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Experimental HIV vaccine gets a boost from ’70s-era discovery

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Although science is known for being a forward-looking field, researchers have found that they can often benefit from a glance over their shoulders. By combining an experimental AIDS vaccine with a long-neglected molecule called poly-IC, Rockefeller University scientists discovered that they were able to significantly improve its effectiveness. Their new, bolstered vaccine not only stimulated the production of HIV-attacking immune cells in mice, but also allowed the rodents to maintain immunity over a significantly longer period of time.

The immunity-directing dendritic cell has long been viewed as a potent resource for vaccine researchers: If they can direct a piece of a pathogen directly to the cell, it should be able to instruct other immune cells to react to the invader.

Prior work by Ralph Steinman, Henry G. Kunkel Professor and head of the Laboratory of Cellular Physiology and Immunology, and others has shown that this is a particularly promising direction for vaccine exploration. He and his colleagues have created dendritic cell vaccines that work by carrying an HIV protein straight to specific receptors on the cell. But while this prompts adaptive immunity — the kind that shifts in reaction to a specific threat — it doesn’t trigger the innate, nonspecific immunity the body uses to attack generalized microorganismal threats. For a vaccine to have a shot at preventing AIDS, it must do both.

So Steinman, research associate Christine Trumpfheller, and their colleagues went looking for something they could use to amplify their

vaccine and elicit an innate immune reaction from the body's T cells. Decades ago, poly-IC had been found to induce a potent immune-simulating chemical called interferon, leading researchers to believe it might work as a stand-alone therapy for infections and cancer. As a primary therapy, it never lived up to its potential and quickly fell out of view. As an adjuvant, however, Steinman hoped it might fulfill some of that forgotten promise.

"Poly-IC has a lot in its favor as a chemically defined adjuvant," Steinman says. It had been used before, so its safety was well documented. Plus, dendritic cells appeared to be enriched in the specific receptor known to interact with poly-IC, making the "vintage" molecule seem as good an adjuvant candidate as any. And it was. "This paper is the first evidence that you can get strong T cell immunity using poly-IC as an adjuvant," Steinman says.

The study, published online in the Proceedings of the National Academy of Sciences, showed that adding poly-IC to their dendritic cell vaccine initiated a strong immune reaction in mice, in which their T cells grew and produced protective molecules against HIV. Even more promising — and necessary for a vaccine to be viable — that protection lasted the duration of the trial, a full seven weeks.

"We think we're inducing immune correlates of protection," he says, "but we won't know for sure until we test it in people." That test isn't terribly far down the road. He and his colleagues plan to begin a phase-one safety trial of the vaccine before the end of the year.

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