CIP2A is Associated with Human Bladder Cancer Aggressivity

Introduction and Objective: Cancerous inhibitor of protein phosphatase 2A (CIP2A) is an oncogenic factor stabilizing c-Myc protein and driving cellular transformation. We evaluate whether CIP2A expression can serve as a marker for bladder cancer and determine its potential as a therapeutic target.
Materials and Methods: Normal and malignant bladder tissues derived from 25 patients with bladder cancer were analyzed for CIP2A mRNA expression using by real-time PCR. CIP2A protein expression was detected in 117 bladder cancers by immunohistochemistry using a tissue microarray annotated with patients follow-up. The functional role of CIP2A in bladder cancer cells was evaluated by small interfering RNA-mediated depletion of the protein followed by an analysis of cell proliferation, migration, invasion, anchorage-independent growth, and xenograft growth.
Results: In 25 bladder cancer tissues examined, 22 of them (88%) exhibited much stronger levels of CIP2A mRNA compared with their corresponding normal tissues. CIP2A protein expression was associated with poor prognosis ($P < 0.001$), lymph node status ($P < 0.001$), tumor stage ($P = 0.003$), histologic grade ($P = 0.011$). Multivariate analysis showed that CIP2A overexpression was an independent prognostic factor ($P = 0.035$). Functionally, CIP2A depletion was shown to inhibit the expression of its target protein c-Myc. Loss of CIP2A also inhibited proliferation, migration, invasion, and anchorage independent growth in bladder cancer cells. Finally, CIP2A was shown to support T24 xenograft growth in nude mice.
Conclusion: Our findings suggest that CIP2A overexpression may play an important role in progression of bladder cancer and CIP2A could be a potential target of bladder cancer therapy.