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IN BRIEF

IMMUNOTHERAPY

Glioblastoma regression obtained with CAR T cells

Data from a case report published in the *New England Journal of Medicine* indicate the feasibility of using chimeric antigen receptor (CAR) T cells in patients with recurrent glioblastoma. In this report, a patient whose glioblastoma had progressed whilst participating in a clinical trial underwent surgical resection of three of five progressing intracranial tumours, followed by infusion of CAR T cells targeting the IL-13α2 receptor, which, in a modification of a previous approach, also had a CD137 co-stimulatory receptor. The patient received weekly intracavitary infusions of these cells for 6 weeks. Owing to the emergence of additional tumours, the route of administration was switched to the right lateral ventricle, enabling access to the cerebrospinal fluid. A further 10 infusions using this approach had a dramatic effect: all tumours shrank by 77–100%, this response was sustained for 7.5 months; however, recurrence did eventually occur and preliminary results suggest these tumours have reduced IL-13α2 expression.

ORIGINAL ARTICLE Brown, C. E. *et al.* Regression of glioblastoma after chimeric antigen receptor T-cell therapy. *N. Engl. J. Med.* **375**, 2561–2569 (2016)

PANCREATIC CANCER

Pancreatic cancer cells digest extracellular protein

The findings of a study using mouse models of pancreatic cancer indicate that malignant cells, unlike their non-malignant counterparts, are able to sequester extracellular proteins via macropinocytosis and then metabolize these proteins to meet metabolic demands. Researchers demonstrated this effect using fluorescently labelled albumin delivered to the pancreas using an implanted reservoir device. Furthermore, researchers found that inhibition of macropinocytosis resulted in a reduction in cellular amino acid levels, thus indicating the importance of extracellular proteins to tumour metabolism and progression. This aggressive macropinocytosis was demonstrated to be restricted to the pancreas, without substantial accumulation in skeletal muscle, following the systemic administration of radiolabelled peptides to these mice.

ORIGINAL ARTICLE Davidson, S. M. *et al.* Direct evidence for cancer-cell-autonomous extracellular protein catabolism in pancreatic tumors. *Nat. Med.* http://dx.doi.org/10.1038/nm.4256 (2016)

CNS CANCER

Local chemotherapy favours antitumour immunity

The selection of the most-effective combinations of chemotherapy and immunotherapy can be challenging, owing to the immunosuppressive effects of certain forms of chemotherapy. Now, researchers have demonstrated that systemically administered carmustine results in severe and persistent lymphodepletion, while local delivery of the same drug from implanted polymers designed to release a constant dose of chemotherapy over a 2-week period left all measured immune-cell populations intact. A similar situation occurred following administration of anti-programmed cell death protein 1 (PD-1) antibodies: the effects of locally delivered carmustine synergized with those of the anti-PD-1 antibodies, whereas systemic chemotherapy resulted in lymphodepletion, thus abrogating the effects of PD-1 inhibition. These findings indicate a need to carefully consider effects on the immune system when designing combination regimens containing chemotherapy and immunotherapy.

ORIGINAL ARTICLE Mathios, D. *et al.* Anti–PD-1 antitumor immunity is enhanced by local and abrogated by systemic chemotherapy in GBM. *Sci. Transl. Med.* **8**, 370ra180 (2016)