Spotlight

By M.O.

With HIV drugs against cancer

Toschi, *et al.*
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Drugs that inhibit the viral protease are critical components of the therapeutic regimen of individuals carrying the HIV virus. While the introduction of these protease inhibitors has dramatically prolonged the life expectancy of HIV-infected patients, the need for lifelong intake has generated concerns about side effects. Indeed, several unwanted symptoms have been observed in those taking the therapy, such as diabetes, lipodystrophy and liver damage.

Here, Toschi and colleagues study a surprising, positive side effect of the drugs: a decrease in HIV-associated cancers. A reduction in the incidence of Kaposi sarcomas, non-Hodgkin lymphomas and cervical cancer has been observed in HIV-infected patients and has been attributed to the improved immune status after therapy. However, the reduction is also observed when therapy fails and immune functions do not improve.

The authors performed experiments in nude mice in the absence of HIV infection and show that two HIV protease inhibitors, indinavir and saquinavir, inhibit the growth of common tumors, such as colon, breast, lung and liver carcinomas. Only saquinavir in unphysiologically high doses inhibited the activity of the cell proteasomes, cellular complexes that break down proteins and that have been implicated in the drugs' activities before. Instead, both inhibitors reduced tumor microvascular densities (40–65%) and invasion of tumor cells *in vivo*, a process linked to the reduced activities of matrix metalloproteinases-2 and -9. The authors propose that protease inhibitors in combination with cytotoxic drugs may be promising new therapeutics that may also help cancer patients not afflicted with HIV infection.