Journal of Vaccines & Clinical Trials

Editorial

A SCITECHNOL JOURNAL

New Ways to Design Vaccines: Nanodelivery, Cancer Vaccines and Systems Biology

Aleš Prokop*

Nanomaterials with defined physico-biochemical properties are versatile drug delivery platforms that may address the key technical challenges facing cancer vaccines and immunotherapy. They are typically made from natural or synthetic materials. Nanoparticles could enable a targeted delivery of tumor antigens and therapeutics and amplify immune activation via the use of new stimuli-responsive or immunostimulatory materials. I will point out here and briefly review the current state-of-the-art in nanoparticle-based strategies designed to potentiate cancer immunotherapies, including cancer vaccines with subunit antigens (e.g., oncoproteins, DNA and mRNA antigens) and whole-cell tumor antigens, dendritic cell-based vaccines, and immunotherapeutics based on cell death immune checkpoint blockade.

For example, by just changing the RNA inside these nanoparticles the immune system could be mobilized against any kind of cancer. Such nanoparticles are easy to produce, and virtually any tumor antigen encoded by RNA could be immobilized and delivered to appropriate immune cells. Thus, the nanoparticulate RNA immunotherapy approach could be adapted to any kind of cancer immunotherapy. This is done in a simple way by introducing the cancer DNA into the immune cells and then injected into a patient. The dendritic immune cells in the spleen, lymph nodes, and bone marrow can do the job afterwards are directed to the body's T cells which can kill the cancer cells in the body. The process here is to enable nanoparticle to enter dendritic cell by a process called internalization. I have edited two books for Springer on this issue [1,2].

Specifically, Kranz et al. [3] prepared lipid nanoparticles that contain RNA encoding tumor antigens and reported that they target dendritic cells and macrophages in mice. Nanoparticle uptake by precursor dendritic cells causes them to develop into mature antigen-presenting dendritic cells that migrate to the T cells. Uptake of nanoparticles by plasma dendritic cells promotes secretion of an initial wave of interferon protein that helps to prime the first steps of T-cell activation. Via internalization of nanoparticles loaded with RNA, the mature dendritic cells express tumor antigens and present them to the T cells. Subsequently, nanoparticle uptake by macrophages leads to a second wave of interferon release, which fully primes the T cells against specific antigens. Such cells then attack tumor cells.

Another way is to employ the check-point inhibitors. Immune checkpoint inhibitors are drugs – often made of antibodies – that allow an immune system attack on cancer cells. Checkpoint inhibitor blockade is considered to be a revolution in cancer therapy, although some patients remain resistant to this therapy. It has been hypothesized that only tumors with high mutation rates generate a natural antitumor T cell response, which could be potentiated via the nanoparticulate delivery. In a special case, PD-1 is a checkpoint protein on immune cells called T cells. It normally acts as a type of "off switch" that helps keep the T cells from attacking other cells in the body. However, when PD-1 attaches to another protein, PD-L1 (present in large quantities in cancer cells); it basically alleviates the immune attack. Here another step is needed. Towards this goal, one can employ monoclonal antibodies that target either PD-1 or PD-L1 via binding and can increase the immune response against cancer cells. These drugs have shown great deals of promise in treating certain cancers. PD-1; PD-L1 (and CTLA-4) are molecules that act as a type of "off switch" to keep the immune system in check.

The combination of nanoparticulate cancer vaccines with checkpoint inhibitor blockade represents another option to improve clinical benefit and a way to reverse resistance to immunomodulators.

Yet, here comes new possibility of blocking the check point status with help of systems biology. Systems biology is defined as quantitative, post genomic, post proteomic, dynamic, multiscale physiology, addresses in an integrative, quantitative manner the shockwave of genetic and proteomic information using computer models [4]. Since cancer is complex multigenic disease, it is necessary to examine both the whole genome of the tumor and the systems-level mechanisms of cell state transition that serve as triggers [5]. It's then necessary to integrate all genetic and non-genetic factors into a network. It would be necessary to understand the gene regulatory networks that control the transition from a normal state to a malignant cancer state and to shift cancer treatment from a strategy centered on eradicating all cancer cells, to one of coaxing the tumor cells to stop metastasis and enter a state of quiescence. Building the approach of using network medicine to perturb cancer cells out of their malignant state is a challenging feat. There are many ways to achieve such goal to build a model-based approach, ranging from relatively coarse genome-wide regulatory and signaling networks to detailed kinetic models of key pathways. A complex check point inhibitor reaction model could in essence be used to interrogate such model in several reaction points (combination therapy) and prevent cancer cell to become resistant. Such approach would be a rational way of designing combination therapy. A rather simplistic PD-1 model was presented recently by Contreras et al. [6]. Inhibitors then could be sought to enable such block.

Good luck with your efforts!

References

1. Prokop A, Editor (2011) Intracellular Delivery. Fundamentals and Applications, Springer Science, Business Media BV, Dordrecht.
2. Prokop A, Iwasaki Y, Jarada A, Eds. (2014) Intracellular delivery II, fundamentals and applications, Springer Science, Business Media BV, Dordrecht.
3. Kranz LM, Diken M, Haas H, Kreiter S, Loquai C, et al. (2016) Systemic RNA delivery to dendritic cells exploits antiviral defence for cancer immunotherapy.

***Corresponding author:** Aleš Prokop, Visiting Scholar, Vanderbilt University, USA, E-mail: ales.prokop@vanderbilt.edu

Received: February 09, 2017 **Accepted:** February 13, 2017 **Published:** February 15, 2017

Nature 534: 396-401.

4. Wikswo JP, Prokop A, Baudenbacher FJ, Cliffel D, Csukas, B, et al. (2006) The engineering challenges of BioMEMS. The integration of microfluidics, micro- and nano-devices, models, and external control for systems biology. IEE Proc Nanobiotech 153: 81-101.
5. Huang S, Zhou J (2014) Cancer treatment: a systems approach. Accessed on February 2nd, 2017.
6. Contreras SAM, Zalba S, Berraondo P, García-Cremades M, Trocóniz IF, et al. (2014) PK/PD modeling of new immunotherapeutic agents in cancer, Abstr 3276.

Author Affiliation

Top

Visiting Scholar, Vanderbilt University, USA