ENDPOINTS NEWS

‘The field is at a flashpoint’: New Chad Mirkin-founded biotech hopes to make more effective cancer vaccines

by **Lei Lei Wu** on January 30th, 2023

Following the success of the mRNA Covid vaccines, cancer vaccines are seeing renewed interest after years of middling results. But a group of researchers suggests that more attention needs to be paid not to what goes into those vaccines, but how the parts are put together.

In a recent paper published in *Nature Biomedical Engineering*, researchers led by Northwestern University’s Chad Mirkin describe how the placement of different antigens in a cancer vaccine impacts its efficacy. The paper builds on past work done by Mirkin’s lab that suggests the structure, or how the parts of a vaccine are arranged, impact a vaccine’s efficacy, not just its components.

And from cancer vaccine research, Mirkin, Boston University professor and the paper’s first author Michelle Teplensky, and Khosla Ventures partner Adam Margolin are co-founding a new biotech known as Flashpoint Therapeutics. Flashpoint is still in its early stages — it’s putting together a seed round — but the biotech already has a lead program where it plans to put its initial focus.

In the paper, the researchers test a cancer vaccine that has two antigen classes: one that triggers cytotoxic T cells and one that triggers helper T cells. The researchers found that a dual-antigen vaccine helped to activate more immune cells to fight the cancer compared to a vaccine with just one kind of antigen.

But rather than just injecting all the necessary components as most vaccines do (what Mirkin terms the "blender approach"), the researchers arrange the antigens on a tiny ball-like structure with nucleotide strings attached to antigens going every which way, called a spherical nucleic acid (SNA). In one vaccine, the helper T cell antigens are placed at the ends of the strings, while the cytotoxic T cell antigens are encapsulated in the middle of the ball. In the other vaccine, the researchers reverse that arrangement.

That SNA technology previously served as the foundation of Exicure, which is currently winding down operations and recently ended its collaborations with AbbVie and Ipsen.

"Think about it. When in the history of pharmaceutical development did structure not matter?" Mirkin said. "Sometimes it's a single atom that makes a difference between a potent drug and one that's totally ineffective. Yet the attention on structure in vaccine development is almost zero, or has been almost zero. And so we're going to change that."

When they gave the dual-antigen vaccines to mice with cancer, they found that the ones that got the second vaccine, where the helper T cell antigens were on the inside, had much slower tumor growth and survived for longer.

They also gave the vaccine in combo with an anti-PD-1 checkpoint inhibitor. Mice who got the combo therapy with the second vaccine also had slower tumor growth and survived for longer compared to the other mice who got only a checkpoint inhibitor or the combo with the first vaccine.

In previous papers as well, Mirkin's lab has shown that changing the structure of a vaccine, but keeping the same composition, can impact the efficacy of a cancer vaccine. To Mirkin and Margolin, the cancer vaccine field is poised for success soon. The field has been marked by repeated failures, both commercial and clinical, but has seen renewed interest following the successes of Moderna and BioNTech's mRNA Covid vaccines. Both biotechs are now working on experimental cancer vaccines.

"I've been in the nucleic acid medicine space for a long time, and in the early days of nucleic acids, [they said] 'well, you'll never be able to make enough of them to really produce drugs.' That's wrong. 'Well, you'll never be able to deliver them to the appropriate cells and tissues to make things work.' Well, that's wrong." Mirkin said.

"You go through low hanging fruit, you go through a lot of failures and you learn, and I think we learned a lot. I think we've learned that admix approaches, while they can be effective in certain cases,

fail in many cases, and in the cancer vaccine space they have had real problems," he continued.

Following the cancer vaccine research that Mirkin and his lab have done, Flashpoint Therapeutics hopes to move those therapies into patients. Flashpoint will be based in Palo Alto, CA, where Margolin is located, but it also has a "strong center of mass in Chicago," and will be operating virtually. Margolin declined to comment on finances beyond the seed round.

Its first indication will be HPV — though as a therapeutic rather than a preventative vaccine, Mirkin noted. Outside of its internal pipeline, Margolin said that partnering will be a significant part of Flashpoint's business, given Big Pharma interest in the space. Moderna is partnered with Merck on its cancer vaccine, where the duo recently released promising early-stage data on a melanoma mRNA cancer vaccine that could reduce the chances a patient's cancer returned and was fatal.

However, that data release was not without debate on how its statistical analysis was conducted.

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Aside from the co-founders, Flashpoint's current team includes Mark Booth, current EVP, commercial at TerSera Therapeutics and former president of Takeda North America; Nick Manusos, former VP of business development at Takeda; Ray Nimrod, who represented the Broad in the CRISPR/Cas9 cases; and Marta New, CEO of Radyus Research.

"We think the field is at a flashpoint — the temperature where a liquid can undergo a phase transition to a gas — and Flashpoint Therapeutics has the technology that can enable the step change efficacy increase that can create a similar phase change in cancer vaccines," Margolin said.

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