



Rhenium Chemotherapeutics: Two Classes of Compounds

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Challenge

- In 2020, 1.8 million new cancer cases diagnosed in the U.S. alone
- Cisplatin and related Pt-based chemotherapeutics: prescribed for ~50% of all cancer patients
 - Testicular, ovarian, bladder, lung, breast, and cervical cancers
 - Critical component of combination therapies for range of solid tumors
- Limitations of current Pt-based chemotherapeutics:
 - Severe side effects: nephrotoxicity, neurotoxicity, ototoxicity, peripheral neuropathy, myelosuppression, nausea and vomiting
 - **Tumor resistance to chemotherapeutics**
 - **No detectable imaging of tumor response**

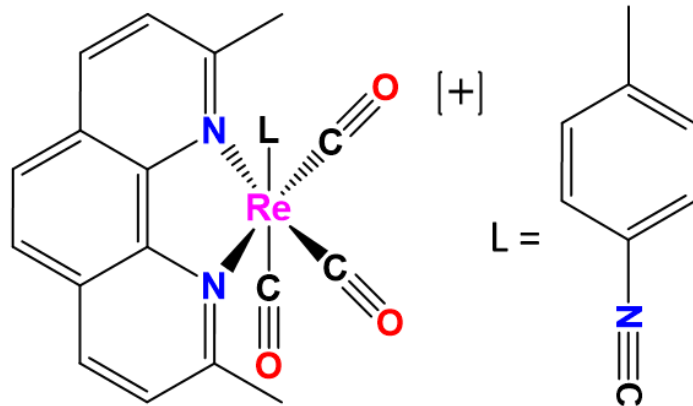
Market: Chemotherapeutics

- **Global chemotherapeutic market:**
 - \$141B in 2019, \$394B by 2027 (11.6% CAGR, *Fortune Business Insights*)
 - Main market driver: increasing prevalence of cancer
 - 18.1M new cancer cases in 2018, expected to rise to 29.4M by 2040 (WHO)
- **Global Pt-based drug market:**
 - \$1.3B in 2018 (4.1% CAGR over 2019-2026, *Polaris Market Research*)
 - Main market drivers:
 - Serious side effects of cisplatin
 - Circumventing Pt-based drug resistance

Essential need for safer, more effective chemotherapeutics

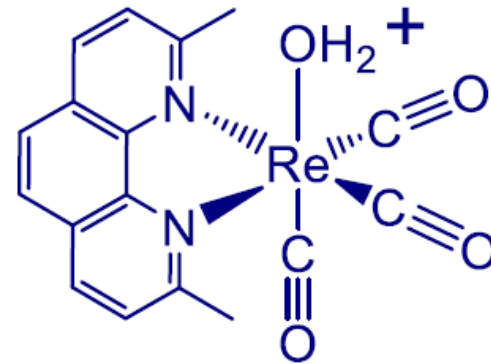
The Inventions

Class A (TRIP-1a)



Induces unfolded protein response-mediated apoptosis (ER stress)

Class B (Aqua)



Cell death *via* non-canonical pathway

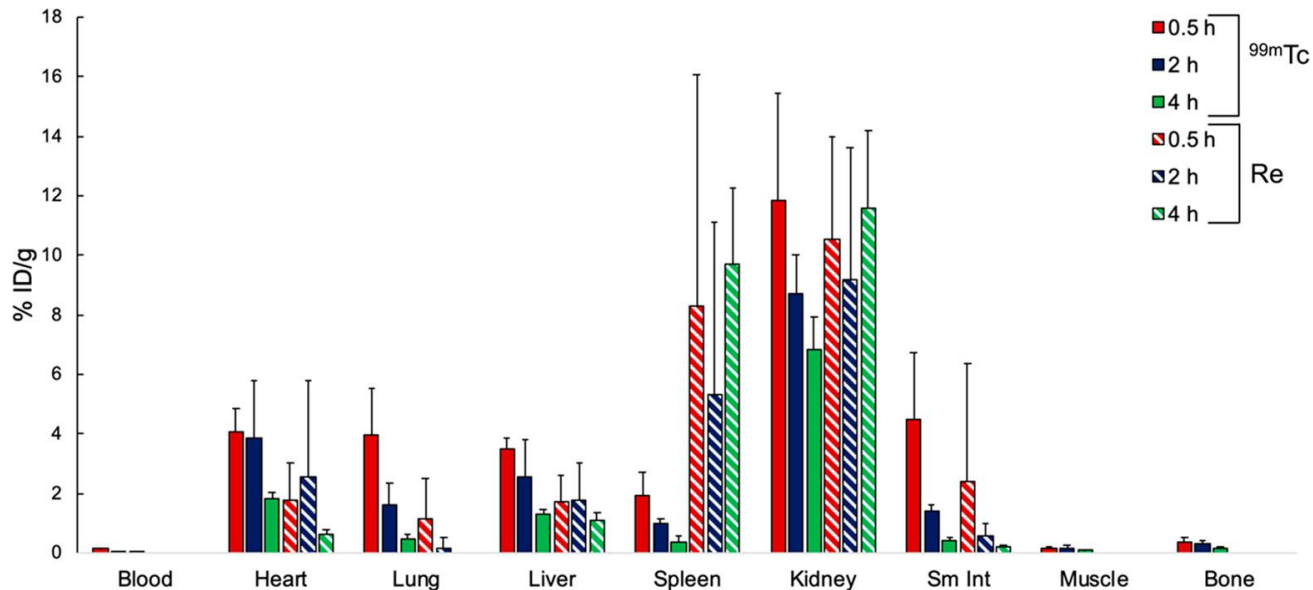
Low-cost, efficient, and scalable manufacturing of water-soluble drugs

Class A shows potency in multiple cancer cell lines

Cell Line	Cell Line Origin	IC ₅₀ (μM)	
		Cisplatin	Class A
A2780	Human ovarian cancer	1.3 ± 0.1	1.7 ± 0.7
A2780CP70	Human cisplatin-resistant ovarian cancer	12 ± 3	1.9 ± 1
HeLa	Human cervical cancer	6.6 ± 0.7	1.4 ± 0.2
A549	Human lung cancer	5.6 ± 0.5	1.4 ± 0.6

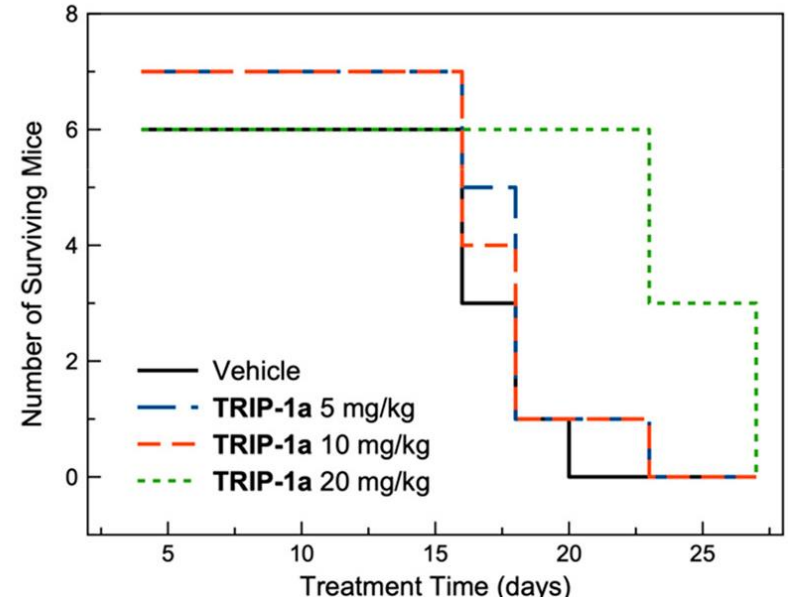
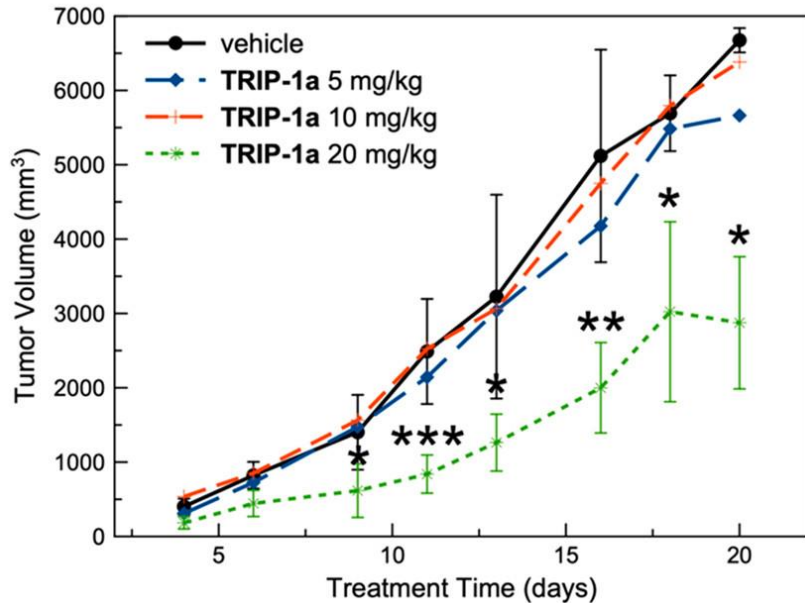
Class A is **6X** more potent than cisplatin in a cisplatin-resistant cell line

Class A is cleared through the liver and kidneys



In BALC/c mice, Class A accumulated in the liver and kidneys (**hepatic and renal clearance**), as well as in the heart and lungs

Class A significantly inhibits tumor growth at 40 mg/kg



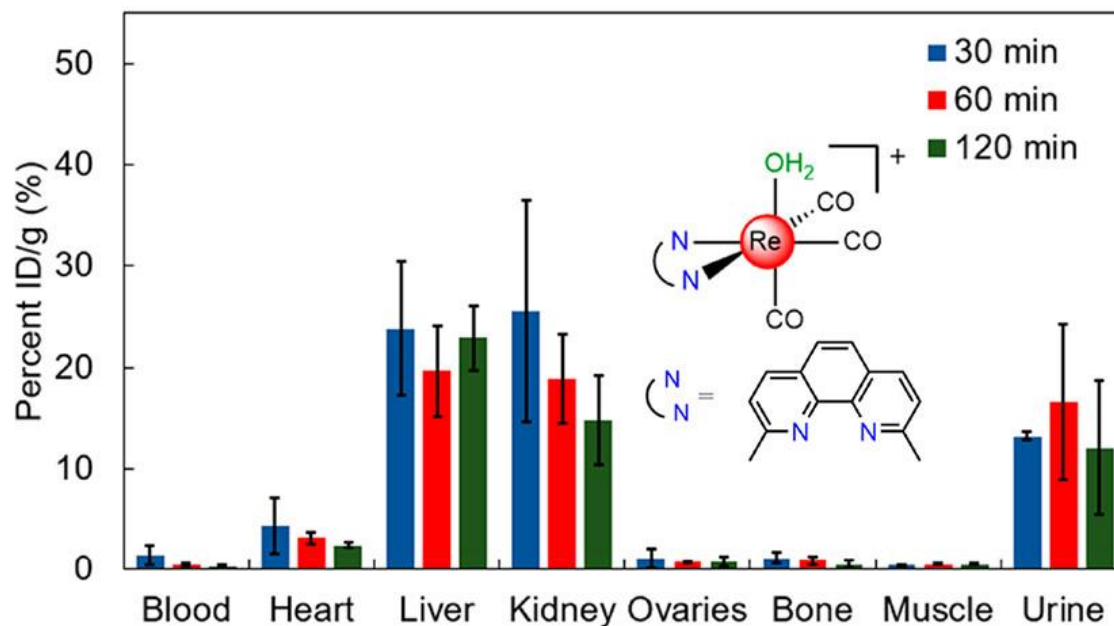
Survival of mice bearing A2780 ovarian cancer xenografts was **extended by 150%** relative to the control group

Class B shows potency in multiple cancer cell lines

Cell Line	Cell Line Origin	IC ₅₀ (μM)	
		Cisplatin	Class B
A2780	Human ovarian cancer	1.3 ± 0.1	2.2 ± 0.2
A2780CP70	Human cisplatin-resistant ovarian cancer	12 ± 3	3.0 ± 0.7
HeLa	Human cervical cancer	6.6 ± 0.7	1.2 ± 0.2
A549	Human lung cancer	5.6 ± 0.5	6.7 ± 4.9

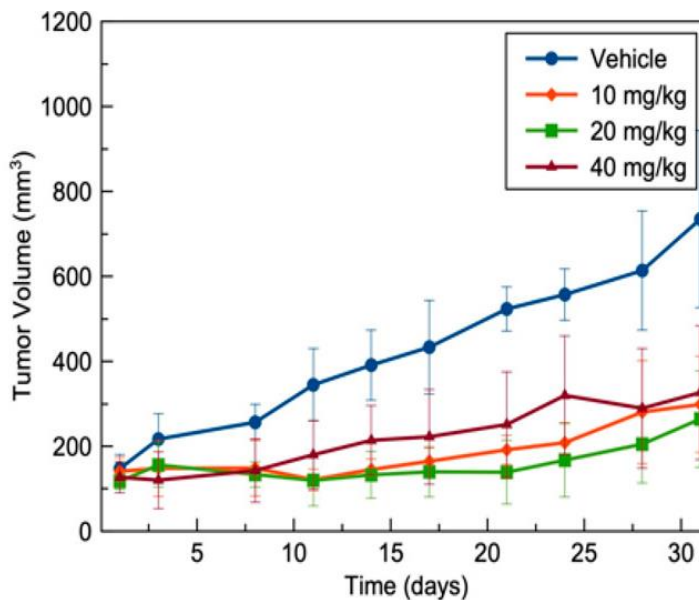
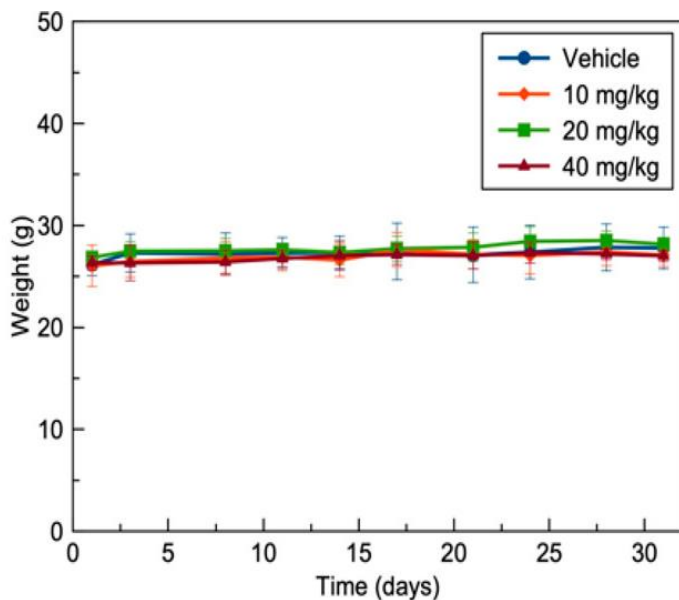
Class B is **4X** more potent than cisplatin in a cisplatin-resistant cell line

Class B is cleared through the liver and kidneys



In BALC/c mice, Class B accumulated in the liver and kidneys (**hepatic and renal clearance**) and showed no toxicity to mice

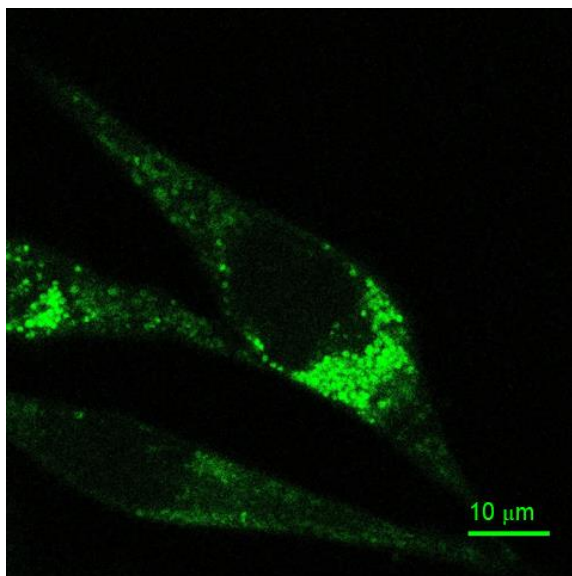
Class B significantly inhibits tumor growth at low concentrations



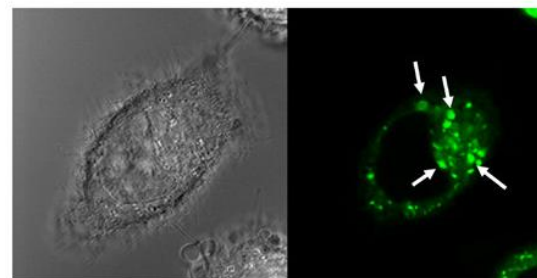
Class B inhibited tumor growth at **10 mg/kg** in mice bearing ovarian cancer xenographs and **did not affect body weight** at any tested concentration

Both classes of Re chemotherapeutics are intrinsically luminescent

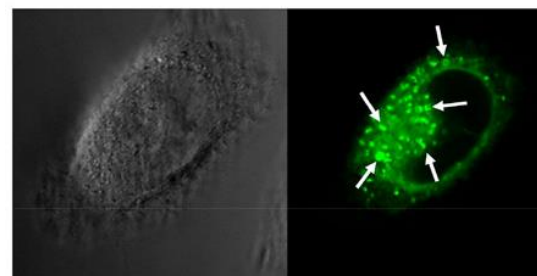
10 μ M, Class A, 4 h



10 μ M
Class B, 24 h



25 μ M
Class B, 4 h



Unlike native cisplatin, both classes are suitable for **theranostic applications** or as **partner imaging agents** with ^{99m}Tc

Targeted Cancers

- Cisplatin is used to treat several cancers (*MacMillan Cancer Support*)
 - Testicular, ovarian, bladder, head and neck, lung, and cervical cancer
 - Its use is being studied in several other cancers
- Cancers sensitive to ER stress-inducing drugs (like **Class A**) include:
 - Multiple myeloma
 - Glioblastoma
 - Pancreatic ductal adenocarcinoma (PDAC)
- For cisplatin-resistant cancers, both Class A and Class B are **highly potent**

Synergism between the classes is being investigated

The Inventor



Justin J. Wilson ([profile](#))

- Associate Professor, Department of Chemistry & Chemical Biology, Cornell University
- Expert in:
 - Medicinal inorganic chemistry
 - Radioactive and non-radioactive metal complexes for both therapeutic and diagnostic applications

Intellectual Property

- “Rhenium Complexes and Methods of Use for Treating Cancer”
 - Generation 1
 - Issued patent 10,973,849
- “Rhenium Complexes and Methods of Use for Treating Cancer”
 - Generation 2
 - U.S. patent filed US20210317151A1

Licensing rights available for both generations

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