Jump-starting cheaper cancer vaccines

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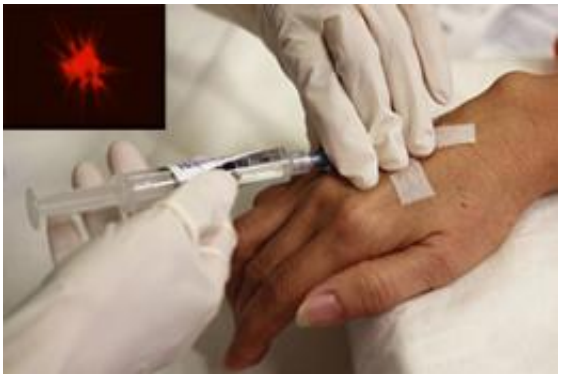

Dendritic cells (top left), derived from human embryonic stem cells, could provide an economical route to produce human cancer therapeutics. Credit: iStockphoto.com/drliwa (main image)

Dendritic cells (DCs)—workhorses of the immune system—derived from human embryonic stem cells (hESCs) may provide an economical way of generating off-the-shelf therapeutic vaccines against cancers, according to research led by Jieming Zeng and Shu Wang from the A*STAR Institute of Bioengineering and Nanotechnology, Singapore.

DCs process and present antigens—substances that stimulate immune responses—to other cells of the immune system that will then eliminate pathogenic cells carrying these antigens. This ability makes DCs ideal as vaccines within the body. As such, the US Food and Drug Administration recently approved the first DC-based vaccine for use. DCs sourced from another individual, however, may be attacked by the

immune system of a recipient. Consequently, DC-based vaccines have been prepared using cells derived from the recipient's own body. This is expensive, the supply of cells is limited, and highly variable results have complicated the evaluation of clinical trials.

Using hESCs, however, it is possible to produce a steady supply of DCs in unlimited numbers, under strict quality control. But, since these DCs are still susceptible to immune attack, Zeng, Wang and co-workers enlisted the aid of invariant natural killer T (iNKT) cells. These cells can be stimulated by compounds attached to molecules of the glycoprotein CD1d and used to boost the activity of DCs, thereby enabling them to trigger the immune response before being eliminated.

First the researchers added genes to DCs generated from hESCs to produce extra CD1d. The greater amount of this glycoprotein produced by the cells then triggered an expansion of iNKT cells in the presence of α-galactosylceramide (α-GC), a ligand or compound which binds to iNKT cells.

Subsequently, they found that α-GC was unnecessary for inducing an anti-tumor response. This is advantageous because previous studies by others with mice had shown that using α-GC for this purpose can lead to uncontrolled iNKT activation. In fact, the researchers showed that pulsing the modified DCs with melanoma antigen was sufficient to prime immune T cells against melanoma tumor cells. The same strategy worked with DCs derived from human monocytes, a type of white blood cell.

"The ability to generate large amounts of uniform hESC-DCs competent in inducing antitumor immunity indicates that they could be used as an unlimited cell source to produce off-the-shelf DC vaccines, to overcome the drawbacks of using an individual's own cells," Wang says. "We are now focusing on developing a simpler process to produce DCs with

similar or even better capabilities."

More information: Zeng, J., Shahbazi, M., Wu, C., Toh, H. C. & Wang, S. Enhancing immunostimulatory function of human embryonic stem cell-derived dendritic cells by CD1d overexpression. *The Journal of Immunology* 188, 4297–4304 (2012). www.jimmunol.org/content/188/9/4297

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