph.D.
  Email: xiaobing_tian@brown.edu

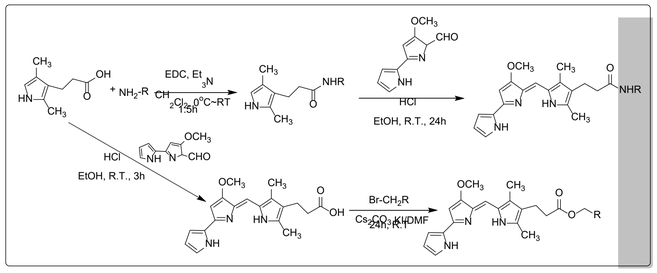
Examples of Scientific Impact

Synthesis of prodigiosin analogues

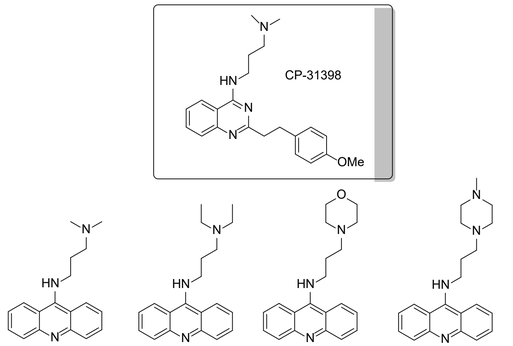
Synthetic route for the analogs of series I



Synthetic routes for the analogs of series III

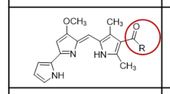
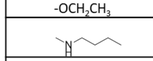
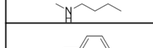
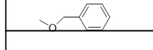
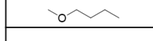
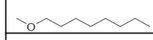


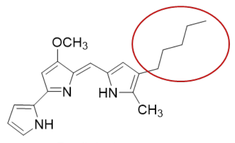
Synthesis of Acridine analogues



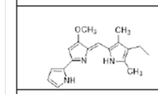
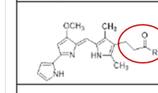
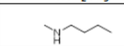
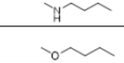
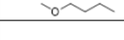
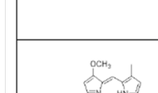
Medicinal Chemistry: Structure Activity Relationships

Prodigiosin Analogs (Series I)

	R	Code
	-OH	PG1-COOH
	$-OCH_2CH_3$	PG1
		PG4
		PG5
		PG6
		PG7
		PG8

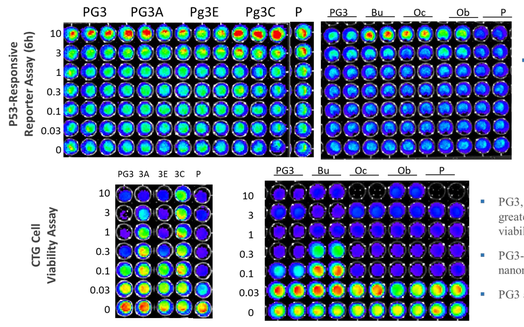


Prodigiosin Analogs (Series III)

	R	Code
		PG3
	-OH	PG3-COOH
	$-OCH_2CH_3$	PG3-E
		PG3-A
		PG3-Bu
		PG3-Oc
		Obatoclax

Medicinal Chemistry: Series III Analogs

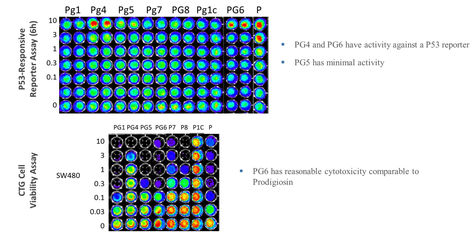
We Studied The Effect of Series III Analogs on the P53 Pathway in SW480 Cells



- PG3, PG3A, PG3E, PG3C, Bu and PG3-Oc have activity on p53 reporter
- PG3, PG3E and PG3-Oc have greatest effect on reducing cell viability
- PG3-Oc was down in the nanomolar range
- PG3 also had comparable activity

Medicinal Chemistry: Series I Analogs

We Studied The Effect of Series I Analogs on the P53 Pathway in SW480 Cells



- PG4 and PG6 have activity against a P53 reporter
- PG5 has minimal activity
- PG6 has reasonable cytotoxicity comparable to Prodigiosin

Issued composition of matter patent on PG3-Oc and PG3; compounds in process of translation through industry collaboration

This work led to a phase 1b clinical trial of Quinacrine + Capecitabine in advanced colorectal cancer. The trial was completed and published in 2020.

Original Study

Check for updates

First-in-Human Phase 1b Trial of Quinacrine Plus Capecitabine in Patients With Refractory Metastatic Colorectal Cancer

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Impact on Users

- Support the generation of new IP at Brown's Legorreta Cancer Center
- Synthetic chemistry to generate analogues of lead compounds

Key Publications

- Tian, X. et al., *Neoplasia*, **2021**, 304-325
- Wang, W. et al, *Cancer Biology & Therapy*, **2005**, 893-898

Future Plans

- Increase user base
- Work on consultation
- Work toward self-sufficient Shared Resource