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Cystatins as inhibitors of metastatic disease

James L. Cox
AT Still University, USA

A tremendous challenge in the treatment and therapy of cancers is due to their propensity to undergo metastasis. Until now there are no effective inhibitors of metastasisin clinical use, excepting perhaps angiogenesis inhibitors. The cystatins are small molecular weight protein inhibitors of cathepsins which have anti-metastatic effects. While certain cathepsins are generally elevated in different tumors, the cystatins are either unchanged or decreased in levels. The cystatins display in general metastasis suppressor actions. Melanoma and a number of other cancers (glioblastoma, breast, prostate and colon) are found to have decreased metastasis when cystatin C is overexpressed in each of the cancer cell types. We noted earlier dramatic inhibition of migration and invasion of melanoma cells overexpressing cystatin. An increase in apoptosis was also noted in a mouse model of metastasis. The cystatins are also known angiogenesis inhibitors which may play a role in reduced metastatic tumor growth. Decreases in melanoma cell signaling and cell migration on collagen are a major current focus. Migration related changes including rhoprotein and calcium regulation are the current approaches we have taken to look at cystatinmechanism of action. The anti-metastatic actions of a natural protein, cystatin, may help unlock future cancer treatment options.

Biography

James Cox obtained his PhD in biochemistry from the University of South Dakota School ofMedicine in 1984. The topic of his doctoral research was DNA repair. From there he did postdoctoral work at Mt. Sinai School of Medicine (NYC). His first position was with Dr. David Calhoun working on E.coli branched chain amino acid gene regulation. The second position was with Dr. Phyllis Shaw and involved the molecular and genetic analysis of cystatin S structure and expression (Cox et al. 1992). He established his own laboratory at AT Still University in Kirksville, Missouri in 1991. At this point he directed his interest in melanoma metastasis and has done much of his work with B16 melanoma cells. He first showed cystatins could block metastasis of melanoma and has directed his studies around this system (Cox et al. 1999, Ervin et al. 2005). He also has broad interests in melanoma and cancer cell biology.

jcox@atsu.edu