



**Figure 1 | Tissue wasting in pancreatic cancer.** The pancreas secretes enzymes into the small intestine that aid the breakdown of food, enabling nutrients to be absorbed (black arrows). Abnormalities in this process can lead to weight loss and tissue wasting. Danai *et al.*<sup>2</sup> investigated the cause and consequences of the weight loss and adipose-tissue wasting that often occur early in pancreatic cancer. They observed that mice with pancreatic tumours had lower blood glucose levels, increased levels of adipose-tissue wasting and a decreased survival rate compared with control mice that did not have a pancreatic tumour. The authors tested whether feeding the mice pancreatic enzymes would result in any improvements, and found that it decreased adipose-tissue wasting and increased blood glucose. However, these changes did not increase the animals' survival rate, providing insights into the debate about whether weight loss is linked to cancer mortality.

result indicates that cachexia does not drive cancer-associated mortality. The result is also consistent with previous clinical evidence<sup>6</sup> that pancreatic-enzyme supplements do not improve survival in pancreatic cancer. Moreover, when Danai *et al.* analysed clinical data to assess adipose-tissue wasting in 782 people with pancreatic cancer, they found that wasting did not correlate with poorer survival rates. However, it was previously reported<sup>13</sup> that the loss of skeletal muscle and adipose tissue is linked to worse cancer survival rates, so Danai and colleagues' results call into question the idea that cachexia affects survival.

As well as regulating exocrine function, the pancreas has endocrine functions — it produces hormones that regulate metabolism. A key component of the endocrine system produced by the pancreas is the hormone insulin. Insulin facilitates glucose uptake into cells, and its absence can cause diabetes. Diabetes can sometimes precede pancreatic-cancer diagnosis by a year or two, and might be a red flag of trouble ahead<sup>14</sup>. Moreover, abnormal glucose metabolism might contribute to adipose- and skeletal-tissue wasting<sup>15</sup>, and diabetes can cause exocrine insufficiency<sup>16</sup>.

Danai and colleagues observed lower insulin and glucose levels in the blood of their model mice compared with the levels in control mice, and this decrease in insulin and glucose might lead to increased breakdown of stored fats, which could, in turn, increase the level of tissue wasting. This potential connection between the endocrine and exocrine systems and weight loss is supported by studies in the fruit fly *Drosophila melanogaster*<sup>17</sup>.

Much remains to be understood about the

role of the exocrine and endocrine systems in pancreatic cancer. One way to address this might be to perform detailed gene- and protein-expression analyses to determine the signalling crosstalk between transplanted cancer cells and the surrounding healthy pancreas in the mouse model used by the authors. Another potential avenue of research would be to investigate pancreatic exocrine insufficiency at the time of cancer diagnosis, especially in people whose tumours do not block the main pancreatic duct.

The authors did not investigate the role of inflammation in cancer-associated weight loss, but this is tricky to investigate because pancreatic tumours are associated with immunosuppression caused by factors such as the protein TGF- $\beta$ . Inhibiting TGF- $\beta$  reduced cachexia in a mouse model of pancreatic cancer<sup>18</sup>, and there is circumstantial evidence that low-level inflammation contributes to pancreatic-exocrine insufficiency<sup>19</sup>. These observations provide tantalizing hints that inflammation warrants further investigation in this context.

It is worth considering whether other mechanisms might contribute to cachexia. For example, appetite loss might in turn reduce enzyme output, so dietary intake could be another key factor. As work such as that of Danai and colleagues improves our understanding of cachexia, the condition comes into focus as a distinct entity, rather than merely an early symptom of cancer. A goal for future research should be to delineate the interactions between exocrine and endocrine function and inflammation in cachexia. Although Danai and colleagues' results cast doubt on whether



## 50 Years Ago

The resignation of two matrons within a short space of time suggests that discontent among hospital staff is on the increase ... matrons simply do not wield today the power they used to. Together with senior nurses they are assuming more and more responsibility, but their opinions are not being taken into account. It would not be a gross exaggeration to say that the concept of an all-powerful, dictatorial matron is fast disappearing, and this is perhaps no bad thing, because no individual can successfully carry the burden of running a hospital. But the answer does not lie in the appointment of honorary members of hospital committees who may be highly capable managers and administrators in their own right, but who have no real knowledge of the problems of nursing staff. What seems to be happening is that these "amateurs" ... are overriding the people with professional knowledge.

From *Nature* 29 June 1968

## 100 Years Ago

Every boy and girl at school who "does science" now learns that metric units are the universal medium of scientific expression, and is practised in their use ... A boy goes home at the end of term and tells his father that he has been doing science, weighing in grams, measuring lengths in centimetres, pressures in millimetres of mercury, and temperatures in degrees centigrade. Surely the most natural remark for any naturally minded parent to make is that his boy need not pay any attention to that, because, if it had any bearing at all upon practical life, he would certainly have been taught to use pounds or grains, inches, and Fahrenheit degrees, and not the outlandish things that nobody uses after he has left school.

From *Nature* 27 June 1918