

Fibrinolytic factors promote inflammatory colonic carcinogenesis through miR-126-mediated targeting of the proteolytic niche

Yousef Salama

An-Najah National University, Palestine

Inflammation is a well-established driver of carcinogenesis and inflammatory bowel disease patients have an increased risk of developing Colorectal Cancer (CRC). We found high intratumoral expression of the fibrinolytic factor Tissue-type Plasminogen Activator (tPA) in human colorectal tissues. Using the azoxymethane/dextran sodium sulfate-induced inflammation-associated colon carcinogenesis model, we demonstrate that tPA and plasmin are up-regulated during colon carcinogenesis. Genetic and pharmacological inhibition of plasmin or tPA suppressed inflammation-induced tumor formation in AOM/DSS induced mice. Mechanistically, tPA downregulated AP2a and miR-126 by activating NF- κ B signaling. Furthermore, tPA via miR126 deregulates factors like HB-EGF, proteases (tPA or MMP9) and CCL2 that are known to promote inflammation-induced CRC. Taken together, our study indicates that targeting plasmin may be useful in the prevention of colon cancer in individuals with inflammatory bowel disease.

Biography

Yousef Salama has completed his PhD from the Institute of Medical Sciences, University of Tokyo, Japan. He is currently working as a Professor at An-Najah National University, School of Medicine. He has published more than 25 papers in reputed journals in the field of cancer and stem cell research.

yousef.ut@gmail.com