THE SHORT ANSWER

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O-GlcNAc occurs cotranslationally to stabilize nascent polypeptide chains

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BACKGROUND:

The addition of O-linked GlcNAc to serine and threonine sidechains (aka O-GlcNAcylation) is a post-translational modification of hundreds of proteins and is involved in all sorts of things, from embryogenesis to insulin resistance to stress response and much more. Relevant to protein homeostasis and this paper in particular, there is now evidence that O-GlcNAcylation affects protein levels and their degree of ubiquitination. Also, the enzyme that transfers GlcNAc, OGT, has been shown to associate with ribosomes.

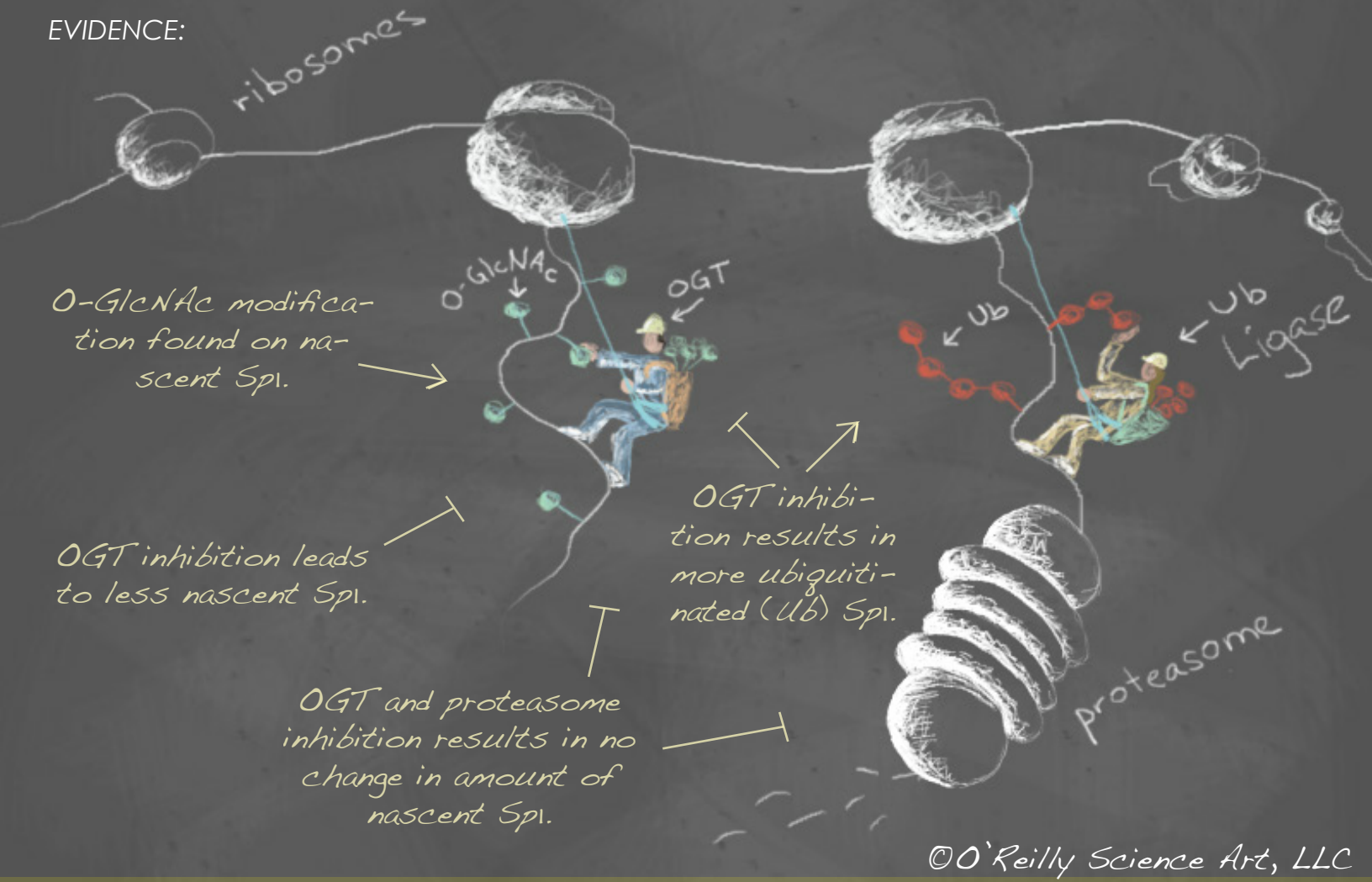
HYPOTHESIS:

O-GlcNAcylation may be a cotranslational modification too, and it may play a role in the quality control system that ensures only fully folded proteins escape proteasomal degradation.

APPROACH:

Send in genes for model protein Sp1 (and Nup62, in supplemental). Send in UDP-GlcNAz, in which an azide group is appended to the acetyl, so a phosphine-biotin probe can be used for detection. Isolate nascent proteins emerging from ribosomes. Isolate model proteins from here via their FLAG tags. Use fluorescent streptavidin to detect O-GlcNAcylation.

EVIDENCE:



CONCLUSIONS:

Some subset of O-GlcNAcylated proteins are modified cotranslationally, protecting them from ubiquitination and proteasomal degradation. Which has left me wondering. Is the GlcNAc there to block ubiquitination? Does it somehow help the nascent protein fold? Or does it add some polarity to regions that are otherwise non-polar and perhaps prone to aggregation? Guess I'll stay tuned.