Exploiting Migration and Metabolism: A Novel Approach to Metastatic Cancers

Lozada, John Roy

Metastatic cancers are associated with a poor prognosis, as current treatments often prove ineffective at targeting every cancer cell and are rather damaging to normal cells. The research reported here suggests a multi-modal therapy for metastatic cancers through the sequestration and targeting of migratory cancer cells. Cells genetically modified to overproduce the potent chemoattractant, CXCL12, were encapsulated within a biocompatible alginate hydrogel to sequester cancer cells bearing CXCR4, the CXCL12 receptor, prominent in most malignancies. Previous work optimized the conditions for cellular encapsulation within the hydrogel. Current work evaluated the efficacy of encapsulated CXCL12 secreting cells on the migratory response of lung (A549), breast (MDA-MB231), and ovarian cancer cells (OVCAR-3), with each demonstrating an increased migratory response ($p<0.01$). These findings suggest potential to redirect cancer cell migration toward the hydrogel structure, restricting metastasis and allowing for the local delivery of anticancer drugs. Interestingly, CXCL12 also demonstrated an apoptotic effect on the cancer cells ($p<0.01$), not observed in non-cancerous HaCaT keratinocytes ($p>0.05$). In conjunction, 3-bromopyruvate was incorporated to further induce apoptosis in the migratory cancer cells through glycolytic inhibition, exploiting cancer's unique metabolic pathway. Akin to CXCL12, 3-bromopyruvate demonstrated an apoptotic effect specific to cancer cells ($p<0.001$). In combination, CXCL12 and 3-bromopyruvate were shown to have a potentially synergistic apoptotic effect. Altogether, these results suggest that a CXCL12 and 3-bromopyruvate laden biocompatible hydrogel has potential to serve as an implantable therapeutic option for a broad spectrum of metastatic cancers.

Awards Won: