Nature Reviews Molecular Cell Biology | AOP, published online 21 January 2015; doi:10.1038/nrm3946-3948

IN BRIEF

METABOLISM

The health benefits of hydrogen sulphide

Dietary restriction has beneficial effects in animal models, such as increased stress resistance and extended longevity; however, the common molecular mechanisms of the nutritional interventions responsible for these effects are unclear. Hine et al. showed that sulphur amino acid restriction increased the expression of cystathionine γ -lyase (CGL) — an enzyme of the trans-sulphuration pathway (TSP) — and increased hydrogen sulphide (H $_2$ S) production. Increased H $_2$ S levels conferred dietary-restriction-mediated stress resistance in vivo. Furthermore, mTOR activation or CGL inhibition blocked TSP induction and H $_2$ S production. Thus, H $_2$ S is a molecular mediator of dietary restriction benefits with clinical potential.

ORIGINAL RESEARCH PAPER Hine, C. et al. Endogenous hydrogen sulfide production is essential for dietary restriction benefits. Cell 160, 1–13 (2015)

AUTOPHAGY

p53-controlled autophagy

The phosphatidylinositol 3-kinase vacuolar protein sorting 34 (Vps34) promotes autophagy and receptor endocytosis and degradation. Xiao et al. observed a negative correlation between levels of the SCF ubiquitin ligase component FBXL20 (a p53-activated gene) and levels of Vps34 and autophagy. Following p53 activation by DNA damage, FBXL20 mRNA levels and SCF-mediated Vps34 ubiquitination and degradation increased, and autophagy decreased; DNA damage-induced phosphorylation of Vps34 increased Vps34–FBXL20 binding. Furthermore, FBXL20 knockdown and p53 activation resulted in an increase and decrease in Vps34-mediated epidermal growth factor receptor (EGFR) degradation, respectively. Thus, p53 activation by DNA damage results in FBXL20 upregulation and increased Vps34 degradation, and inhibits autophagy and receptor degradation.

ORIGINAL RESEARCH PAPER Xiao, J. et al. FBXL20-mediated Vps34 ubiquitination as a p53 controlled checkpoint in regulating autophagy and receptor degradation. *Genes Dev.* http://dx.doi.org/10.1101/qad.252528.114 (2015)

NUCLEAR ORGANIZATION

Targeting chromatin to the lamina

Genomic variable lamina-associated domains (vLADs) bind the nuclear lamina and repress genes in a cell-state-specific manner. Harr et al. developed the tagged chromosomal insertion site (TCIS) system to integrate short (<2.5-kb) DNA fragments into the genome, identified mouse fibroblast-specific vLADs and derived lamina-associated sequences (LASs) from their borders. Several LAS insertions could target chromatin to the lamina by binding the transcriptional repressor YY1. Targeting of both LAS-containing TCISs and endogenous LADs to the lamina required YY1 and lamin C, as well as the facultative heterochromatin marks H3K27me3 and H3K9me2/3.

ORIGINAL RESEARCH PAPER Harr, J. C., et al. Directed targeting of chromatin to the nuclear lamina is mediated by chromatin state and A-type lamins. J. Cell Biol. **208**, 33–52 (2015)