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Human microRNA miR-888 cluster is a novel oncogenic network in the prostate involved in cancer progression pathways

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Prostate cancer (PCa) is the 2nd leading cause of cancer-related male deaths in the US. Clinicians lack effective clinical options for advanced disease and metastatic PCa remains incurable and lethal. MicroRNAs (miRNAs) are often dysregulated in human PCa. It is poorly understood how these small non-coding RNAs function in the prostate to promote cancer progression. In a screen for miRNAs correlating with advanced disease, we found miR-888 was enriched in aggressive, castration-resistant human PCa cell lines and in tumors from PCa patients. This miRNA was elevated in an innovative prostatic fluid biomarker source called expressed prostatic secretions in urine (EPS urine) from PCa patients with high-grade disease. We postulated that miR-888 plays an oncogenic role in the prostate. Indeed, we noted miR-888 promoted prostate cell proliferation, migration and colony formation *in vitro*. miR-888 belongs to a genomic cluster of seven miRNAs (miR-892c, -890, -888, -892a, -892b, -891b, -891a) located on chromosome Xq27.3 and lies within HPCX1 (hereditary PCa, X-linked 1), a region associated with hereditary PCa. miR-888 cluster members were similarly elevated in aggressive PC3 cell lines and enriched in EPS urine exosomes from high-grade PCa patients. Our *in vitro* assays indicated that this cluster modulated prostate cell growth, migration, invasion, and ability to grow in soft agar. miR-888 and miR-891a were validated as bona fide pro-oncogenic factors and accelerated prostate tumorigenesis in mice. We are testing if miR-888 cluster inactivation using antimir reagents blocks disease progression in animal models. This work will lead to effective clinical tools for aggressive PCa.

Biography

Aurora Esquela-Kerscher completed her MS in Biotechnology and PhD in Biochemistry, Cellular and Molecular Biology at the Johns Hopkins University School of Medicine. She conducted a Post-doctoral Fellowship in Frank Slack's laboratory at Yale University where she began her studies on the role of microRNAs during development and disease. She is currently working as an Associate Professor in the Department of Microbiology and Molecular Cell Biology and Member of the Leroy T Canoles Jr. Cancer Research Center at Eastern Virginia Medical School in Norfolk, Virginia. Her lab aims to develop novel diagnostic and therapeutic targets for aggressive forms of prostate cancer.

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