approaches have been able to reduce IL-2 toxicity or even allow administration of the intended number of IL-2 doses, let alone increase IL-2 doses.

Samlowski *et al.* tested M40403 in three different mouse tumor models, all different in terms of patterns of disease and sensitivity to IL-2 antitumor effects[3]. In none of the three tumor systems did M40403 impair IL-2 antitumor efficacy, while allowing a twofold increase in IL-2 to be administered. The reversal of IL-2-induced hypotension and increased survival was associated with elevation in circulating catecholamines.

Most impressively, in the two mouse tumor models not very sensitive to IL-2 (RENCA and MethA), IL-2 and M40403 led to a much greater antitumor effect, with long-term cures, even when combined with standard minimally effective IL-2 doses.

How does M40403 enhance IL-2 efficacy? In a small series of *in vitro* and *in vivo* experiments, M40403 seemed to enhance the IL-2-mediated generation of lymphokine-activated killer activity through an expansion of cells capable of cytolysis not restricted by major histocompatibility class. It seems that adherent macrophage populations may suppress lymphokine-activated killer activity through the production of $O_2^{\bullet-}$. Blocking $O_2^{\bullet-}$production prevents macrophage-mediated immunosuppression. This combination may limit IL-2 toxicity while enhancing antitumor efficacy (**Fig. 1**).

Even now, there are other approaches that may offer the same hope, including retinoids (all-*trans*-retinoic acid) and inhibitors of vascular endothelial growth factor[11,12]. It is clear that much work needs to be done, but translating the results of Samlowski *et al.* for use in cancer patients may allow others to join those few long-term survivors with advanced melanoma or renal cancer.

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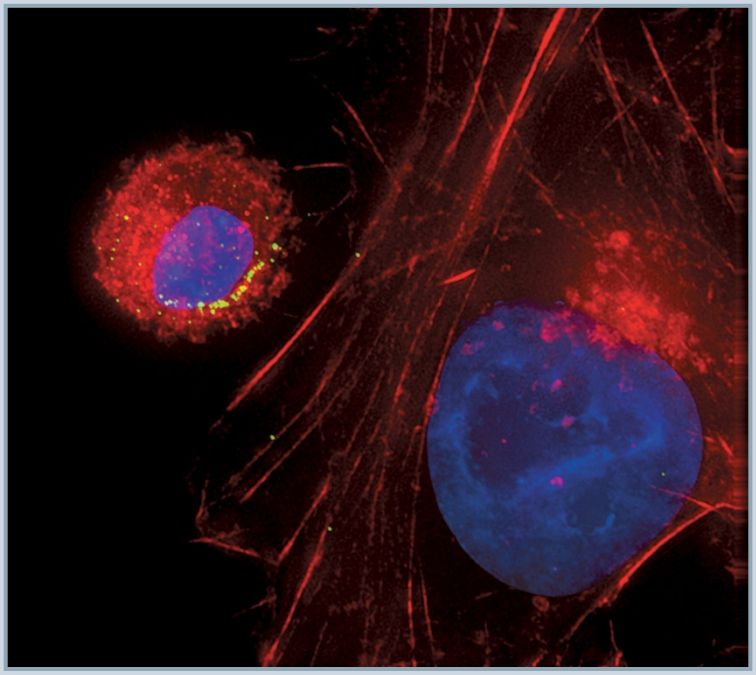
HIV hijacks dendritic cells

Dendritic cells take up invading pathogens and other antigens, process them and present them to T cells. In the 1 May issue of *Sciencexpress*, David McDonald *et al.* report that HIV exploits this function to infect more T cells, its primary target.

Dendritic cells take up HIV particles and gather them in protected vesicles. The investigators found that when a dendritic cell (left; see **Supplementary Movie 1** online) meets a target cell (right; DNA in blue and actin in red), the virus particles (green) scattered around the dendritic cell mobilize and cluster along the contact surface between the two cells. At the same time, HIV receptors also travel to the contact site. The flurry of activity at the interface enables some of the HIV particles to cross the divide into the target cell as shown here. The target cell in this image is a fibroblast transfected with the HIV receptor CD4 and its coreceptor CXCR4; the authors noted similar behavior using T cells as the targets.

The authors propose that HIV takes advantage of the large surface area of dendritic cells to get as many particles taken up as possible and then concentrate them at the interface with the target cell, thereby increasing the chance of productive T-cell infection. Recent studies with other pathogens suggest that this exploitation may be fairly widespread, say the authors.



Courtesy of Dave McDonald and Tom Hope

Pierrette Lo