



OFFICE OF SPONSORED RESEARCH



## **Chemosensitizing Agents for Multidrug Resistance (MDR) & Chemotherapy**

### **Overview:**

McGill University is seeking to outlicense intellectual property relating to compounds for reversing multidrug resistance. The invention provides potent first in class flavonoid analogs that reverse resistance of tumors to common chemotherapeutics. Remarkably, the compounds also manifest chemosensitization of pentamidine and sodium stibogluconate resistance in *Leishmania in vitro*. and exhibit intrinsic anti-Leishmanial activity against promastigotes and amastigotes.

### **Medical need & Opportunity**

Multidrug resistance (MDR) is responsible for many forms of resistance in bacteria, fungi and human tumors. The MDR phenotype is a major determinant of clinical outcome in cancer treatment. The resistance of tumor cells is often the result of the enhanced ability of these cells to impair efficacy of cytotoxics through increased drug conjugation and upregulation of drug efflux. The latter is mediated by for instance by P-glycoprotein (MDR1) or multidrug resistance protein 1 (MRP1).

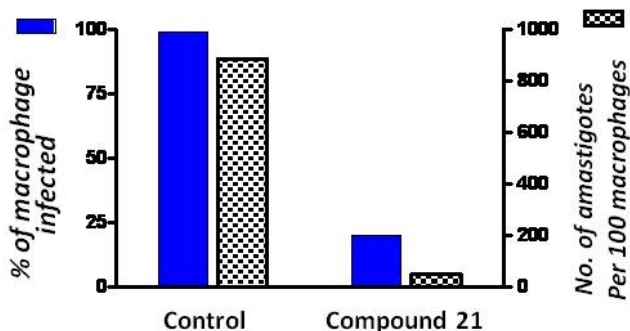
Pentavalent antimonial compounds are the mainstay in the treatment of the various forms of leishmaniasis. Pentamidine and amphotericin B are second-line treatment in cutaneous leishmaniasis. The compounds of the invention present new alternatives indicated as chemosensitizing agents in drug resistant chemotherapy.

## Technology

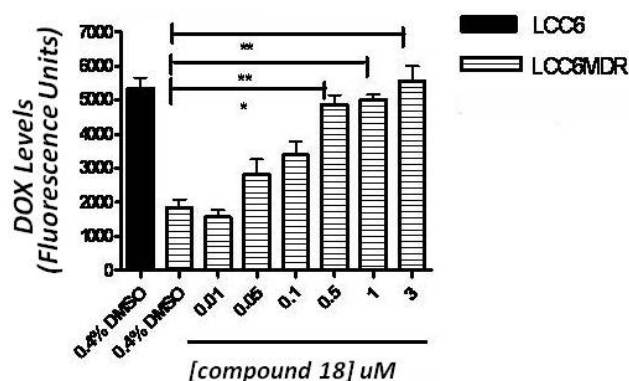
Proof of concept is demonstrated in three drug resistant tumor cell lines: (i) MDA435/LCC6 human breast cancer cells (ii) murine *P388/ADR* leukemic cells and (iii) *2008/MRP1* ovarian carcinoma cells. The chemosensitization of drug resistant tumor cell lines is demonstrated for taxol, doxorubicin, daunomycin, vincristine and vinblastine and others. The compounds are effective in killing parasites resistant to the other current clinically used antileishmanials.

### *In vitro* anti-amastigote activity of compound 21

mouse peritoneal elicited macrophages (PEM) infected with sodium SSG-resistant Ld39 promastigotes, allowed to transform into amastigotes,



### Accumulation of Doxorubicin as a function of [compound 18]



## The Inventors



**Dr. Tak-Hang (Bill) Chan** is Professor Emeritus, McGill University and Honorary Professor, Academia Sinica, Peking University, Lanzhou University. Dr. Chan received his B. Sc. from the University of Toronto in 1962, his M. A. from Princeton University in 1963 and his Ph. D. from Princeton University in 1965. Professor Chan has been the recipient of many awards and distinctions: Merck Sharpe & Dohme Award, 1982 Senior Killam Fellow, 1983-85 R. U. Lemieux Award, 1993 Fellow, Royal Society of Canada



**Dr. Larry M. C. Chow** is Associate Professor & Associate Head at Hong Kong Polytechnic University. He received his B. Sc. from the Imperial College London in 1990 and his Sc.D. from Harvard University in 1996. Dr. Chow was the recipient of the Young Investigator Award in 1995 and of the President's Awards for Outstanding Performance/Achievement from Hong Kong Polytechnic University in 2000.

### CONTACT:

John Di Maio  
Office of Sponsored Research  
McGill University  
Tel: 514-398-8949  
Email: john.dimaio@mcgill.ca  
Reference code: ROI 06083, 09052, 09086  
Opportunity: Exclusive license or research collaboration



L'Institut de recherche  
du Centre universitaire de santé McGill  
The Research Institute  
of the McGill University Health Centre



**McGill**