HIV uses autophagy for its own means
Virus avoids degradation and turns pathway into a helping hand for virion production.

Not satisfied with simply thwarting its host’s defensive maneuvers, HIV actually twists one to its advantage, based on new findings from Kyei et al. (1). The research suggests that autophagy—often used to capture and destroy invaders—aids in protein processing steps essential to HIV proliferation.

Autophagy is probably better known for its role in stress response pathways, particularly during bouts of nutritional deprivation. But in 2004, independent publications from the laboratories of Vojo Deretic and Tamotsu Yoshimori implicated autophagy in mammalian cell-autonomous defense mechanisms against pathogens (2, 3). Many publications have since revealed that a range of intracellular pathogens from bacteria to viruses to protozoa are targets for autophagosomes, which eventually acidify and become lytic bags of bug destruction (4).

Deretic figured the pathogenic targets didn’t necessarily stop there. “We thought that autophagy would be a cool device to capture and digest incoming HIV virions,” he says. “So, we thought if we induced autophagy, maybe it would digest HIV.” In the new work, his group shows that the opposite occurred—virus levels were increased when they thought, might thereby block acidification steps necessary to make a degradative organelle—did not occur.

The group then sought the viral agitator that blocks autophagosome maturation and allows Gag processing. Their primary candidate was an HIV protein called Nef, which interacts with the vacuolar proton ATPase and, if blocking autophagosome maturation, might be far down the road. If the idea is to kill the virus using drugs such as rapamycin, which induces autophagy, it will first be necessary to block Nef, notes Deretic. The idea is not without natural support. “There were cases in Australia involving HIV strains that lacked Nef,” he says. “And these people would not progress to AIDS, meaning the virus is disabled.”

Deretic has other exciting ideas. Highly active anti-retroviral therapy often does a smashing job clearing viral loads from the blood. But the pathogen can persist in particular locales such as gut lymphoid tissue (8). "My hope," says Deretic, “is to go after these reservoirs and chew up the virus that for some reason is not readily accessible or susceptible to the anti-retroviral therapy. I have great hope that autophagy will help us with that. This is something we didn’t have on our radar screens just five years ago.”

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