IN BRIEF

BREAST CANCER

The importance of recycling

Ben-Chetrit *et al.* identified amplification of synaptojanin 2 (SYNJ2), which encodes a phosphoinositol lipid phosphatase implicated in vesicle trafficking, in 4% of 1,980 patients with breast cancer and found that SYNJ2 amplification or overexpression correlated with poor survival. Cells lacking SYNJ2 had defective epidermal growth factor receptor (EGFR) recycling at lamellipodia, which reduced cell migration and invasion *in vitro*. Knockdown of SYNJ2 also reduced lung metastasis of xenograft tumours. Finally, the authors identified an inhibitor of SYNJ2 that blocked cell invasion, which should be tested in animal models in future studies.

ORIGINAL RESEARCH PAPER Ben-Chetrit, N. *et al.* Synaptojanin 2 is a druggable mediator of metastasis and the gene is overexpressed and amplified in breast cancer. *Sci. Signal.* **8**, ra7 (2015)

TUMOUR HETEROGENEITY

A free ride

Why do tumours maintain intratumour heterogeneity under selective pressures? One explanation is that tumour cells of different subclones cooperate and depend on each other for survival. Archetti *et al.* found that heterogeneity can also be maintained without strict interdependence between subclones. Neuroendocrine pancreatic cancer cells that do not express insulin-like growth factor 2 (IGF2) have a growth advantage over cells that express IGF2 in co-cultures, but IGF2-producing cells are not out-competed. This can be explained by game theory: IGF2 acts as a 'public good' that can be exploited by non-producer cells.

ORIGINAL RESEARCH PAPER Archetti, M., Ferraro, D. A. & Christofori, G. Heterogeneity for IGF-II production maintained by public goods dynamics in neuroendocrine pancreatic cancer. Proc. Natl Acad. Sci. USA <u>http://dx.doi.org/10.1073/pnas.1414653112</u> (2015)

RADIOTHERAPY

Healing the brain

Radiotherapy can be very effective in the treatment of brain tumours, but it is associated with significant and irreversible long-term side effects, especially in children. Piao *et al.* transplanted oligodendrocyte progenitors (hOPCs) derived from human embryonic stem cells in the irradiated brains of young (4-week-old) rats. Injection of hOPCs in the forebrain remyelinated the brain and rescued cognitive deficits, whereas hOPC grafts in the cerebellum restored lost motor skills.

ORIGINAL RESEARCH PAPER Piao, J. *et al.* Human embryonic stem cell-derived oligodendrocyte progenitors remyelinate the brain and rescue behavioral deficits following radiation *Cell Stem Cell* **16**, 198–210 (2015)

THERAPEUTICS

Give it a shock

To maintain a high local concentration of chemotherapy, Byrne *et al.* have created two devices, implantable and transdermal, that rely on iontophoresis (the flow of charged molecules in an electric field). The devices improved the delivery and efficacy of gemcitabine in an orthotopic patient-derived xenograft mouse model of pancreatic cancer, as well as of cisplatin in two aggressive orthotopic mouse models of breast cancer, increasing both tumour growth inhibition and overall survival. The devices also showed favourable pharmacokinetic profiles, maintaining high local drug concentrations and low systemic exposure.

ORIGINAL RESEARCH PAPER Byrne, J. D. et al. Local iontophoretic administration of cytotoxic therapies to solid tumors. *Sci. Transl. Med.* **7**, 273ra14 (2015)