IN BRIEF

MATHEMATICAL MODELS

Network analysis of oncogenic Ras activation in cancer

Stites, E. C., Trampont, P. C., Ma, Z. & Ravichandran, K. S. *Science* **318**, 463–467 (2007)

Mutation of Ras is a common occurrence in many human tumours. To understand more about the many pathways that mutated Ras can affect, Edward Stites and colleagues developed a mathematical model of Ras signalling. Their model and subsequent *in vitro* experiments indicate why only point mutations that render Ras insensitive to GTPase activating protein are commonly found in human tumours. Moreover, their model predicted novel drugs that might inhibit the cancerous Ras network more effectively than the wild-type network.

IMAGING

Detecting tumor response to treatment using hyperpolarized ^{13}C magnetic resonance imaging and spectroscopy

Day, S. E. *et al. Nature Med.* **13**, 1382–1387 (2007)

Many groups are now investigating ways of imaging biochemical changes in tumours *in vivo* that are indicative of an early therapeutic response to treatment. Kevin Brindle and colleagues have identified a new method for detecting changes in the activity of lactate dehydrogenase (LDH) in tumours using hyperpolarized [1-^{13}C]pyruvate. The hyperpolarized ^{13}C label is transferred between pyruvate and lactate in a reaction that is catalysed by LDH, and this flux is reduced after treatment with chemotherapeutic drugs owing to the induction of cell death. Such changes can be clearly seen using magnetic resonance spectroscopy and spectroscopic imaging, and could provide a new method for assessing response to therapies in the clinic.

CANCER SYMPTOMS

Tumor-induced anorexia and weight loss are mediated by the TGF-β superfamily cytokine MIC-1

Johnen, H. *et al. Nature Med.* **13**, 1333–1340 (2007)

Patients with late-stage cancer often experience a wasting syndrome that includes anorexia and weight loss. Although this is thought to be cytokine-mediated, Johnen *et al.* now demonstrate a direct connection between levels of macrophage inhibitory cytokine 1 (MIC1) and cancer-associated weight loss in both humans with prostate cancer and mice with xenografted prostate tumours. Weight loss could be reversed in mice with tumours using an antibody against MIC1, and normal mice that were given systemic MIC1 had reduced body weight.

CANCER STEM CELLS

Colon cancer stem cells dictate tumor growth and resist cell death by production of interleukin-4

Todaro, M. *et al. Cell Stem Cell* **1**, 389–402 (2007)

Todaro *et al.* have shown that cells from primary human colon tumours that express the stem-cell marker CD133 are both necessary and sufficient to form subcutaneous tumours in immunodeficient mice. The $CD133^+$ cells were resistant to death induced by various chemotherapeutic drugs, and the authors showed that this was because of interleukin 4 (IL4) produced by the $CD133^+$ cells. Consistent with this, treatment of mice with an IL4-neutralizing antibody or an IL4 receptor-α antagonist improved the anti-tumour efficacy of chemotherapy.