MELANOMA AND MELANOCYTIC NAEVI

THE IMMUNOSUPPRESSIVE FUNCTION AND UNDERLYING MECHANISMS OF MONOCYTE-DERIVED TOLEROGENIC LANGERHANS CELLS ON THE DEVELOPMENT OF MELANOMA

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It has been reported that different langerhans cell (LC) subsets play different roles in the early development and metastasis of melanoma. However, the phenotype and function of LC subset which exerts an immunotolerigenic effect on melanoma still remain unknown. Our findings showed that there were two subsets of LCs with different origin in melanoma, namely epidermal resident Ly6C-CD11b+CD207+LCs (rLCs) and monocyte-derived Ly6C+CD11b+CD207+LCs (moLCs) by flow cytometry and confocal. moLCs were mainly distributed on the edge of melanoma. With the development of melanoma, The frequency of rLCs gradually decreased due to its migration to the tumor-draining lymph node (TDLN) while moLCs were recruited and supplemented the shortage of rLCs. The declined expression of MHCII but increased expression of PD-L1 on the surface of moLCs induced by the gradually elevated concentrations of TGF-β in tumor microenvironment suggested an immunosuppressive phenotype. Elimination of moLCs with Anti-Ly6C monoclonal antibody could increase the proportion of CD8+PD-1+ T cells in both melanoma tissues and TDLN and significantly inhibit tumor growth and metastasis in vivo. However, the elimination of rLCs from Langerin-DTR transgenic mouse with diphtheria toxin could increase the percentage of Tregs in TDLN. Finally, we also confirmed the existence of moLCs (CD14+CD207+) in human melanoma specimens by immunohistochemical staining. In conclusion, our study identified for the first time the subset of monocyte-derived tolerogenic moLCs with an immunosuppressive function and demonstrated its contribution to the development of melanoma, thus providing a new theoretical basis on immune tolerance as well as a potential therapeutic target for melanoma.