Introduction

Adult muscle precursor cells (MPCs) are envisioned as a cellular therapy for stress urinary incontinence. However, the results of recent animal studies and first human trials show a wide range of outcomes.1-2 The quality of cells used might be a key factor influencing muscle formation and functional outcome.

In order to define which muscle would be most suitable for biopsy, we investigated biopsies of predominately slow-twitch fibers, fast-twitch fibers, weight-bearing and non-weight-bearing muscles. Biopsies were taken, characterized and functionally investigated in vivo.

Materials and Methods

Muscle biopsies from the quadriceps, rectus and soleus muscles of Lewis rats were obtained, histologically analysed, and their MPCs expanded in culture. Precursor cell density (Pax7) and myofiber type were determined by immunohistochemistry and histomorphometry. MPCs of each group were characterized by FACS analysis (Actinin, Desmin, MyoD and MHC). Cell expansion potential was evaluated and compared by proliferation assays. In vivo muscle tissue formation and function were assessed by injecting 10 x 10^6 MPCs s.c. into nude mice. After 2 weeks, a gross examination, immunohistochemistry and functional organ-bath studies (40V / 32Hz) of the engineered muscles were performed.

Results

Histomorphometric analysis showed a higher number of Pax7-positive cells in the soleus muscle (23.9% ± 7.4%), whereas the expression was lower in the rectus muscle (18.8% ± 4.8%) and quadriceps muscle (12.4% ± 0.8%). Table 1 shows FACS analysis of marker expression on different MPCs at P2. We were successful in engineering muscle tissue from all sources. However, the weight of the bioengineered muscles of the soleus group was 53.15 ± 11.45mg, whereas the weight of the quadriceps and rectus group was lower (37.2 ± 2.4mg and 35.5 ± 6.4mg, respectively, Figure 1A). The same trend was seen in the functional organ-bath studies on Electrical Field Stimulation (EFS) at 40V and 32Hz with the highest contraction per 100mg tissue for the soleus MPCs (671 ± 47.2mg), whereas the rectus MPCs (433 ± 255mg) and quadriceps MPCs (183 ± 98mg) had lower contraction rates (Figure 1B).

Discussion and Conclusions

With an increase in life expectancy, the significance of stress urinary incontinence in the elderly is also increasing. Improving sphincter function by applying autologous stem cells and tissue engineering seems to be a logical step to treat patients with sphincter insufficiency, and promising results have been reported.3-4 In our study we demonstrated that the origin of muscle samples has a significant impact on muscle tissue engineering with differences in expansion potential, tissue formation and muscle contraction. The presented data suggest that MPCs harvested from slow-twitch and weight-bearing muscles (soleus) will result in the best functional outcome for the engineering of sphincter muscle.

References


Disclosures

The authors have nothing to disclose