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Another Twist on ADCs

Researchers at Johns Hopkins University have developed a new twist on antibody-drug-conjugates (ADCs): a drug related to the plant poison thapsigargin, coupled to a peptide that binds to prostate-specifi c membrane antigen (PSMA), which is not really prostate-specifi c, but instead is expressed on endothelial cells in the microenvironment of many solid tumors. Thapsigargin is a poison that inhibits SERCA, a calcium pump which is critical for cells to maintain their membrane potential. Untargeted, the drug is far too toxic to use medically. But the authors showed that by combining it with the PSMA targeting peptide, they were able to make a prodrug, G202, which achieved "substantial tumor regression against a panel of human cancer xenografts *in vivo* at doses that were minimally toxic to the host." These results appeared in the June 28, 2012, issue of *Science Translational Medicine*. G202 is being developed by GenSpera Inc. The drug is currently in Phase I trials.