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Dual role of the TGF- β superfamily cytokine MIC-1/GDF15 in tumorigenesis in prostate cancer prone TRAMP mice

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MIC-1/GDF15 is a TGF- β superfamily cytokine, which was first cloned by author's group from activated macrophages. It is reported to play role in a range of biological activities including inflammation, metabolism and cancer. MIC-1/GDF15 expression is upregulated in prostate cancer (PCa) and other common cancers raising its serum levels in proportion to stage and extent of disease. In advanced cancer, these serum levels can increase by 10-50 folds leading to cancer anorexia/cachexia. In present study, the effect of MIC-1/GDF15 on PCa development and spread in the TRAMP transgenic model of prostate cancer was evaluated. TRAMP mice was crossed with MIC-1/GDF15 overexpressing MIC-1^{fms} mice to generate TRAMP^{fmsmic-1} mice and then compared the development and spread of PCa in both mouse lines. It was further compared metastasis of androgen independent TC1-T5 TRAMP cell line that lacks MIC-1/GDF15 expression, by injecting intravenously into MIC-1^{fms} and WT mice. TRAMP^{fmsmic-1} had significantly smaller genitourinary tumors, lower PCa grades and on average, survived 7 weeks longer than TRAMP mice. Contrary to this, a much larger number of TRAMP^{fmsmic-1} mice developed distant organ metastases. Following intravenous injection of TC1-T5 cells; a significantly higher number of lung tumor colonies were observed in MIC-1^{fms} mice than WT mice. The studies provide strong evidence that MIC-1/GDF15 has complex actions on tumor behavior: It inhibits primary tumor growth but with advancing disease, may promote metastases. As MIC-1/GDF15 is induced by all cancer therapies and metastasis is the major cause of cancer treatment failure, these results may have a direct impact on patient care.

Biography

Yasmin Husaini has completed her PhD from Banaras Hindu University in 1994. She has done her Postdoctoral studies in Molecular Biology and Cancer from University of New South Wales, University of Sydney and University of Technology Sydney, Australia. She has been working on prostate cancer since 2005. At present she is leading a research team investigating the role of MIC-1/GDF15 in the biology of cancer at St Vincent's Centre for Applied Medical Research, St Vincent's Hospital, and Sydney, Australia. She has published more than 20 papers in reputed journals.

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