Progress Toward an Antitumor Vaccine

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How can we induce the body to use its own weapon, the immune system, to battle cancer?

In principle, by the same means used against infectious diseases: immunization. The production of a selective vaccine is not a trivial task, however. A team led by Horst Kunst at the University of Mainz has now found a way to bind a molecule that is typical for tumors to a carrier protein without irritating the immune system. As they report in the journal *Angewandte Chemie*, their method is based on an immunocompatible connection by way of a sulfur atom, namely, a thioether.

Epithelial tumor cells have unusually large amounts of mucin MUC1 on their surface. This MUC1, in comparison with its “normal” cousins, is also modified in a very characteristic manner. Mucins are mucilaginous substances that protect the surfaces of mucus membranes. They are glycoproteins—macromolecules with a central protein chain and long side chains made of polysaccharides. The modified MUC1 would be a good target molecule (antigen) for antibodies in immunological antitumor therapy.

The difficulty with this approach is that such sugar-containing compounds are completely ineffective at stimulating the immune system to form antibodies. “Immunization is only successful if the vaccine is anchored to an immunizing carrier protein by means of a spacer,” explains Kunz. This would be very easy to accomplish with polysaccharides, but turns out to be very complicated with glycoproteins,

because the protein portion of the molecule has many reactive groups that are attacked in the coupling reaction. “In addition,” says Kunz, “many of the structures that make suitable anchors are themselves highly immunogenic, which can suppress the immune response against the true target, the glycoprotein.”

This team has now found a good anchoring technique: Their anchor is a thioether (two carbon atoms coupled together through a sulfur atom). To this end, the carrier protein is first equipped with a spacer, which has an allyl group (two carbon atoms attached by a double bond) at its end. The glycopeptide is coupled to a building block that causes thiols (sulfur–hydrogen groups) to protrude from the molecule. In the next, light-initiated (photochemical) reaction, only the desired thioether bonds are formed—no side reactions occur at other locations in the peptide chain.

“Synthetic glycopeptide antigens containing structural elements typical of tumors in the sugar as well as the protein segment,” explains Kunz, “can thus be attached to the carrier protein in a controlled fashion. The largely nonimmunogenic thioether bridges could clear the way for the development of vaccines for immunization against tumor cells.”

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