Zong Sheng Guo, PhD, PI; M. Haroon Choudry, MD, Co-PI
University of Pittsburgh
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Treating PMP Using Small Molecule Inhibitors of Gel-forming Mucin Production

Research Update as of 10/18/2011

Pseudomyxoma peritonei (PMP) is a rare malignancy characterized by intra-peritoneal accumulation of mucinous ascites and predominantly occurs in the setting of appendiceal neoplasms. The clinical course is determined by the degree of epithelial differentiation and extent of extra-cellular mucin production. Progressive accumulation mucin compresses intra-abdominal organs leading to organ dysfunction, morbidity and eventual patient demise. We hypothesize that targeted reduction of mucin production may minimize disease-associated symptoms, tumor recurrence and the need for repeated surgical interventions.

We have demonstrated successful inhibition of MUC2 mRNA expression in mucin secreting LS174T cells and decreased mucninous tumor growth in a subcutaneous LS174T murine xenograft model and an intra-peritoneal murine xenograft model of PMP developed in our laboratory after therapy with two anti-inflammatory drugs, dexamethasone and celebrex, and an MEK 1/2 inhibitor RDEA119. Preliminary analysis using comparative genomic hybridization array technology has identified unique genomic aberrations that may represent potential therapeutic targets, if found to be consistently present across multiple tumor samples in subsequent studies. Further research will identify additional potential targeted therapies and elucidate their mechanisms of MUC2 inhibition.