Abstract

Cancer cell invasion and metastasis are hallmarks of cancer. It is becoming apparent that the interaction between cancer cells and the surrounding microenvironment are involved in their ability to invade and metastasise. In general, cancer cells can either migrate individually, in an amoeboid or mesenchymal manner, or collectively. The first aim of this thesis was to analyse the role of NG2 in amoeboid to mesenchymal transition (AMT) and Rho/ROCK signalling. We found that NG2 promotes an amoeboid morphology, and increased invasiveness, in a Rho-dependent manner. Secondly, we analysed the role of the major tumour microenvironment (TME) component, cancer-associated fibroblasts (CAFs), on melanoma cell invasiveness. We found the CAF interaction with melanoma cells leads to increased levels of interleukin-6 (IL-6) and IL-8, and this leads to increased invasiveness. Simultaneous blocking of IL-6 and IL-8, using neutralising antibodies, inhibits CAF-dependent invasion. Further analysis of another major component in the melanoma TME, keratinocytes, has highlighted the importance of the tumour cell niche in invasion. Our results indicate that cancer cells have the ability to change morphology, and that the TME plays an important role in melanoma cell invasiveness. Metastatic melanoma treatment has proven difficult over the years, and the use of natural compounds may be desirable. We analysed the effect of natural curcumin, purified from turmeric, on melanoma invasion and found that curcumin inhibits invasion of melanoma cells, in 3D. These results demonstrate the importance of the tumour cell-TME interaction.

Keywords: Melanoma, invasion, fibroblasts, microenvironment, interleukins