Introduction

Hepatocellular carcinoma (HCC) ranks among the 10 most common cancers worldwide. The fact that HCC is resistant to conventional chemotherapy and is rarely amenable to radio-therapy leaves this disease with no effective therapeutic options and a very poor prognosis. Therefore, the development of more effective therapeutic tools and strategies is much needed.

In this project we investigate mesenchymal stem cells (MSCs) as vehicles for specific delivery of therapeutic genes, e.g. death ligand tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL) into tumors, because MSCs may contribute to the formation of tumor stroma and tumor blood vessels.

TRAIL is a potent inducer of apoptosis in transformed cells, while sparing most normal cell types.

Methods

- For therapeutic intervention, lentiviral vectors were constructed for expression of TRAIL. MSCs were selected from intraoperatively harvested bone marrow. Migration of MSCs to cancer cells was detected in an in vitro spheroid-assay. MSCs were stained with CellTracker Red and spheroids with CellTracker Green.

- Sensitivity of established human prostate carcinoma cells towards lentiviral TRAIL was tested by annexin-staining followed by flow cytometry.

Conclusion

• Autologous MSCs may be a powerful tool for the transfer of therapeutic genes into tumors, e.g. for specific induction of tumor apoptosis.

Outlook

• Co-culture of cancer cells with MSCs infected with lentiviral TRAIL (Donor/Target Kill Assays)
• Transfer of therapeutic genes via MSCs in liver xenograft models and analysis of tumor growth and tumor apoptosis
• Repetition of apoptosis induction by lentiviral TRAIL with liver carcinoma cells