**Role of Microsatellite Stability and Mismatch DNA Repair Mechanism in the Response to 5­Fluorouacil Treatment in African American Colon Cancer Cell Lines**

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Despite progress in closing the gap, health disparities still persist among African American (AA) colon cancer patients both in incidence and death rates as well as worse prognosis after treatment with 5­Fluorouacil (5­FU) when compared to Caucasian American (CA) patients. In addition, AA colon cancer patients have higher incidence of mutations on the mismatch DNA repair mechanism (MMR) than CA patients and previous studies have shown a correlation between mutations in MMR and microsatellite instability (MSI) to resistance

to 5­FU. Therefore, we aim to examine if differential MSI and MMR play a role in the efficacy of 5­FU treatment in AAs.

Methods: We examined the microsatellite status and MMR mutations found in the tumors from AA colon cancer patients at our institution from 2010 to 2017 and utilized the AA tumor­derived colon cancer cell line SB­521, generated in Dr. Williams’ laboratory, and the CA colon cancer cell line HT­29 for in vitro studies. In order to assess the response to 5­FU, we used the protein levels of the ribonucleotide reductase catalytic subunit M1 (RRM1) protein as a marker for drug resistance, the cleavage of Caspase­3 for apoptosis initiation, c­Jun N­terminal kinases (JNK) phosphorylation as indicator of cellular stress and Histone 3 protein levels as reference of gene methylation changes.

Results: Our retrospective data (N=83 patients) demonstrated that up to 20% of our colon cancer patients have MSI and up to 30% showed MMR mutations. As hypothesized, the protein levels of the chosen targets in the two cell lines exhibited differences after treatment with 5­FU. The AA cell line SB­521 appears to be more sensitive to the chemotherapeutic in terms of apoptosis, stress response and drug resistance when compared to HT­29 cells.

Conclusions: Altogether, our results illustrate the range of MSI, MMR and protein patterns in AA tumors and cell line. The cell line SB­521 is a potential model to study 5­FU treatment for patients with MSI and MMR mutations as it has high MSI, does not express MLH1, has reduced MSH2 and overexpresses MSH6 (MMR proteins). Previous data suggests that lack of a functional MMR mechanism may play a role in the response to this chemotherapeutic. Further studies are needed to elucidate the differences in chemotherapy treatment responses between AAs and CAs and their role in colon cancer health disparities.