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Macrophage inhibitory cytokine-1 (*MIC-1/GDF15*) has dual role in tumorigenesis in prostate cancer prone TRAMP mice

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MIC-1/GDF15 is a member of the TGF-β superfamily that plays role in the pathogenesis of a number of disease processes including cancer. MIC-1/GDF15 is overexpressed in prostate cancer (PCa) and other common malignancies and its expression is linked to cancer outcome. We have evaluated the effect of MIC-1/GDF15 overexpression and deletion on the evolution of PCa in transgenic TRAMP prostate cancer prone mice. We generated two syngeneic TRAMP mouse lines, one that overexpresses MIC-1/GDF15 ($TRAMP^{fmsmic\text{-}1}$) and the other that lacks MIC-1/GDF15 expression ($TRAMP^{MIC\text{-}/\text{-}}$). We then compared their survival, prostate tumor size, histopathological grade and extent of metastases with that of TRAMP mice. $TRAMP^{MIC\text{-}/\text{-}}$ had 4-5 weeks shorter survival but had larger prostate tumors at necropsy than TRAMP mice. However, $TRAMP^{fmsmic\text{-}1}$ mice had 7 weeks longer survival, smaller genitourinary tumors and lower PCa grades but had higher incidence of metastasis than TRAMP mice. To confirm this, we compared metastasis of TC1-T5, an androgen independent TRAMP cell line that lacks MIC-1/GDF15 expression, by injecting intravenously into MIC-1/GDF15 overexpressing ($MIC\text{-}1^{fms)}$ and syngeneic WT C57BL/6 mice. We observed a significantly higher number of TC1-T5 lung tumor colonies in $MIC\text{-}1^{fms}$ mice than WT C57BL/6 mice. Our studies suggest that MIC-1/GDF15 plays a different role in early compared to advanced cancer: Early in disease it may protect from and slows the growth of PCa. However, with advancing disease, MIC-1/GDF15 overexpression may promote metastases. As all cancer treatments induce MIC-1/GDF15 expression 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, India 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, Sydney, Australia. She has published more than 20 papers in reputed journals.

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