

Dystrophin production induced by myoblast transfer therapy in Duchenne muscular dystrophy

SIR,—Myoblast transfer therapy (MTT) is being developed to prevent and to alleviate hereditary skeletal muscle degeneration.¹⁻⁴ We report here the results of the first application of MTT in man.

The safety and efficacy of MTT was assessed by injecting the left extensor digitorum brevis muscle of a 9-year-old adopted boy with Duchenne muscular dystrophy (DMD) with about 8×10^6 myoblasts. Donor myoblasts were cloned from satellite cells derived from a 1 g rectus femoris biopsy specimen of the normal, legal father. The only immunosuppressive agent administered was cyclosporin, at a dose of 5-7 mg/kg body weight divided into two daily doses. The dosage was varied to maintain serum trough concentrations in the range 100-150 ng/ml.

Donor myoblasts survived, developed, and produced dystrophin in the fibres from the myoblast-injected extensor digitorum brevis (fig 1). Dystrophin was not found in the contralateral muscle sham-injected with an equal volume (0.4 ml) of the carrier solution. Dystrophin was immunocytochemically localised⁵ at the sarcolemma. Dystrophin-positive fibres were present in clusters.

A western immunoblot⁶ confirmed the dystrophin in the myoblast-injected muscle and its absence in the sham-injected muscle (fig 2).

At no time during the 92 days after myoblast injection was there any sign of erythema, swelling, tenderness, or inflammation at the injection sites. Serial laboratory evaluation, including electrolytes, creatinine, and urea, did not reveal any significant changes before or after MTT. There was no clinical evidence of an adverse reaction to MTT or to cyclosporin.

Through natural cell fusion, which is inherent in myogenesis and muscle regeneration, donor myoblasts insert full complements of normal genes into dystrophic muscle cells.³ Therefore, it does not matter which gene is abnormal or which protein is missing. MTT has potential application for many hereditary muscle diseases. It repairs degenerating cells and replenishes lost cells.^{1,3} This first case

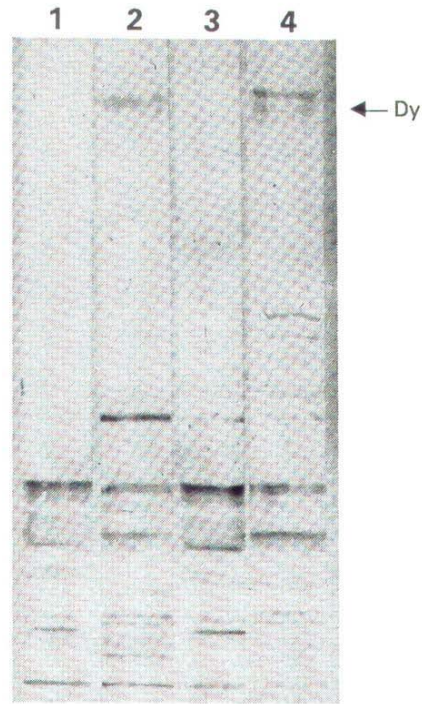


Fig 2—Immunoblot analyses of dystrophin (Dy) in muscle samples.

(1) *Mdx* mouse; (2) myoblast-injected muscle of DMD boy; (3) sham-injected muscle of DMD boy; and (4) normal C57BL/6 control mouse.

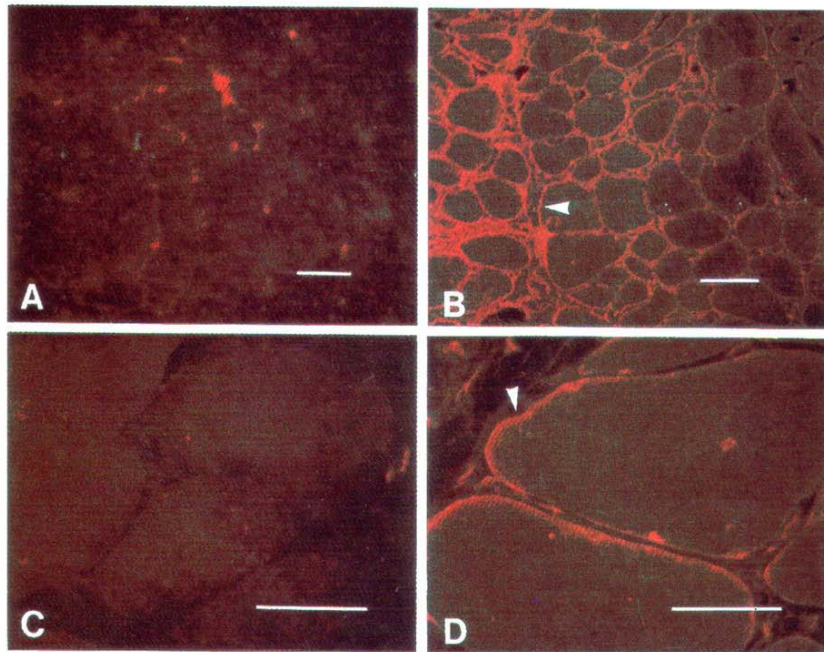


Fig 1—Immunocytochemical demonstration of dystrophin.

Dystrophin absent in sham injected muscle (A, C), but present in myoblast-injected muscle (B, D). Dystrophin was immunocytochemically localised at the sarcolemma (arrows). Cross-sections; bar = 100 μ m.

suggests that MTT offers a safe and effective means for alleviating biochemical deficit(s) inherent in muscles of DMD.

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