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### **Retinoic acid treatment of glioblastoma multiforme microtumors suppresses key metastatic parameters and induces tumor cell death**

Although clinical studies have shown consistent aberrations of retinoic acid (RA) metabolism in the brain tumor malignancy, glioblastoma (GBM), currently there is no consensus regarding its potential application to patient treatment. Specifically, increased levels of a key enzyme involved in its synthesis, aldehyde dehydrogenase 1 (ALDH1), have been identified in many human cancers, including GBM. Elevated ALDH1 levels occur at GBM invasion zones that interface normal brain tissue in patients with GBM, and this metastatic parameter is a prognostic biomarker since there is an inverse correlation between patient survival and ALDH levels at these invasion zones. Increased ALDH1 levels result in increased production of RA, which has been implicated as an important contributor to cell “stemness”, a phenotype linked to sustained tumorigenesis. Recent studies at our Cancer Biology Research Laboratory suggest that retinoic acid treatment of GBM microtumors suppresses the formation of tumor invasion zones and substrate attachment, ultimately resulting in tumor cell death. I propose that this effect is due to feedback inhibition of ALDH (whose levels are high in these invasion zones) by exogenous RA. This model suggests that the cancer stem cell (CSC) phenotype is at least in part sustained by ALDH1 mediated effects on cell motility and invasive parameters normally restricted to developing neural tissue. This research suggests that Vitamin A, known to play an important role in normal embryonic neural tissue development, may also counteract the activity of a critical pathway involved in the malignant transformation of glioma cells by classic negative feedback regulation.

#### **Biography**

Sarah Adelaide Crawford is Professor of Genetics at Southern Connecticut State University. She received a PhD from Columbia University College of Physicians and Surgeons, an MS degree in biochemistry from Princeton University, and a BS degree from Marymount Manhattan College. She is director of the Cancer Biology Research at Southern Connecticut State University.

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