

SEMINAR ANNOUNCEMENT

Targeting DNA Base Excision Repair in Tumor Drug Resistance - An Application to Anti-Cancer Drug Analysis

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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/apyrimidinic (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.

Thursday, January 29, 2009

12:00 – 1:00 pm

Room 117

Pizza and refreshments will be served before the seminar.