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## **Proteolytic pathways involved in muscular dystrophy in mdx, dy/dy and mdf mice: a preliminary study**

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(DMEM/BSA). The amplitude of IGF-1 stimulated AIB uptake (about 300% of basal) and protein synthesis (about 130% of basal) did not differ between lines, whereas the IGF-1-stimulated DG uptake was higher in myotubes from the FG line than from the SG line ( $F_{(1,69)} = 4, P < 0.01; 168 \pm 12\%$  vs  $145 \pm 8\%$  of basal, respectively). Following 24 h incubation of the myotubes in DMEM containing 0.5% Ultrosor, protein degradation was similar in both lines (about 22%).

Our data show that DNA synthesis by satellite cells from FG chicks is higher than that of cells from SG chicks in the presence of FCS or IGF-1. On the contrary, metabolic parameters of satellite cell derived myotubes and their response to IGF-1 were not affected by selection except for glucose uptake. Therefore, some growth-related pathways, but not all, have been modified by genetic selection for faster growth.

**Proteolytic pathways involved in muscular dystrophy in mdx, dy/dy and mdf mice: a preliminary study.** L Combaret<sup>1</sup>, D Taillandier<sup>1</sup>, E Aourousseau<sup>1</sup>, L Voisin<sup>1</sup>, D Meynial-Denis<sup>1</sup>, O Boespflug-Tanguy<sup>2</sup>, JL Guénet<sup>3</sup>, D Attaix<sup>1</sup> (<sup>1</sup> *INRA-Theix, Centre de Recherche en Nutrition Humaine et Unité d'Étude du Métabolisme Azoté, 63122 Saint-Genès-Champanelle*; <sup>2</sup> *Laboratoire de Biochimie, Faculté de Médecine, 63001 Clermont-Ferrand Cedex*; <sup>3</sup> *Unité de Génétique des Mammifères, Institut Pasteur, 75015 Paris, France*)

Alterations in the structural, functional and metabolic properties of skeletal muscle or protein loss observed in muscular dystrophy may result from variations in protein synthesis and/or protein breakdown. The aim of the present study was to identify the proteolytic systems responsible for such alterations using Northern blot procedures, since mRNA levels proteases could be a sensitive index of increased protein breakdown [Attaix *et al* (1994) *Reprod Nutr Dev* 583-597] in mdx (lacking dystrophin and reproducing the Duchenne de Boulogne myopathy) in dy/dy (exhibiting muscle atrophy presumably due to neuronal defects) and mdf mice (characterized by a preferential loss of type I fibers).

Three groups of mdx, dy/dy and mdf dysotrophic mice ( $n = 3 - 6$ ) were studied at 6, 6 and 8 weeks of age respectively. mdx, dy/dy and

mdf animals were compared to control Black 6, OF1, and Black 6 mice, respectively, of the same age. Muscle atrophy was estimated by comparing the tibialis anterior muscle mass divided by the body weight, to compare dystrophic and control mice with slightly different live weights. The Northern blot procedures used to measure mRNA levels for cathepsin D, m-calpain, ubiquitin, and proteasome subunits were described by Taillandier [(1993) Thèse de Doctorat de l'Université Blaise-Pascal, Clermont-Ferrand II, France].

The mdx mice did not exhibit any muscle atrophy. Only the mRNA levels for m-calpain, but not for cathepsin D or ubiquitin, were higher in mdx mice than in controls, suggesting a selective activation of the  $Ca^{2+}$ -dependent proteolytic pathway, in accordance with previous observations by Turner *et al* [(1988) *Nature* 335, 735-738]. By contrast, in dy/dy mice that present a small atrophy of the tibialis anterior muscle (26%,  $P > 0.05$ ) only the expression of polyubiquitin was higher than in control mice, mRNA levels for cathepsin D, m-calpain and the C2 proteasome subunit being systematically lower than in controls. These data suggest a possible inhibition of the different proteolytic pathways in dy/dy mice. Finally, the large atrophy of the tibialis anterior muscle observed in mdf mice (71%,  $P < 0.001$ ) probably totally resulted from impaired protein synthesis, since no variation in mRNA levels for cathepsin D, m-calpain, ubiquitin and C9 the proteasome subunit was observed in this model of dystrophy.

Taken together, these preliminary data clearly indicate that the activation of a given proteolytic system totally depends on the type of muscular dystrophy.

**Effect of lipoprotein lipase polymorphisms on lipid levels in obese patients before and after a hypocaloric diet.** R Jemaa, S Tuzet, F Fumeron, D Betoulle, M Apfelbaum (*INSERM, U 286, Faculté Xavier-Bichat, rue H-Huchard, 75018 Paris, France*)

Obesity is frequently associated with hypertriglyceridemia and hypoHDLemia [Crique *et al* (1986) *Circulation* 73 (suppl 1), 140-150]. A hypocaloric diet is accompanied by a decrease in lipid levels. Individual variations in the response to dietary modification are likely to be attributable to both environmental and genetic factors. The lipoprotein lipase (LPL) plays a key role in the