COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar

Wednesday, March 30, 2022
4:00pm
2548 NUB or Zoom

"Viral Mimicry NanoVaccine Boosting B Immunity to Enhance Anti-cancer Efficacy'

Presented by:

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Abstract: The role of B cell cancer vaccines is controversial, and T cell cancer vaccines achieve limited efficacy. Here, we designed a virus mimicry B cell nanovaccine (VSMVax) that, when combined with αPD-1, achieved long-term tumor remission by promoting the T follicular helper (Tfh)-dependent B cell response and remodeling tumor immune microenvironment. VSMVax resembled a viral structure with optimal distance between antigen clusters, and optimal local antigen density. VSMVax penetrated deep and accessed the medullary regions of lymph nodes and crosslinked with B cell receptors for early B cell activation. VSMVax increased Tfh-dependent germinal center responses and antigen-specific B cells in lymph nodes. Strikingly, VSMVax promoted tumor immune cell infiltration and remodeled tumor immune microenvironment. VSMVax represents a novel cancer vaccine design that stimulates a unique B cell immunity to achieve long-term cancer remission
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Although B cell vaccines have been successfully used to prevent viral infections (such as SARS-CoV-2, HPV, and many other viruses), B cell vaccines are rarely designed for cancer treatment since the role of B cell immunity in cancer treatment is controversial. However, several recent studies have demonstrated that regardless of the T cell infiltration, high densities of B cells in the tumor are strongly associated with a better clinical response to ICB therapy in various types of cancers. These findings point to the need to develop a new generation of B cell cancer vaccines that promote B cell activation and tumor infiltration, in addition to generating neutralizing antibodies, to boost anticancer immunotherapy.

In this study, We engineered a virus mimicry nanovaccine (VSMVax) which had an optimal distance between antigen clusters (5–10 nm), and had high local antigen density in each cluster. These unique features are essential to crosslink B cell receptors (BCRs) to elicit extensive early B cell activation and subsequent robust GC responses for antigen specific long-term B cell generation. We also hypothesize that stronger B cell response elicited by VSM may also lead to better B cell access into the tumor microenvironment. To mimic the clustered antigen topography of viruses, we generated nanoparticles with spikes and conjugated HER2 peptides that contained a B cell epitope (SNTAPLQPEQLQ) and CD4+ T helper cell epitope (PESFDGDPA) onto the spikes of VSMVax. To enhance the remodeling of tumor immune microenvironment, we also introduced LIGHT, a member of the tumor necrosis factor (TNF) ligand family, into the VSMVax platform. Surprisingly, VSMVax with LIGHT, in combination with anti-PD1 antibody, achieved long-term tumor remission (>240 days) with a complete response (CR) rate of 44% in mice with HER2 breast cancer.

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