

FUNCTION OF SKELETAL MUSCLE TISSUE FORMED AFTER MYOBLAST TRANSPLANTATION INTO IRRADIATED MOUSE MUSCLES

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Pretreatment of host muscles with ionising radiation enhances the formation of donor-derived tissue after myoblast transplantation in the mouse but there is little evidence for improvement of muscle function. To investigate this, we implanted myoblasts from an expanded, male-donor derived, primary culture (i28) into X-ray irradiated (16 Gy) or irradiated and damaged soleus muscles of female syngenic mice (Balb/c). Three to 6 months later the isometric contractile properties of transplanted and control muscles were studied *in vitro*, and the Y chromosome positive progeny of the implanted cells was visualised on muscle cross-sections.

Irradiated and vehicle-injected muscles had significantly smaller weights than untreated solei and produced less twitch and tetanic tension (all about 18%). Such deficits were not found in irradiated solei implanted with 10^6 myoblasts. Increase of muscle mass and strength was due to the integration of donor-derived cells. No deficits in nerve-evoked tension were found.

Repeated freezing/thawing *in situ* of irradiated muscles led to formation of soleus remnants devoid of or containing only small amounts of contractile tissue (1-50 muscle fibres). Myoblasts (10^6) implanted into such destructed muscles generated numerous muscle fibres (1200-5000 per muscle). Upon direct electrical stimulation these fibres produced considerable twitch (53% of normal) and tetanic tensions (35%). The newly-formed muscles were, however, insufficiently innervated presumably due to radiation mediated arrest of Schwann cells. Separate studies on nerve regeneration following x-irradiation and nerve crush or botulinum application will be demonstrated. In any case, even after complete muscle destruction the disorganised suspension of donor cells will produce new organised contractile tissue thus replacing the host muscle. Limiting factor is the reduced capacity of the nerve to regenerate after x-irradiation.

Apart from these results, the role of the satellite cell in muscle fiber repair as well as a possible source for pluripotent stem cells will be discussed. The deviating behaviour of human myogenic cells in their limited proliferative capacity and telomere length related senescence will be mentioned.

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