was first thought. Finely self-tuning machine than that the proteasome is a more degradation delay, it is clear that the proteasome is partly responsible for HIV RTC transport to the nucleus.

The team has now set about an unbiased task to find other nuclear import factors. Through multiple cell fractionation steps, they identified an RNA component capable of supporting Ubp6, the team shows, actually delays the rate of protein destruction. Proteasomes purified from yeast Ubp6 deletion mutants that view. Ubp6, the team argues, temper the destructive force of the proteasome is tempered by one of its own components, report John Hanna, Daniel Finley, and colleagues (Harvard Medical School, Boston, MA).

The traditional view of the proteasome was, says Finley, “like a pencil sharpener,” mindlessly chewing away at ubiquitinated proteins. The characterization of one proteasome-associated factor now changes that view. Ubp6, the team shows, actually delays the rate of protein destruction. Proteasomes purified from yeast Ubp6 deletion mutants degraded ubiquitinated cyclin B protein faster than did those from their wild-type counterparts.

Ubp6 is a deubiquitinase, but this activity was not responsible for delaying degradation. Inhibiting its deubiquitinase active site did not speed up degradation. Ubp6 also needed to be bound to the proteasome to delay degradation, which would not be necessary if the delay tactic was simply to prevent targeting of proteins to the proteasome by removing ubiquitin moieties.

Instead, Ubp6 seems to delay degradation, at least in part, by inhibiting the action of a second proteasome component, called Rpn11. Rpn11 is itself a deubiquitinase whose activity is strictly coupled with degradation, unlike Ubp6.

Though Rpn11 inhibition might not be the sole cause for the degradation delay, it is clear that the proteasome is a more finely self-tuning machine than was first thought.

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**HIV tRNA transport to the nucleus**

HIV rides the tRNA train to the nucleus, according to Lyubov Zaitseva, Richard Myers, and Ariberto Fassati (University College, London, UK).

For HIV to propagate inside cells, it must first enter the nucleus and, using its reverse transcription complex (RTC), integrate into the host genome. Fassati and his team previously showed that a nuclear import protein called importin 7 was partly responsible for HIV RTC transport to the nucleus.

Ubp6 delays force of destruction

**T**he team has now set about an unbiased task to find other nuclear import factors. Through multiple cell fractionation steps, they identified an RNA component capable of supporting nuclear import of HIV RTC. Sequencing revealed that the component was tRNA. Sure that tRNAs—instrumental for cytoplasmic protein translation—could not be responsible, Fassati thought, “Oh no! It’s all wrong, we’ve got to start all over again.” Only after multiple repetitions was the team convinced that the tRNA was not merely a contaminant.

Virtually all the tRNAs isolated from the active fraction (the one capable of nuclear import) had defective 3’ ends and were thus incapable of supporting translation. Wild-type tRNAs, on the other hand, had very little nuclear import activity.

Fassati speculates that perhaps the defective tRNAs get shuttled back to the nucleus for repair or degradation. Nuclear import costs energy, but the expense is probably worthwhile to ensure undisturbed protein translation. Whatever the host cell’s cost, HIV enjoys a free ride.

Reference: Zaitseva, L., et al. 2006. PLoS. 4:1689–1706.

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**Point of no return for senescence**

Senescent cells live on but can never again divide. This proliferative block is thought to safeguard against rampant oncogenic cell division. Akiko Takahashi, Eiji Hara, and colleagues (University of Tokushima, Japan) now show that, to enforce this irreversible stasis, cells switch on a self-perpetuating loop that suppresses cytokinesis.

Stable cell cycle arrest is induced by activating the retinoblastoma (RB) tumor suppressor. In senescent human cells, unlike nonsenescent cells, subsequent inactivation of RB leads to the reinitiation of DNA replication but no proliferation, suggesting that a second safety mechanism arrests senescent cells in G2 or M phase.

This second arrest only works in cells that are grown in mitogen-rich (and thus tumor friendly) conditions, the authors now find. The mitogens induce reactive oxygen species (ROS), which then start a self-perpetuating loop. The team observed that ROS remained high in senescent cells even after RB inactivation.

ROS, which are thought to induce senescence, are known to activate PKCδ, which studies suggest in turn activates ROS production. Consistent with this positive feedback, levels of PKCδ were also high in the permanently arrested cells.

High PKCδ, the team showed, suppressed the WARTS cytokinesis activator. Inhibiting PKCδ released this suppression and enabled senescent cells that managed to escape the early RB-induced block to proliferate.

Reference: Takahashi, A., et al. 2006. Nat. Cell Biol. doi:10.1038/ncb1491.