



Effect of administration timing of postchemotherapy granulocyte colony-stimulating factor on host-immune cell recovery and CD8+ T-cell response.

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Abstract:

Granulocyte colony-stimulating factor (G-CSF), a hematopoietic growth factor, is a standard supportive therapy given during cancer treatment. It induces acceleration in neutrophil recovery through stimulation of mobilization of hematopoietic progenitors. Given that the latter is also induced by chemotherapy itself, the timing of administration of G-CSF postchemotherapy might impact the resultant overall effects. The present study aimed to determine the optimal timing of G-CSF postchemotherapy to exert its optimal effects on the immune cell recovery and its impact on antigen-specific CD8+ T-cell response. B6 mice were treated once with cyclophosphamide (4 mg/mouse; CTX) and then daily with G-CSF (5 g/mouse) from Days 1-5, 2-5 or 5-9 post-CTX treatment. The total numbers of various immune cell types were analyzed on Days 7, 9 and 12 post-CTX treatment. To evaluate effects on CD8+ T-cell response, a pmel-1 transgenic mouse model was used in combination with prime boost peptide vaccination therapy. The total number of white blood cells (WBC), neutrophils, monocytes, lymphocytes, granulocytes and dendritic cells (DC) were significantly increased after G-CSF treatment in particular when G-CSF was administered from Days 2-5 post-CTX treatment. Application of this timing of G-CSF and CTX treatment after adoptive transfer of T-cells followed by prime-boost vaccination with antigenic peptide did not block the expansion of the donor pmel-1 CD8+ T-cells. In conclusion, adjusting the timing of treatment with G-CSF postchemotherapy can optimize its promoting effects on recovery of myeloid cells without altering the associated antigen-specific immunity.

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