Expression of dystrophin and utrophin in the skeletal muscles of patients with Duchenne/Becker muscular dystrophy and of female gene carriers of Duchenne muscular dystrophy

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Immunohistochemical expressions of dystrophin and utrophin were studied in biopsied skeletal muscle. The subjects were five cases of Duchenne type muscular dystrophy (DMD), four cases of Becker type muscular dystrophy (BMD), and two cases of symptomatic women with DMD carrier. The utrophin-positive rate (the mean) in dystrophin-negative cells was 99.0% in DMD, and 17.9% in DMD carriers. In contrast, the utrophin-negative rate (the mean) in dystrophin-positive cells was 99.5% in BMD and 99.9% in DMD carriers. In skeletal muscles, the manifestation of the utrophin had an extremely close relation to dystrophin.

Expression of dystrophin (DYS) and utrophin (DRP) in skeletal muscle was studied in patients with Duchenne muscular dystrophy (DMD) or Becker-type muscular dystrophy (BMD), and in manifesting female DMD gene carriers to clarify the relationship between the synthesis of dystrophin and of utrophin [1,2].

Table 1. Patients of enrolled in the present stady.

Type	Case No.	Age/sex	Deleted exons*	Biopsied muscle	No. of examined muscle cells
DMD	1	6/M	-	Vastus lateralis	594
	2	10/M	-	Vastus lateralis	2438
	3	10/M	-	Vastus lateralis	1666
	4	11/M	44	Vastus lateralis	1068
	5	11/M	not detected	Vastus lateralis	446
BMD	1	16/M	not detected	Vastus lateralis	1373
	2	43/M	45-52	Deltoideus	1380
	3	59/M	45-48	Gastrocnemius	1340
	4	64/M	45-48	Deltoideus	520
DMD	1	33/F	-	Deltoideus	870
carrier	2	51/F	-	Deltoideus	1905

*: examined by PCR or Southern blot.

Immunostainings were carried out for dystrophin using anti-dystrophin antibody (DYS2, Novocastra Inc.) and for utrophin using anti-utrophin antibody (MANCHO 7 provided by Dr. Morris). This was done in serial sections of biopsied muscle obtained from patients with DMD or BMD, and from female DMD gene carriers. In cross-sections, the cells were classified into three groups based on the immunostaining patterns of dystrophin or utrophin on cell membranes: "+" cell, definitely stained throughout the entire membrane; "±" cell, patchy or faint staining; and "-" cell, no staining on the cell membrane.

In DMD muscles, 99.1% and 90.5% of the cells were DYS "-" and DRP "±", respectively. In BMD muscles, 97.2% and 99.4% of the cells were DYS"±" and DRP "-" respectively. In DMD carrier's muscles, 5.3% of the cells were DYS "-", 71.5% were DYS "±", 23.2% were DYS"+", and 98.9% were DRP"-". In the serial sections, DYS"-" plus DRP"±" cells comprised 91.1%, and DYS"+" plus DRP"-" cells comprised 75.0% of the total number of cells in DMD muscles, DYS"±" or "+" plus DRP"-" cells comprised approximately 100% of the total number of cells in BMD muscles, DYS"-" plus DRP"-" cells comprised 81.8%, and DYS"+" or "±" plus DRP"-" cells comprised approximately 100% of the total number of cells in DMD carriers.

The expression of dystrophin on most of the dystrophic muscle cells was reciprocal to that of utrophin, suggesting a close relationship between the expressions of dystrophin and utrophin. The expression of utrophin may be regulated by the expression of dystrophin, and a minimal expression of dystrophin may completely suppress utrophin expression. However, there was a small number of non –reciprocal cells, suggesting a defect in the system which regulates the synthesis of dystrophin and utrophin.

References

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