Secreted phospholipase A2, lipid metabolism and breast cancer cell survival

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Tumour cells display metabolic changes that fuel cell growth and proliferation and enable cell survival during metabolic stress. One of the fundamental metabolic perturbations in cancer is the acquisition of a lipogenic phenotype, characterised by increased dependency on *de novo* fatty acid production to support membrane phospholipid synthesis and thereby cell growth. Recent studies have revealed that the transformed properties of tumour cells may also depend on changes in triacylglycerol (TAG) lipolysis and fatty acid (FA) oxidation. The mechanisms enabling the transformations of phospholipid and lipid metabolism in cancer cells are however still largely unknown. Secreted phospholipases A2 (sPLA2s) act on phospholipids in cell membranes and lipoproteins to release FAs and lysophospholipids. Their involvement in cancer is not clear and it has been postulated that their effects on cell growth and proliferation are a consequence of their ability to modulate lipid mediator signaling. Contrary to expectations, we have recently found that sPLA2 induces TAG synthesis and cytosolic lipid droplet (LD) formation in invasive breast cancer cells, stimulates their proliferation and prevents their death during prolonged starvation. The sPLA2-induced resistance to starvation-induced cell death is dependent on LD lipolysis and FA oxidation and is associated with the activation of AMP-activated protein kinase (AMPK), a decrease in lipid synthesis and enrichment of polyunsaturated fatty acids (PUFAs) in LDs of breast cancer cells. We identify sPLA2 as a novel modulator of lipid metabolism that promotes the growth and survival of invasive breast cancer cells by stimulating LD biosynthesis and FA oxidation.