# Design, Synthesis, and Biological Evaluation of Adenine-Targeted Platinum–Acridinylthiourea Derivatives: A Structure–Activity Relationship Study

Rajsekhar Guddneppanavar[1], Gilda Saluta[2], Gregory L. Kucera[2], and Ulrich Bierbach[1,2]

*[1]Department of Chemistry, Wake Forest University, [2]Comprehensive Cancer Center, Wake Forest University School of Medicine*

Sequence- and groove-specific DNA-targeted molecules play an important role in drug discovery. We have reported a novel platinum-acridine conjugate, [PtCl(en)-(ACRAMTU)]$(NO_3)_2$ (ACRAMTU = 1-[2-(acridin-9-ylamino)ethyl]-1,3-dimethylthiourea) that binds to DNA through a combination of monofunctional metalation of nucleobase nitrogen and intercalation of the acridine chromophore into the DNA base stack. To tune the sequence and groove specificity of this agent, we are making systematic changes to the acridine moiety. Seven new ACRAMTU derivatives were synthesized and fully characterized. The binding with poly(dG-dC)$_2$ and poly(dA-dT)$_2$ of these derivatives was studied using ethidium-DNA fluorescence quenching assays.

Platinum-conjugates of the above seven new ACRAMTU derivatives were synthesized (**1**-**7**) and characterized. The activity of both ACRAMTU derivatives and their platinum-conjugates were tested against HL-60 leukemia cells and possible structure-activity relationships will be discussed.