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MEETING ABSTRACT Open Access

IL-6-mediated migration of human metastatic melanoma cells is reduced by simvastatin treatment

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Background

In 1987 the HMG-CoA reductase inhibitors, statins, were first marketed and are now widely used as well-tolerated therapeutics for hypercholesterolemia. High interleukin 6 (IL-6) plasma levels in melanoma patients are linked to a higher tumour burden and reduced overall survival. We have recently shown that simvastatin triggers apoptosis in human metastatic melanoma cells which is associated with concentration-dependent changes in autocrine IL-6 secretion. Here, we investigated IL-6 signalling with respect to proliferation and migration in human metastatic melanoma cells under statin application.

Methods

For this approach, human metastatic melanoma cells (A375, 518a2) were used for quantification of surface expression of the IL-6 receptor (IL-6-R/gp130) and for cell cycle with FACS analysis. Additionally, migration assays were carried out with simvastatin and/or IL-6 administration over time.

Results

Increasing concentrations of simvastatin led to morphological changes and detachment of the melanoma cells. After reseeding of the detached cells, A375 cells had a normal cell cycle profile while 518a2 cells underwent apoptosis resulting in cell death. Moreover, simvastatin treatment enhanced the surface expression of the IL-6-R and the gp130 subunit in a time- and concentration-dependent manner. Both cell lines responded to IL-6 treatment with increased proliferation and migration which was inhibited by simvastatin.

Conclusion

We demonstrate that simvastatin up-regulates the IL-6 pathway on the level of the heteromeric IL-6 receptor. Although increased IL-6 receptor expression would imply a stronger IL-6 signal, this is not seen in the presence of simvastatin. A novel therapeutic concept for simvastatin may emerge from the suppression of the IL-6-mediated proliferation and migration in metastatic melanoma cells.

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