Programa Multicêntrico em Bioquímica e Biologia Molecular da SBBq

PROVA DE SUFICIÊNCIA EM INGLÊS

08/11/2016

NOME DO CANDIDATO:_____

IES: _____

Abaixo encontram-se dois textos, aos quais se referem as questões. Os textos foram retirados de:

Texto 1- Regulation by S-Nitrosylation of Protein. Post-translational Modification.
Douglas T. Hess and Jonathan S. Stamler . J. Biol. Chem. 2012, 287:4411-4418
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Texto 2- Glyceraldehyde 3-phosphate dehydrogenase
(Wikipedia)

Texto 1:
It has been established over the past decade that S -nitrosylation, the addition of an NO group to a Cys thiol to form an S -nitrosoprotein (SNO-protein), regulates a broad spectrum of proteins in all functional protein classes and cell types examined. The literature now encompasses some 3000 S -nitrosoproteins (including those identified with exogenously administered, physiological, nitrosylating agents), which may represent only the tip of the iceberg in light of the emerging role of denitrosylases in determining detectable levels of protein S -nitrosylation. As illustrated in this minireview, the picture that has formed indicates that the propagation or modulation of cell signals by S -nitrosylation often entails crosstalk with signaling modalities mediated by other principal mechanisms of post-translational modification. Indeed, it appears to date that, among post-translational modifications that convey cell signals, the breadth of the influence of S -nitrosylation may be comparable with that of phosphorylation and ubiquitylation, where signal crosstalk is established as a central operating principle.

Important new insight into the regulation of nuclear S -nitrosylation has been provided recently by Snyder and coworkers.
These investigators established a role for the enzyme GAPDH (**Glyceraldehyde 3-phosphate dehydrogenase**) in conveying S -

nitrosylation-based signals from the cytosol to the nucleus: GAPDH

that is S –nitrosylated at the single (active site) Cys-150, by NO generated endogenously in the context of apoptotic signaling, binds to an enzyme (the E3 ubiquitin ligase Siah1) and is thereby co-translocated to the nucleus. Subsequently, they reported that S –nitrosylation of GAPDH promoted its binding to nuclear substrates, including HDAC2 and the Class III deacetylase sirtuin-1, followed by transfer of the NO group from SNO-GAPDH to binding partners. Furthermore, trans-S nitrosylation inhibited sirtuin-1 activity and its effects on transcription.

Texto 2:

Glyceraldehyde 3-phosphate dehydrogenase (abbreviated as **GAPDH** or less commonly as G3PDH) (EC 1.2.1.12) is an enzyme of ~37kDa that catalyzes the sixth step of glycolysis and thus serves to break down glucose for energy and carbon molecules. In addition to this long established metabolic function, GAPDH has recently been implicated in several non-metabolic processes, including transcription activation, initiation of apoptosis.

Under normal cellular conditions, cytoplasmic GAPDH exists primarily as a tetramer. This form is composed of four identical 37-kDa subunits containing a single catalytic thiol group each and critical to the enzyme's catalytic function. Nuclear GAPDH has increased isoelectric point (pI) of pH 8.3–8.7. Of note, the cysteine residue C152 in the enzyme's active site is required for the induction of apoptosis by oxidative stress. Notably, post-translational modifications of cytoplasmic GAPDH contribute to its functions outside of glycolysis.

Cellular distribution

All steps of glycolysis take place in the cytosol and so does the reaction catalysed by GAPDH. In red blood cells, GAPDH and several other glycolytic enzymes assemble in complexes on the inside of the cell membrane. The process appears to be regulated by phosphorylation and oxygenation. Bringing several glycolytic enzymes close to each other is expected to greatly increase the

overall speed of glucose breakdown. Recent studies have also revealed that GAPDH is expressed in an iron dependent fashion on

the exterior of the cell membrane a where it plays a role in maintenance of cellular iron homeostasis.

Function

Metabolic

As its name indicates, glyceraldehyde 3-phosphate dehydrogenase (GAPDH) catalyses the conversion of glyceraldehyde 3-phosphate to D-glycerate 1,3-bisphosphate. This is the 6th step in the glycolytic breakdown of glucose, an important pathway of energy and carbon molecule supply which takes place in the cytosol of eukaryotic cells. The conversion occurs in two coupled steps. The first is favourable and allows the second unfavourable step to occur.

Transcription and apoptosis

GAPDH can itself activate transcription. The *OCA-S* transcriptional coactivator complex contains GAPDH and lactate dehydrogenase, two proteins previously only thought to be involved in metabolism. GAPDH moves between the cytosol and the nucleus and may thus link the metabolic state to gene transcription.

Com base nos dois textos, responda às Questões:

1. No que consiste a S-nitrosilação de proteinas e qual sua função?

2. Qual o papel de S-nitrosilação da Gliceraldeido-3- fosfato desidrogenase? Qual o resíduo modificado?

3. Qual a reação catalizada pela Gliceraldeido-3- fosfato desidrogenase no citoplasma, qual a sua estrutura quaternária e a qual via metabólica pertence?

4. Cite resumidamente (em uma frase), qual é a vantagem da associação (em complexos) de enzimas da via glicolítica, como a GPDH e outras.