news

Sourcing natural killer cells for antitumor immunotherapy

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Human embryonic stem cells (hESCs) might one day provide treatments for cancer, report Minnesota-based scientists Dan Kaufman and Jeffrey Miller. The researchers and their colleagues have converted hESCs into natural killer (NK) cells, a type of immune cell that can destroy cancer cells [1]. It will be several years, warn Kaufman and Miller, before hESC-derived NK cells will be ready to try in patients but hESCs could provide an unlimited source of NK cells for cancer therapy.

NK cells for cancer killing

Unlike T and B lymphocytes, components of the adaptive immune system that make specific responses to foreign antigens, NK cells (part of the innate immune system) kill cells that have lost expression of major histocompatibility complex class I molecules. Tumor cells often downregulate class I expression, explains Miller, Associate Director of Molecular and Cellular Therapeutics in the Department of Medicine and Cancer Center, University of Minnesota, USA, 'and we have known for about 30 years that NK cells purified from the blood can kill some tumor targets'. Attempts to treat cancer by boosting endogenous NK activity in patients with cancer have proven ineffective, however, possibly because NK cell activity is inhibited by receptors on the tumor cells that the NK cells recognize as self.

To circumvent this problem, Miller recently tested NK cells isolated from the blood of closely related donors. These, he reasoned, would be different enough from the host's cells to be able to recognize and kill tumor cells efficiently. In a small Phase II trial, Miller and co-workers found that donor haploidentical NK cells survived in patients with acute myeloid leukemia (AML) for about a month and induced remissions in some patients for whom standard therapy had failed [2].

The stem cell option

Miller now plans to test whether umbilical cord blood might be a better source of NK cells for cancer immunotherapy than adult blood. Cord blood contains more hematopoietic stem cells – cells that renew themselves but also differentiate into specific types of blood cell – than adult blood. 'We hope to start testing the safety of NK cells produced from HLA half-matched cord blood in patients with AML in the next few months', says Miller. 'If cord blood proves to be a better source of NK cells for tumor therapy than adult blood, then hESCs may be an even better source.'

Embryonic stem cells can differentiate into any cell type present in the adult body. The first hESC lines were isolated in 1998 but, says Stephen Minger, Director of the Stem Cell Biology Laboratory at King's College London, UK, 'large numbers of lines have been freely available for only 3–4 years so researchers are only just learning how to persuade them to differentiate down specific pathways. hESCs may eventually provide unlimited cells for regenerative medicine – for example, neurons to repair nervous system damage – and highly enriched human cell populations for use in drug screening and toxicology.'

By deriving functional NK cells from a hESC line in a two-step process, Kaufman, an assistant professor in the Stem Cell Institute of the University of Minnesota, USA, is working towards a third potential use of hESCs, that of a source of cells for cancer immunotherapy [1]. The NK cells we have derived, says Kaufman, 'express inhibitory and activating receptors typical of mature NK cells and can kill human tumor cells in culture'. He now plans to test whether these NK cells can kill human tumor cells implanted in animals.

According to Minger, 'designing conditions that generate a highly enriched population of any cell type that may have therapeutic potential from hESCs is a good step forward'. Dario Campana, Professor of Pediatrics at St Jude Children's Research Hospital, Memphis, USA, also comments that the University of Minnesota study is exciting and may help to identify new molecules that regulate NK cell expansion, which could then be used to produce sufficient NK cells for clinical use. Campana himself recently described a method for growing large numbers of NK cells from peripheral blood [3].

Kaufman and Miller both agree that additional work is needed to find ways to make sufficient hESC-derived NK cells for clinical use, but, says Kaufman, 'if we can make the system efficient enough, we might open up the possibility of using hESCs as a renewable source of NK cells that can be matched to individual tumors to improve killing efficiency'.

References

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Nanomedicine transforms drug delivery

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The marriage of nanotechnology and biotechnology has come as a surprise for the older generation. Few expected those two crazy kids to run off together, but, upon reflection, it seems inevitable. Biomolecules represent the ultimate nanoscale 'machines.' It was only a matter of time before engineers attempted to imitate them. Now surprising advances in nanotechnology stand poised to change all the rules for drug discovery. Did you think your compound was insoluble? Did you discard it because it doesn't cross the blood–brain barrier? Think again.

Treatment at the single-molecule scale

Nanomedicine encompasses medical diagnosis, monitoring, or treatment at the single-molecule scale. This new field is so promising that the National Institutes of Health have included a Nanomedicine initiative in the NIH Roadmap.

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