4 - 57 Increase in Expression of Indoleamine 2,3-dioxygenase in Iron-ion Irradiation-induced Bone Marrow Dendritic Cells Damage in Mice

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High linear energy transfer radiation is known to deposit higher energy in tissues and cause greater damage than low-LET irradiation[1]. Local immunosuppression is frequently observed after irradiation (IR). Dendritic cells (DCs) play important roles in the initiation and maintenance of the immune response[2]. The dysfunction of DCs contributes to tumor evasion and growth. However, molecular mechanisms underlying the establishment of immune tolerance induced by heavy ion IR through this DC population are poorly understood. Therefore, here we report our findings on the dysfunction of bone marrow-derived dendritic cells (BMDCs) induced by iron ion radiation and promotions of expressions of JNK1/2/3, indoleamine 2, 3-dioxygenase 1 (IDO1), p-ERK1/2 and p38/MARK; and decrease of IDO2, MHC class II, CD40, CD80 expressions and IFN-γ, TNF-α secretion after total-body IR in mice in Fig. 1. $JNK^{+}IDO1^{+}$ BMDCs showed up-expression of p-ERK1/2 and p-p38/MARK, reduced expression of MHC class II and CD80, and were not able to effectively stimulate allogeneic spleen T cells. Inhibition of IDO1 expressions could partly restore the function of BMDCs. In all, our study shows that elevated JNK and IDO1 expression induced by Fe ion IR resulted in dysfunction of BMDCs via p-p38/MARK and p-ERK1/2 signal pathway, and may represent a new mechanism in radiation-induced immune tolerance. These findings provide important knowledge for the role of JNK/IDO1 signal pathway in dysfunction of BMDCs response to radiation.

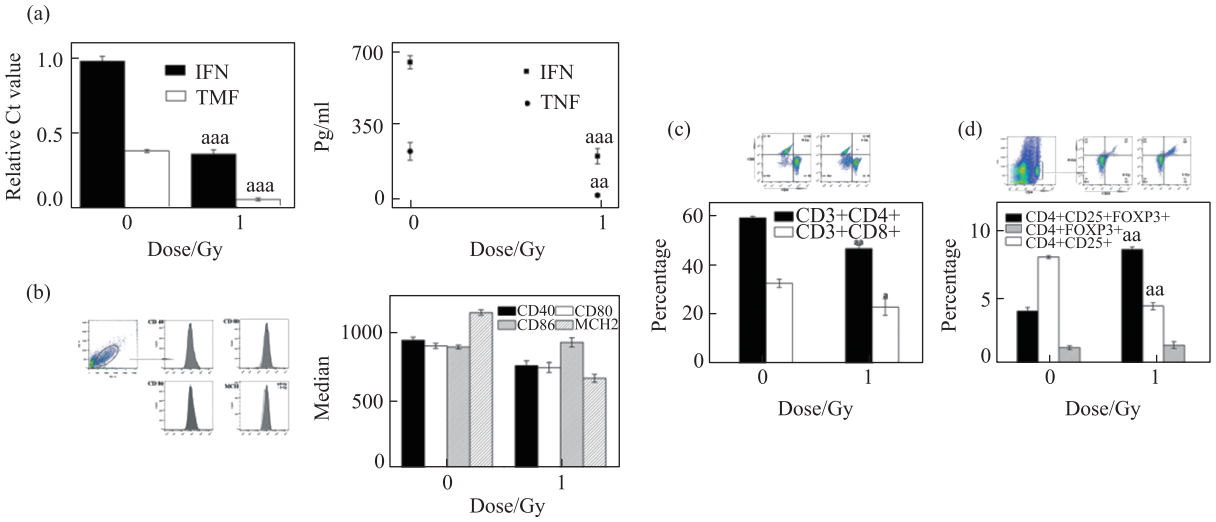

Fig. 1 (color online) Dysfunction of BMDCs induced by iron ion IR.

References

[1] S. A. Hamilton, M. J. Pecaut, D. S. Gridley, et al., J. Appl. Physiol., 101(2006)789.

[2] Y. Zhang, H. Wang, Immunol., 135(2012)268.