Trastuzumab-grafted PAMAM dendrimers for the selective delivery of anticancer drugs to HER2-positive breast cancer

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Video Abstract

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Abstract

An international team of researchers has developed a way to target HER2-positive breast cancer, a highly aggressive form of the disease that is notoriously difficult to treat. Although some drugs are already available, most cause serious side effects because they also impact healthy cells. To avoid those unwanted responses, the researchers combined two existing drugs in a clever new formulation that targets only HER2-positive breast cancer cells. Two drugs used in standard therapy are trastuzumab, or TZ, and docetaxel, or DTX. TZ is an antibody that binds to HER2. It is selective and toxic on its own, but it works much better in combination with other chemotherapies. DTX, on the other hand, is very toxic, but it doesn't discriminate between healthy and cancerous cells. To try and get the best of both drugs, the team brought the molecules together with dendrimers – tiny synthetic polymers with a branching, tree-like structure. This unique structure allows DTX to be loaded inside, at the bases of the branches, while TZ can be added to the branch tips. DTX is thus shielded from healthy cells while TZ is free to target cancerous cells. When the team tested the drug on a HER2-positive breast cancer cell line, they found that it was rapidly taken up by the cells. It was also almost 4 times better at killing the cells when it included the TZ antibody compared to DTX alone. But the TZ-DTX combo was no more effective in pursuing HER2-negative cancer cells than dendrimers with DTX alone, highlighting the drug's selectivity. The shielding effect of the antibody also improved the biocompatibility of the dendrimers. Antibody-free complexes caused significant lysis to red blood cells, but complexes containing antibody caused no such damage. The precise targeting of this new formulation could potentially avoid many of the side effects of standard chemotherapy. By further testing the DTX complexes and even applying the dendrimer technology to other drugs, promising new tools that might one day help eradicate breast cancer may soon be on the horizon.