gene product (MC066L) that was 74% identical to human glutathione peroxidase, a major cellular scavenger of reactive and toxic oxygen metabolites and one of the few known enzymes that requires covalently bound selenium as a cofactor.

The importance of this remarkable sequence similarity was further underscored by the discovery of a predicted stem-loop selenocysteine insertion sequence (SECIS) motif within the 3′ untranslated region of MC066L. Hairpin SECIS structures in mRNA allow cellular translational machinery that makes the protein to read through an internal UGA codon that would ordinarily stop translation. By inserting a specific selenocysteine suppressor tRNA instead of stopping when the UGA occurs, the ribosome continues to the next downstream stop to make the full-length selenoprotein. Similar sequence motifs have been reported for other viruses (*10*), notably human immunodeficiency virus–1 (HIV-1) and Ebola, but actual synthesis of viral selenoproteins had never been demonstrated. The MCV gene has an in-frame UGA at codon 64, and the incorporation of ^{75}Se into expressed 30-kD MC066L protein (*7*) supported the contention that at least some of the translated viral protein resulted from readthrough all the way to the downstream stop at codon 221. Furthermore, transfection experiments in HeLa cells and immortalized HaCaT keratinocytes revealed that MC066L expression protects against cell death induced by ultraviolet treatment or hydrogen peroxide but not by either tumor necrosis factor ligand or FAS-antibody, which act by triggering programmed cell death (*7*).

So what does glutathione peroxidase actually do for MCV? Unfortunately, MCV does not grow in cultured cells, and no animal models exist to test the effects of gene deletions on viral pathogenesis. Nevertheless, certain predictions can be made from what is known about the glutathione peroxidase–reductase cycle that couples peroxide and hydroxyl radical detoxification with the oxidation of reduced glutathione. Along with catalase and superoxide dismutase, glutathione peroxidase is a major protectant against reactive oxygen metabolites, which can not only damage viral macromolecules directly, but are also potent inducers of apoptosis by virtue of their ability to trigger mitochondrial membrane permeability transitions (*11*, *12*). In fact, reduced glutathione peroxidase activity caused by selenium deficiency is associated with increased susceptibility to apoptosis (*13*) and excessive oxidant-induced cellular damage in HIV-1 infection (*14*).

Shisler *et al.* (*7*) speculate that MC066L might protect MCV—an exclusively dermatrophic virus that replicates only in suprabasal layers of differentiating keratinocytes—from intracellular peroxide toxicity or free radicals generated directly by ultraviolet light exposure. However, there is another possibility that is difficult to dismiss—that MC066L also serves as an intracellular protective mechanism against the toxic effects of diffused peroxide produced from dermal phagocytic leukocytes (*15*). Before regression, MCV lesions contain few inflammatory cells, although some tissue phagocytes may patrol below the basement membrane. Because hydrogen peroxide released during an oxidative burst by activated phagocytic cells can readily penetrate membrane barriers and produce damaging hydroxyl radicals within infected target cells, even small amounts could be significantly toxic for the relatively slow-growing MCV, particularly because virus replication likely represses the expression of all cellular anti-oxidant genes. Thus, in a manner that is analogous to how some tumor cells have hijacked the glutathione redox system to protect against peroxide cytotoxicity (*16*), active viral glutathione peroxidase could be the most effective countermeasure against phagocyte-derived peroxide for a virus-infected cell.

Taken in this light, it seems appropriate that the biological treasure-trove of the poxvirus family has not only introduced us to the extracellular Star Wars technologies, but is also the first to teach us that viruses can be equally adept at the kind of intracellular hand-to-hand combat normally associated with ground-level warfare as well.

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NOTE BENE: OPTICAL PHYSICS

Sweeping the Field

The payoffs for inventing new ways to compress pulses of light are substantial: data flow faster through optical fibers and all-optical switches for next-generation computers. But cleverness has a price, in that most methods require high nonlinearity—the ability of light to change the optical properties of the material it passes through—which in turn demands high optical power. One way out is to use a second optical pump wave to induce the nonlinearity and allow the weaker signal pulse to exploit it (*1*). Recently, Broderick *et al.* of the University of Southampton have demonstrated an elegant technique for molding short pulses—the "optical pushbroom" effect (*2*). They start with a useful device called a fiber Bragg grating, a resonant structure in which a lot of optical energy can be stored by a low-power continuous beam. Then they introduce a powerful but relatively long pulse that traverses the grating. As it passes through the grating, the strong pulse puts a slight "chirp" or frequency shift on the continuous beam, with some parts made higher and some lower pitch. But the Bragg grating itself is a highly dispersive medium, so the high frequency parts speed up and overtake the low frequency parts, causing a drastic pile-up of optical energy. In effect, the long pump pulse gathers up probe energy in a short spike on its leading edge, much as a broom piles up debris as it is swept along the floor. The result: a purely optical conversion of easily crafted long pulses into useful shorter ones.

–David Voss

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