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VACCINES

Stem cell hope for cancer treatment

Autologous induced pluripotent stem cell (iPSC)-based vaccines have been shown to elicit antitumour responses *in vivo* against multiple types of cancer, according to a new report in *Cell Stem Cell*.

As embryonic cells and tumour cells share gene expression profiles and antigens, immunization with embryonic material can lead to tumour rejection. However, ethical constraints prevent the development of embryonic stem cell (ESC)-based cancer vaccines. Kooreman and colleagues show that the transcriptome of human iPSCs overlaps with that of cancer cells and human ESCs. Thus, iPSCs may potentially be used to prime the immune system against tumour-associated antigens.

In a mouse model of breast cancer (FVB mice injected with DB7 cells), a 4-week vaccination schedule of once weekly injections of autologous irradiated iPSCs plus the adjuvant CpG oligodeoxynucleotides (iPSC/CpG ODNs) led to strong *ex vivo* T cell responses to tumour lysate and to the production of DB7-specific IgG *in vivo*. Remarkably, compared to injection of a vehicle control or of either iPSCs or CpG ODNs alone, this vaccination schedule protected against tumour growth in the FVB-DB7 model, as well as in a mouse model of melanoma (C57BL/6 mice injected with B16F0 cells) and in a clinically relevant orthotopic mouse model of breast cancer. Moreover, two iPSC/CpG ODN-immunized FVB mice injected with DB7 cells survived to 1 year (most mice did not survive 2 weeks beyond the end of the experiment) and rejected a subsequent challenge with DB7 cells.

Flow cytometric analyses of iPSC/CpG ODN-vaccinated C57BL/6 mice 2 weeks after B16F0 tumour injection showed a decrease in the number of regulatory T cells in the blood and increases in T helper (T_H) cells and antigen-presenting cells (APCs) in tumour-draining lymph nodes. In addition, iPSC/CpG ODN-vaccinated FVB mice had increased numbers of T_H cells, cytotoxic T cells and APCs in draining lymph nodes, suggesting that iPSC/CpG ODN vaccination upregulates antigen presentation and T cell activity.

> “injections of autologous irradiated iPSCs plus the adjuvant CpG [ODNs] led to strong *ex vivo* T cell responses”

Notably, the adoptive transfer of T cells from iPSC/CpG ODN-vaccinated FVB mice to other FVB mice conferred protection against DB7 tumour growth. In addition, the transfer of tumour-experienced lymphocytes from iPSC/CpG ODN-vaccinated animals protected immunodeficient mice from developing teratomas induced by iPSC inoculation. These data suggest that the iPSC/CpG ODN vaccine provides immunity against epitopes that are shared between iPSCs and cancer cells.

In an alternative model of vaccination, CBA/J mice were vaccinated either with iPSC/CpG ODN or with CpG ODNs plus irradiated AC29 cancer cells (AC29/CpG ODN), and then inoculated with AC29 cancer cells. Immune profiling showed that tumour-infiltrating lymphocytes in the iPSC/CpG ODN and AC29/CpG ODN vaccination groups had an inflammatory profile. Furthermore, in the iPSC/CpG ODN vaccination group, the presence of B cells and T cells that express IL-2, IL-4 and IL-5 was predictive of tumour regression.

Finally, the authors assessed whether the iPSC/CpG ODN vaccine could protect against tumour recurrence after resection. C57BL/6 mice were injected with B16F0 tumour cells and the resulting tumours were resected after 2 weeks. A vaccination programme with flank injection sites induced a reduction in tumour cell load in the draining lymph nodes of animals vaccinated with CpG ODNs or iPSC/CpG ODN. Whereas for vaccination injections distal to the tumour, only the iPSC/CpG ODN vaccinated group had a lower tumour recurrence in the resected area, indicating a systemic reactivation of the immune system.

In summary, irradiated iPSC-based vaccines are effective at inducing immunity against multiple cancer types in mice and may represent a future prophylactic cancer vaccine and/or adjuvant therapy after tumour resection.

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ORIGINAL ARTICLE Kooreman, N. G. *et al.* Autologous iPSC-based vaccines elicit anti-tumour responses *in vivo*. *Cell Stem Cell* **22**, 1–13 (2018)

FURTHER READING Finn, O. J. The dawn of vaccines for cancer prevention. *Nat. Rev. Immunol.* https://doi.org/10.1038/nri.2017.140 (2017)