# Targeting immunometabolism in patient-derived breast cancer explant cultures

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Combining explorative or standard anticancer therapies with immunotherapies holds great promise in the treatment of advanced cancers, with variable response due to influence from the tumor immune microenvironment (TIME). Therefore, there is a clear need for pharmacologically tractable models of the TIME to dissect its influence on individualized treatment response. We have established a Patient Derived Explant Culture (PDEC) model of breast cancer, which retains the immune contexture of the original tumor, recapitulating cytokine profiles and CD8+ T cell cytotoxic activity. We explored the therapeutic action of standard of care chemo paclitaxel and a MYC synthetic lethal BCL2 inhibitor venetoclax + metformin drug combination ex vivo, discovering metformin cannot overcome the specific lymphodepleting action of venetoclax. Instead, metformin exerts mitochondrial complex I dependent immunomodulatory effects on populations of antigen presenting cells, increasing their capacity to co-stimulate CD4+ T cells and thus facilitating anti-tumor immunity. Our results highlight PDECs as a feasible model to identify immuno-metabolic functions of anticancer drugs in the context of patient-specific TIME.