NSPl1: a new factor in the GLUT4 translocation

We have demonstrated that a novel intracellular protein in skeletal muscle cells may be involved in GLUT4 translocation, and functions as a regulator of blood glucose concentration in the body .

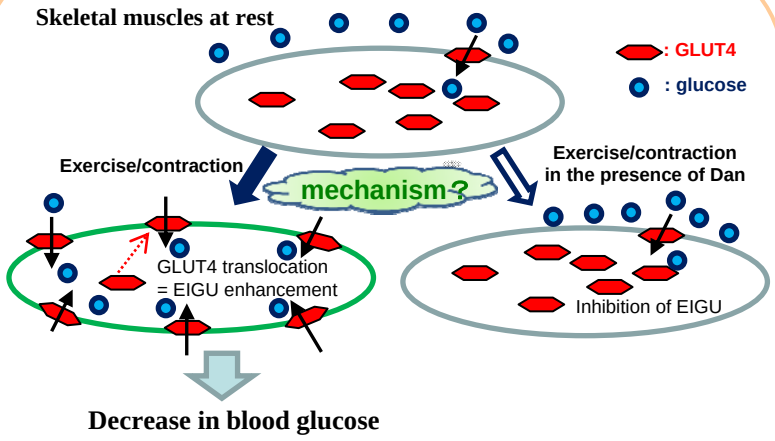

Fig 1 Exercise-induced glucose uptake in skeletal muscles

Exercise-induced glucose uptake is considered to be the result of translocation of GLUT4 from internal stores to the cell membrane. GLUT4 translocation in skeletal muscles induced by exercise decreases blood glucose levels.

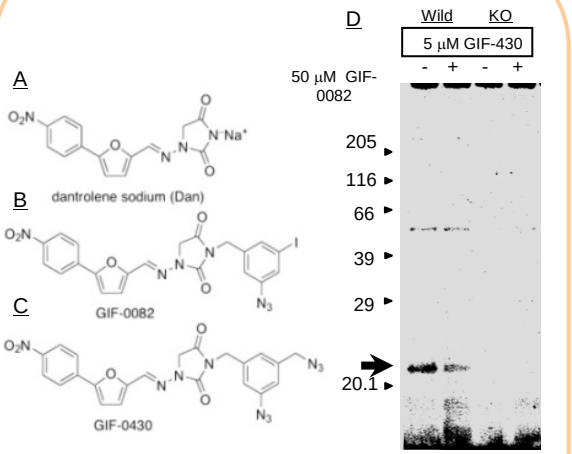

Fig 2 Discovery of novel dantrolene receptor, NSPl1

Dantrolene derivatives (A, B, C) can specifically label 23-kDa sk-NSPl1 by photo-irradiation (D, Wild, →). No labeling is detected in sk-NSPl1-deficient muscles (D, KO).

Exercise-induced glucose uptake (EIGU) into skeletal muscle cells have been thought to be one of the most important regulatory systems of blood glucose levels in the body, however, the molecular mechanisms underlying this function remained unclear. Recently, we discovered that dantrolene (Dan), which inhibits EIGU, can bind to skeletal-type neuroendocrine-specific protein-like 1 (sk-NSPl1) with photo-reactive Dan derivatives. sk-NSPl1 plays an important role in membrane translocation of GLUT4 induced by contraction/exercise. The sk-NSPl1 may also be involved in the regulation of glucose levels in the body (*Diabetes*).

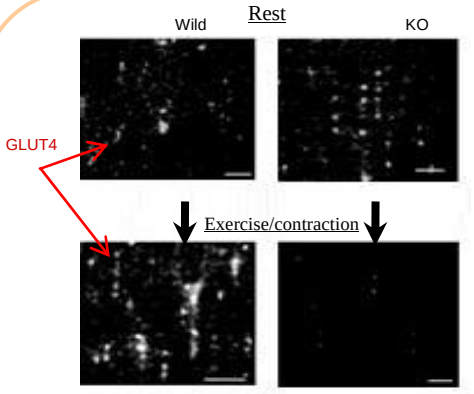

Fig 3 Confocal imaging of GLUT4 translocation in wild and sk-NSPl1-deficient muscle

GLUT4 increased markedly at the sarcolemma when wild-type skeletal muscle was electrically stimulated (EIGU, Wild), while in the sk-NSPl1-deficient muscle (KO) it remained almost unchanged.

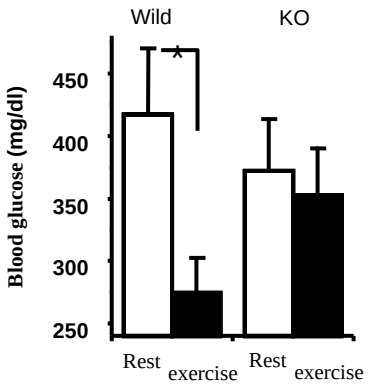

Fig 4 Effects of exercise on blood glucose concentration of sk-NSPl1-deficient mice

In wild-type mice, electrical stimulation of hind limbs reduced blood glucose levels. In sk-NSPl1–deficient mice, long-lasting electrical stimulation of hind limbs showed no change in blood glucose levels.

Future directions

Considering that NSPl1 was discovered to be a receptor for dantrolene, and that it can change blood glucose levels in the body, further studies using the imaging technology available at the Center for Molecular Imaging Science (CMIS) may lead to the understanding of the molecular mechanisms underlying different life-style related diseases, such as Type 2 diabetes, and the development of preventive or therapeutic agents for those diseases.

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