MedicalXpress

Modified antibodies trigger immune response, point to novel vaccine design strategies

January 7 2013, by Matt Fearer

In an approach with the potential to aid therapeutic vaccine development, Whitehead Institute scientists have shown that enzymatically modified antibodies can be used to generate highly targeted, potent responses from cells of the immune system.

The approach, referred to as "sortagging," relies on the bacterial enzyme sortase A to modify antibodies to carry various payloads, such as peptides, lipids, fluorophores, and proteins. In this case, the scientists, whose findings are reported online this week in the journal *PNAS*, attached a variety of small antigens to an antibody directed at the surface of key immune cells. Through sortagging, the scientists were quickly able to prepare various antibody-antigen fusions and to deliver the antigens to their intended targets and track them as the immune cells mounted their intricate responses.

"Sortagging is remarkably specific and efficient," says Lee Kim Swee, first author of the *PNAS* paper and a postdoctoral researcher in the lab of Whitehead Member Hidde Ploegh. "We were able to create 50 different constructs (antibody-protein attachments), which wouldn't have been feasible if we had relied on the more traditional approach of genetic fusion."

Swee and colleagues tested the approach in a mouse model of herpes virus, sortagging 19 known viral epitopes to a cell-specific antibody.

They created a vaccine cocktail and immunized a group of mice. Upon subsequent re-exposure to the virus, vaccinated mice showed a 10-fold reduction in the amount of circulating virus.

"This is proof of principle that one could in fact use sortagging on antibodies to easily attach a tailored set of antigens, toward which the immune system can be educated," Swee says. "This technique also helps us understand how to design better antibody-based vaccines."

For paper co-author Carla Guimaraes, sortagging's value is bolstered by its flexibility. She likens it to "playing with Legos," because it allows "you to mix and match" proteins of diverse shapes, sizes, and functions. The process can be used, for example, to attach the relatively large green fluorescent protein (GFP) to antibodies without hindering GFP's desirable fluorescing activity or the binding of the conveying antibody to its intended target.

"Imagination is really your only limitation," says Guimaraes, who is also a postdoctoral researcher in the Ploegh lab. "You could for example, use sortase to attach a toxin to an antibody and use that antibody to deliver the toxin to specific cells." Such an approach, she notes, would be an appealing strategy for developing better-tolerated cancer therapies.

More information: "Sortase-mediated modification of αDEC205 affords optimization of antigen presentation and immunization against a set of viral epitopes" *PNAS*, online, January 7, 2013

Provided by Whitehead Institute for Biomedical Research