

UC Davis researchers report new molecule that targets leukemia and lymphoma cells

Research not possible without radioactive isotopes

Press release
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Testing in dogs with naturally occurring non-Hodgkin's lymphoma is under way

UC Davis Cancer Center researchers have developed a novel peptide that binds to the surface of leukemia and lymphoma cells with extremely high affinity, specificity and stability, and demonstrates remarkable promise as a tool to help image tumors and deliver anti-cancer drugs. The research is reported in the July issue of *Nature Chemical Biology*.

"We believe that this peptide has great potential for becoming a new, effective imaging and therapeutic agent for patients with lymphoid cancers," said Kit Lam, professor and chief of hematology and oncology at UC Davis Cancer Center and senior author of the paper.

The peptide – named LLP2A by Lam – binds to a receptor found on the surface of lymphocytes. In the *Nature Chemical Biology* paper, Lam reports that LLP2A is attracted specifically to malignant lymphocytes, not healthy ones.

The next step will be to evaluate the binding of LLP2A in a larger number of human lymphoma biopsy samples. If those results are positive, Lam plans to test the peptide as a lymphoma imaging agent in patients. Experiments are already under way at the UC Davis School of Veterinary Medicine to evaluate LLP2A in dogs with naturally occurring non-Hodgkin's lymphoma. In addition, Lam and his colleagues have begun testing the peptide as a drug-delivery vehicle for lymphoma tumors in mice.

LLP2A is intended to work like a monoclonal antibody – but a peptide is much smaller than an antibody and has the potential to infiltrate cancer cells more successfully. Monoclonal antibodies, engineered to lock onto a specific target molecule, are used to carry radioactive isotopes or anti-cancer drugs directly to a tumor. Three monoclonal antibodies, rituximab (Rituxan), ibritumomab tiuxetan (Zevalin), and tositumomab (Bexxar), have already been approved by the Food and Drug Administration for the treatment of B-cell lymphoma. These antibodies have drawbacks, however: They bind to healthy lymphocytes along with malignant ones; in addition, they do not bind to T cells and therefore can't be used to treat T-cell lymphoma.

In contrast, LLP2A binds to both B-cell and T-cell lymphoid cancer lines, and has low affinity for normal T or B lymphocytes. It also has lower uptake in the liver and spleen than the monoclonal antibodies now on the market for lymphoma treatment.

"We believe LLP2A may be an ideal vehicle for the delivery of radionuclides, cytotoxic agents, toxins, cytokines and nanoparticles to lymphoid cancers which include non-Hodgkin's lymphoma and acute lymphocytic leukemia," Lam said.

In their paper, Lam and his colleagues report that they have already used LLP2A to successfully image lymphoid tumors in living mice. The researchers coupled near-infrared fluorescent dyes to LLP2A peptides; when the dye-tagged peptides found and locked onto a tumor, the tumor became visible to a near-infrared scanner.

LLP2A was identified using a combinatorial chemistry method Lam developed more than a decade ago. Known as the "one-bead-one-compound" method, Lam's technique allows scientists to synthesize millions of novel compounds in less than a week and analyze them in a few days.

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UC Davis Cancer Center is a National Cancer Institute–designated cancer center serving the Central Valley and inland Northern California, a region of more than 6 million people. Its research program is made up of 180 scientists on three campuses: the UC Davis Medical Center campus in Sacramento, the UC Davis main campus in Davis, Calif., and the Lawrence Livermore National Laboratory in Livermore, Calif.

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