# Changes in oligomeric structure of muscle fructose 1,6-bisphasphatase influence internal structure of mitochondria by regulating its interaction with mitofilin

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**L. Pietras**[I], B. Budziak[I], M. Migocka-Patrzałek[II], A. Gizak[I]

[I]Department of Molecular Physiology and Neurobiology, Faculty of Biological Sciences, University of Wroclaw, Wroclaw, Poland, [II]Department of Animal Developmental Biology, Institute of Experimental Biology, Faculty of Biological Sciences, University of Wroclaw, Wroclaw, Poland

Mitochondria serve as the powerhouses of the cell by producing ATP. The cellular network of these organelles undergoes dynamic changes that are crucial to maintaining the proper quality of these organelles. In cardiac myocytes, appropriate intracellular distribution of mitochondria is essential for sequestration and release of Ca2+, regulating (together with ER cisterns) its local and global concentration. The organelles' trafficking is also responsible for meeting the cellular region-specific energy requirements and for the efficient removal of excess lactate from the cytoplasm. Fructose 1,6-bisphosphatase 2 (Fbp2) is a glyconeogenic enzyme and a multifunctional protein, whose cellular function depends on its oligomeric state – dimeric or tetrameric. Quite recently, we have shown that in the HL-1 cardiomyocyte cells, chemically induced tetramerization of Fbp2 results in a disturbance of tubulin network, significant restriction of mitochondrial trafficking, and intensification of mitophagy. Here, we provide a piece of evidence that this intensification results from disruption of the internal structure of mitochondria. Studies using electron microscopy reveal that tetramerization of Fbp2 leads to alteration in the morphology of mitochondrial cristae. Results of proteomic studies and proximity ligation assays suggest that at the basis of the phenomenon lies the interaction of dimeric Fbp2 with Mic60/mitofilin - the core component for the cristae organizing system (MICOS). Disruption of this interaction by reduction of the cellular pool of available Fbp2 dimers (using chemically induced tetramerization or partial silencing of Fbp2 expression) is sufficient to induce defects in the organization of inner mitochondrial membrane. These results emphasize the significance of oligomerization for regulating the physiological role of Fbp2 in the cell, and suggest involvement of the protein in cardiac diseases originating from mitochondrial defect.