MS07-P03 | Structural and functional characterization of Phosphoglucomutase 5

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Phosphoglucomutase-like protein 5 (PGM5), also known as “Aciculin” or phosphoglucomutase-related protein (PGM-RP) is a member of the phosphohexose mutase protein family.

It is closely related to phosphoglucomutase 1 (PGM1), which catalyzes isomerization of glucose-1-phosphate to glucose-6-phosphate via its phosphotransferase activity.

PGM5 is expressed in smooth and cardiac muscle at high levels, it is localized at intercalated disks of cardiac muscle and myotendinous junctions of skeletal muscle, is part of the mature Z-disk and has been found to be a highly dynamic and mobile protein which is essential for myofibril formation, maintenance and remodelling. Knockdown of PGM5 has been shown to lead to failure of myofibril assembly, alignment and membrane attachment. The protein is also involved in areas of myofibrillar damage [1].

It has first been described as a novel dystrophin and utrophin binding protein [2], which has a purely structural role and lacks phosphoglucomutase activity [3]. Recently, the list of binding partners has been extended to also include striated muscle Z-disk proteins filamin C, Xin [1] and FATZ-1.

Revisiting the studies done in the early 90s, we can show in biochemical assays that PGM5 does possess phosphoglucomutase activity, albeit less than PGM1 and present the first crystal structure of the protein obtained in complex with an inhibitor of PGM1, fructose-1,6-bisphosphate, at 1.57 Å resolution.

[1] Molt S., et al., J Cell Sci. (2014) 127, 3578-92
[2] Molseeva, E. P., et al., Eur. J. Biochem. (1996) 235, 103-113
[3] Belkin, A.M., et al., Journal of Cell Science (1994) 107, 159-173