Muscle Precursor Cells are safe for the treatment of urinary incontinence after surgery for prostate cancer

Meline N L Stölting1; Stefanie Kramer2; Simon Ametamey2; Stefano Ferrari3; Attila Becskei4; Tullio Sulser1; Daniel Eberli1

1Laboratory for Urologic Tissue Engineering and Stem Cell Therapy, Department of Urology, University of Zurich, Zurich, Switzerland
2 Institute of Pharmaceutical Sciences Department of Chemistry and Applied Biosciences, ETH Zurich, Zurich, Switzerland
3 Institute of Molecular Cancer Research, University of Zurich, Zürich, Switzerland
4 Institute of Molecular Biology, University of Zurich, Zürich, Switzerland
5 Biozentrum, Focal Area Growth and Development, University of Basel, Basel, Switzerland

Introduction

Skeletal muscle encloses sources of Muscle Precursor Cells (MPCs), which are capable of reconstructing muscle fiber upon injury. MPCs are studied for the treatment of urinary incontinence, also for patients after prostatectomy. However, the safety of injecting these cells in proximity of a potential location of tumor recurrence has not yet been investigated.

Materials and Methods

We have injected human MPCs, isolated from muscle biopsies harvested from the rectus abdominis, together with different types of prostate cancer, DU145, PC3 and LnCAP (ATCC-LGC Standard) in vivo. Tumor sizes were measured with caliper twice a week for 6 weeks. Lymph node metastasis and tumor phenotypes were analyzed by histology. Tissue physiological activity was assessed by PET scan with F-choline. After harvest tissues were examined by IHC evaluating myogenic differentiation apoptosis and cell cycle arrest of the retrieved tumor. Data was analyzed with SPSS v11 (SPSS Inc, Chicago, IL) by independent samples t-tests or one way ANOVA (p<0.05 is considered significant).

Results

When co-injected with MPCs, Prostate carcinoma growth was reduced up to 5 fold (fig.1), while lymph node metastases were reduced from 100% after 6 weeks to only 10%. Lymph node and bone metastasis were identified by PET scan with F-choline (Fig.2) on the animals injected with tumor alone. In contrast, no animal bearing tumor co-injected with MPCs presented positive lymph node or metastasis. Histology demonstrates that MPCs differentiated in vivo developing into organized and functional muscle, while the tumor in its proximity were undergoing apoptosis (Caspase3 positive), cell cycle arrest (p21 positive) and expressing the tumor suppressor (BIN1).

Fig.2. Bone and Lymph node Metastasis on control by PET

Discussion and Conclusions

In this study, we report that the use of MPCs in proximity of prostate cancer is safe in vivo. Further, it decreased tumor growth and metastasis formation could be demonstrated. These results suggest that MPCs can be safely injected on the pelvic floor after prostatectomy.

Acknowledgments

We thank the technical assistance of Dr. Marten Schneider, Dr. Irina Agarkova and Fatma K Pfiffner. This work was supported by the Hartmann-Müller Foundation, Abbott AG and SNF.

Disclosures

Authors have nothing to disclose.