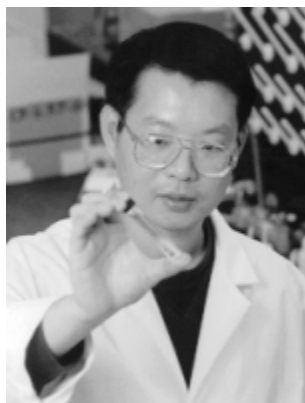


Fall 2009 Seminar Program*Friday, November 6th WBSH, Room 6030 - 3:15 p.m.*

Dr. Yan Xu
Professor and Director of Graduate Programs

Department of Chemistry
Cleveland State University

“Targeting DNA Base Excision Repair in Tumor Drug Resistance - An Application of Analytical Chemistry to Cancer Research”

ABSTRACT

Alkylating agents remain the backbone of cancer chemotherapy. These substances vitiate tumor cells by directly adding alkyl groups to the nucleotide bases in the cellular DNA. A major obstacle to effective cancer treatment with alkylating agents is the presence of elaborate mechanisms of cellular DNA repair. For example, methylating agents, such as temozolomide (TMZ), form cytotoxic and genotoxic O6-methylguanine (O6mG, 6%), N7-methylguanine (N7mG, 70%), and N3-methyladenine (N3mA, 3%) purine base adducts. The effectiveness of alkylating agents for cancer treatment is diminished by at least two DNA repair mechanisms. First, the O6mG base-adduct is repaired by O6mG DNA-methyltransferase (MGMT), and second the N7mG and N3mA base adducts are removed by the base excision repair (BER) pathway. These repair mechanisms result in tumor resistance to alkylating agents, thus limiting drug efficiency and leading to treatment failure.

The goal is to overcome tumor resistance to alkylating agents, which, in turn, should lead to a significant impact on cancer therapy and clinical outcome. A strategy is currently being developed by Dr. Stanton L. Gerson's group at the Case Comprehensive Cancer Center in collaboration with Dr. Xu's group at Cleveland State University aiming at interrupting DNA base excision repair using a safe and effective apurinic/aprimidinic (AP)-site blocking agent to achieve cytotoxic killing of the tumor cells. This talk will present the quantitative work in association of with the modulation of DNA base excision pathway using liquid chromatograph tandem mass spectrometry.

BIO

Dr. Yan Xu is a Professor of Chemistry. He currently serves as Associate Chair and Director of the Chemistry Graduate Program. Dr. Xu received his MS from California State University at Fresno, and his Ph.D. from University of Cincinnati. He joined Cleveland State University in 1991 as an Assistant Professor. He was a Visiting Scientist to the Division of Clinical Sciences at the National Cancer Institute during 2000-2001. Dr. Xu is also an Adjunct Staff in the Department of Molecular Cardiology at Lerner Research Institute, and an Adjunct Faculty in the Department of Medicine at Case Western Reserve University. Dr. Xu has developed a solid scholarly reputation in the field of bioanalytical chemistry with external funding from National Cancer Institute, American Cancer Society and National Institutes of Health, and had over 100 scientific publications and presentations. In addition to Dr. Xu's administrative responsibility in the Department, he has served on the University Judicial Board, University Graduate Petition Committee, University Undergraduate Petition Committee, University Global Learning Task Force, President's Advisory Council on Equal Access & Opportunity, Northeastern Ohio Science and Engineering Fair as Judge, American Chemical Society Cleveland Section as Alternate Councilor and Analytical Topical Group Leader.