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one further mannose ring from $Man_8GlcNAc_2$ to make $Man_7GlcNAc_2$. This was unexpected because no mannosidase activity was detected when Htm1p was first characterized (although it homologous to mannosidase enzymes).

$Man_7GlcNAc_2$ is then recognized by a protein called Yos9p. This protein specifically binds to the exposed mannose residue left after Htm1p's trimming. Yos9p was already thought to "proofread" glycans that signal protein misfolding and target them for degradation, but until now the specific signal sought by Yos9p wasn't clear. The work therefore provides important insights into how this arbiter of protein quality control operates in the ER.

Clerc, S., et al. 2009. *J. Cell Biol.* doi:10.1083/jcb.200809198.

Lamin B locks up Oct-1

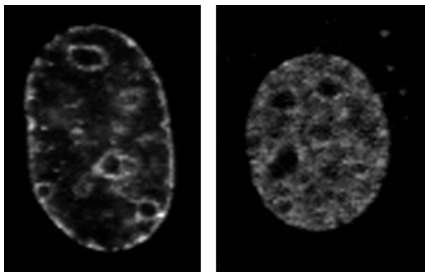
A large fraction of the transcription factor Oct-1 is associated with the inner nuclear envelope, but how and why it is retained there was unknown.

As for how, Malhas et al. show that Oct-1 binds to lamin B1, a prominent intermediate filament that lines the nuclear envelope, and in cells expressing a drastically truncated mutant of lamin B1, Oct-1 was disassociated from the nuclear envelope.

This left the question, why? The authors asked whether disrupting lamin B1–Oct-1 interactions could affect the expression of genes regulated by Oct-1. Indeed, in cells with truncated lamin B1, they found that expression of several Oct-1–regulated genes was altered because more Oct-1 could bind at these genes' promoters. Among the genes was a group involved in the oxidative stress response. As a result, these mutant cells accumulated higher levels of reactive oxygen species than wild-type cells.

It remains to be seen whether and how lamin B1–Oct-1 interactions are actively regulated in cells to help control gene expression. But, it is evident from these results that perturbation of lamin B1–Oct-1 interactions can make cells more vulnerable to oxidative stress. This could be particularly important in aging cells, where nuclear envelope integrity (and lamin B1 localization) is often perturbed, says author David Vaux. Lamins support the structure of the nucleus, and compromised nuclear structure has been a suspected cause of aging; another type of lamin, lamin A, is known to cause a premature aging disease when faulty. Increased production of reactive oxygen species—due to the perturbation of lamin B1 in mature cells—could be another way in which lamins contribute to the aging process.

Malhas, A.N., et al. 2009. *J. Cell Biol.* doi:10.1083/jcb.200804155.



Oct-1 localizes to the nuclear envelope in wild-type (left) but not lamin B mutant cells (right).

CERT loss puts the brakes on growth

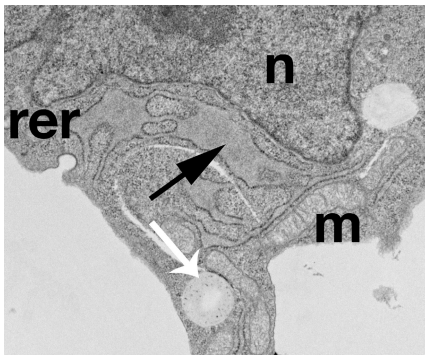
Wang et al. provide new insights into how ceramide transfer protein (CERT) affects cell growth and survival.

Many cancer therapeutic agents cause ceramide-dependent apoptosis, but the cell biology of this lipid is poorly understood. Recently, it was shown that CERT is required to transport ceramide from the endoplasmic reticulum (ER), where it is synthesized, to the Golgi, where it undergoes processing to create complex sphingolipids including sphingomyelin—a major component of plasma membranes. To learn more about CERT and ceramide in vivo, Wang et al. made CERT-deficient mice.

CERT-deficient embryos, they found, die around embryonic day 11.5. To explore whether increased ceramide levels and subsequent apoptosis could be to blame, the authors examined the embryos' cells. The ER of CERT-deficient cells was swollen, as ceramide was trapped in the organelle. This impaired ER function and also activated cellular stress pathways. Some of the trapped ceramide overflowed into mitochondria, causing these organelles to bloat too. How ceramide is transmitted from the ER to mitochondria remains unclear, but as with the ER, the ceramide accumulation impaired mitochondrial function.

Surprisingly, the stress and organelle malfunctions were not enough to kill the cells, as the cells up-regulated several adaptive responses. The cells did exhibit impaired growth rates however, as they adapted to these stressful conditions. In the growing embryos, this resulted in retarded organogenesis—the animals died when their hearts failed to develop properly. The implication for cancer therapy, on the other hand, is that targeting the CERT pathway might slow or stop a tumor's growth, but may not kill it.

Wang, X., et al. 2009. *J. Cell Biol.* doi:10.1083/jcb.200807176.



CERT-deficient cells have swollen rough ER (black arrow) and distended or disintegrating mitochondria (white arrow).