**Amplification of USP13 drives ovarian cancer metabolism**

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Dysregulated energetic metabolism has been recently identified as a hallmark of cancer. Although mutations in metabolic enzymes hardwire metabolism to tumourigenesis, they are relatively infrequent in ovarian cancer. More often, cancer metabolism is re-engineered by altered abundance and activity of the metabolic enzymes. Here we identify ubiquitin-specific peptidase 13 (USP13) as a master regulator that drives ovarian cancer metabolism. USP13 specifically deubiquitinates and thus upregulates ATP citrate lyase and oxoglutarate dehydrogenase, two key enzymes that determine mitochondrial respiration, glutaminolysis and fatty acid synthesis. The *USP13* gene is co-amplified with *PIK3CA* in 29.3% of high-grade serous ovarian cancers and its overexpression is significantly associated with poor clinical outcome. Inhibiting USP13 remarkably suppresses ovarian tumour progression and sensitizes tumour cells to the treatment of PI3K/AKT inhibitor. Our results reveal an important metabolism-centric role of USP13, which may lead to potential therapeutics targeting USP13 in ovarian cancers.