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Molecular switches as a way to better control CAR-T cells

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Among the many oncology therapies, few have generated as much excitement as CAR-T. The success of CAR therapy would not have been possible without the many discoveries that preceded it, most notably, the Nobel Prize-winning breakthroughs in cellular immunity. However, despite the fact that CAR-T already offers not only hope for development, but measurable results in the treatment of hematological malignancies, CAR-T still cannot be safely applied to solid tumors. The reason for this is, among other things, the lack of tumor-specific antigens which, in therapy, threatens to cause a lethal attack of lymphocytes on healthy cells. In the case of hematological malignancies, dangerous complications such as cytokine release syndrome may occur. Scientists have responded to these clinical challenges with molecular switches. They make it possible to remotely control CAR lymphocytes after they have already been administered to the patient. Moreover, they offer many additional capabilities. For example, they can be used to switch CAR antigenic specificity, create logic gates, or produce local activation under heat or light. They can also be coupled with costimulatory domains, used for the regulation of interleukin secretion, or to prevent CAR exhaustion. More complex modifications will probably require a combination of reprogramming (iPSc) technology with genome editing (CRISPR) and allogenic (off the shelf) CAR-T production.