Appendix A

ANTI-CANCER DRUGS

Work on this project involved collaboration with Dr. Lali Medina-Kauwe, now at Cedars-Sinai Medical Center, on the development of corroles as anti-cancer drugs. Given the high fluorescence of corroles, and their known toxicity to cancerous cells[6], the water-soluble corroles seemed an ideal place to start on a search for drugs. While Dr. Medina-Kauwe worked on developing a protein to specifically enter cancer cells, we provided compounds for testing in cellular systems with model proteins, in particular with HSA. It was hoped that the fluorescent corroles could be used as a diagnostic tool for early cancer detection. If the corrole is bound to a transport protein specific for cancer cells, unknown cells could be exposed to the mixture and tested for the fluorescent markers. It was then hoped to develop a phosphorescent corrole that could be delivered to the cells and used to activate triplet oxygen in the cell to singlet oxygen, inducing cell death in a photodynamic therapy manner. If the absorbance of the corroles could not be shifted into tissue penetrating wavelengths, we planned to put more effort into developing a corrole that could activate a catalytic oxygen cycle, based on the findings that the chromium complex of **1** catalyzes the aerobic oxidation of phosphines[72].

While **2**, **2-Ga**, **2-Mn**, and **2-Sn** were all used to varying extents in the project, it was **2-Ga** that served as the best model compound. It was found that a transport protein could indeed deliver this corrole compound into cells (see figure A.1). Even more remarkable was the

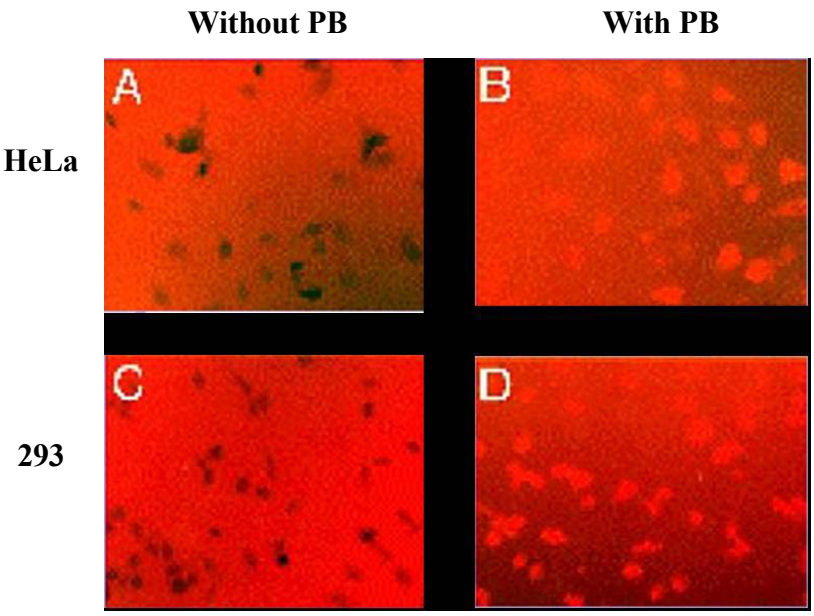

Figure A.1. Corrole delivery to cells. PB: a proven gene delivery protein. HeLa: human cervical carcinoma cells. 293: monkey kidney cells. Micrographs (courtesy of Dr. Medina-Kauwe) were taken under UV light at 10x magnification.

increased toxicity the corrole seemed to show toward cancer cells versus non-cancerous cells. The mechanism of this specific toxicity is still under investigation. This toxicity was seen with **2** and **2-Mn** as well. Work with **2-Sn** is underway.