Artificial enzymes facilitate targeted cancer therapy

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Video Abstract

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Abstract

Despite their known benefits, chemotherapy and other cancer treatments can take a toll on patients. Side effects such as hair loss, nausea, immune system suppression, fatigue, cognitive impairment, and infertility are common. The reason is that many cancer-fighting treatments target cells that quickly reproduce, which is true of cancer cells but also of other, healthy cells in the body, including blood cells and those lining the gastrointestinal tract. Is it possible to target only cancerous tissues with therapeutic drugs so that healthy organs remain unaffected? Researchers at the RIKEN Cluster for Pioneering Research in Japan are engineering molecules to do just that. The team showed that artificially designed gold-based enzymes (or metalloenzymes) can be used to guide drug delivery through a technique called selective cell tagging therapy. These metalloenzymes are studded with sugar molecules that can bind to specific proteins called lectins displayed on the surface of cancer cells. When the researchers injected their metalloenzyme into mice that had also been injected with cancer cells, the sugar-molecule anchors bound specifically to the lectins on the cancer cells. The team then introduced a therapeutic tagging agent that prevents cancer cells from clustering into tumors and becomes functional only after reacting with the metalloenzyme. After 81 days, 40% of the mice treated with both the enzyme and tagging agent had survived, showing an overall disruption in tumor development and growth. Meanwhile, mice injected with cancer cells but not given the dual treatment all developed tumors and died. In a second experiment, the researchers looked at the effects on mice with experimentally induced tumors that had already formed. This time, the tagging agent was a form of the chemotherapy drug doxorubicin that becomes toxic when it interacts with the metalloenzyme. Just like in the first experiment, the mice receiving the full treatment presented higher survival and reduced tumor growth over 77 days. These results demonstrate that administering both the metalloenzyme and tagging agent suppresses not only tumor development but also tumor growth. While further research is needed to better understand how metalloenzymes behave in humans, these findings are promising. Selective cell tagging therapy could pave the way toward targeted cancer treatments that are effective and leave healthy tissues unharmed.