IN BRIEF

METABOLISM

Conscious decoupling

Aerobic metabolism is assumed to rely predominantly on glucose as fuel for the tricarboxylic acid (TCA) cycle and mitochondrial respiration. Hui *et al.* showed that lactate derived from the circulation can predominantly fuel the TCA cycle in most tissues. They investigated circulatory fluxes of metabolites through stable isotopic tracing in fed and fasted mice and found that, in both states, the flux of lactate was highest among all metabolites tested, including glucose. During the fasted state, glucose-derived carbons contributed to the TCA cycle mainly indirectly, via circulating lactate. Finally, in genetically engineered mouse models of lung and pancreatic cancer, circulating lactate was identified as the primary substrate for the TCA cycle. Overall, this study shows how aerobic energy production is decoupled from glycolysis, thereby allowing independent regulation of these processes across tissues.

ORIGINAL ARTICLE Hui, S. *et al.* Glucose feeds the TCA cycle via circulating lactate. *Nature* **551**, 115–118 (2017)

LEUKAEMIA

Crowd control

In acute myeloid leukaemia (AML), accumulating leukaemic blasts occupy specialized niches in the bone marrow (BM). However, the extent to which normal haematopoiesis is affected in AML cannot be fully accounted for by this anatomical crowding of the BM. Boyd *et al.* found that the adipocyte BM niche is disrupted in human AML, causing defective myelo-erythroid maturation of haematopoietic stem and progenitor cells (HSPCs). Analysis of AML patient samples through *in vitro* co-culture and patient-derived xenografts (PDXs) in mice identified that BM adipogenesis was disrupted in AML. Whereas normal HSPCs promoted adipogenesis of mesenchymal stem cells (MSCs) in co-culture, leukaemic cells inhibited adipogenesis of MSCs. Adipogenesis in the BM was also severely impaired in PDXs. Importantly, pro-adipogenic therapy restored the adipocyte BM niche, protected normal haematopoiesis and repressed leukaemic growth in PDXs.

ORIGINAL ARTICLE Boyd, A. L. *et al.* Acute myeloid leukaemia disrupts endogenous myelo-erythropoiesis by compromising the adipocyte bone marrow niche. *Nat. Cell Biol.* **19**, 1336–1347 (2017)

TUMOUR BIOMARKERS

A mark is a marker

Early detection of cancer is crucial to improve prognosis, and circulating tumour DNA (ctDNA) presents a minimally invasive screening tool. In contrast to mutation patterns, DNA methylation patterns in ctDNA resemble that of cancer tissue. Xu *et al.* showed that ctDNA methylation patterns can be used as biomarkers for diagnosis and prediction in hepatocellular carcinoma (HCC). Through analysis of differential methylation profiles in HCC tissues and blood leukocytes in healthy individuals, they identified a panel of methylation markers enriched in HCC. They successfully validated this panel in matched DNA from HCC tumour tissue and plasma. Using ctDNA from a cohort of 1,098 patients with HCC and 835 normal controls, the researchers developed diagnostic and prognostic prediction models. These models strongly correlated with tumour burden, stage and therapy response, and reliably predicted clinical outcomes.

ORIGINAL ARTICLE Xu, R. *et al.* Circulating tumour DNA methylation markers for diagnosis and prognosis of hepatocellular carcinoma. *Nat. Mater.* http://dx.doi.org/10.1038/nmat4997 (2017)