

Dynamic O-GlcNAc modification in response to glucose deprivation

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About 2~5% of extra-cellular glucose is converted into uridine diphosphate-N-acetyl glucosamine (UDP-GlcNAc) through hexosamine biosynthetic pathway (HBP). UDP-GlcNAc could be used for O-GlcNAc modification of nuclear-cytoplasmic proteins by aid of O-GlcNAc transferase (OGT). Accordingly the concentration of extra-cellular glucose is tightly related not only with HBP but also with O-GlcNAc modification. At glucose deprivation condition, generally, the levels of UDP-GlcNAc and O-GlcNAc modification of proteins decrease. However, in A549, human lung cancer cell line, O-GlcNAc modification increases in response to glucose deprivation in a time dependant manner. On the other hand, the level of OGT is not changeable at this condition. This reflects that OGT activity increases in response to starvation in A549. Moreover the activity of GFAT, the first and rate-limiting enzyme in the hexosamine biosynthesis pathway, increases steadily in glucose starvation condition. We used sWGA precipitation method and MALDI-MS to identify the proteins in which O-GlcNAc modification increased at glucose deprivation condition. In view of the results so far achieved, we could identify several cytoskeletons, heat shock protein (HSP-70), ribosomal proteins etc. HSP-70 is known not only to be O-GlcNAc modified, but also to bind to other O-GlcNAc modified proteins. Thus, we will focus on revealing how the O-GlcNAc modification protects some proteins from degradation in response to glucose deprivation.