Adenoid cystic carcinoma (ACC) is a rare, glandular carcinoma whose incidence rate and limited 2D cell culture capability make it difficult to study primary patient samples. Although well-characterized ACC patient-derived xenografts (PDX) have proven to be a useful model to study disease mechanisms and therapeutic sensitivities, animal drug studies are relatively throughput-costly, and take months to accomplish. Ex vivo 3D cell culture can provide a high-throughput, less costly, and significantly faster platform for these drug studies but are hampered by the rarity of tissue. To address this unmet need for models of rare tumor types we developed 3D spherical (3D-\textit{XPDX}™) and microtumor (3D-\textit{XPDX-m™}) models of ACC using PDX as the primary tissue source. ACC PDX cells readily formed spheroids in our 3D-\textit{XPDX}™ platform, remained viable for up to 14 days, and maintained disease-relevant biomarkers such as MYB and c-KIT. 3D-\textit{XPDX}™ represent a more complex model of ACC by incorporating extracellular matrix. ACC 3D-\textit{XPDX}™ displayed tumor-like morphologies corresponding with the parental tumors and exhibited MYB and c-KIT biomarker expression for up to 56 days in culture. Drug response profiling (DRP) was performed using the 3D-\textit{XPDX}™ ACC model with KIYATEC’s validated KIY-A-PREDICT™ DRP platform. The screening panel consisted of drugs and drug-like compounds currently in use or under investigation for use in ACC, including broad-spectrum chemotherapies and targeted agents. Individualized drug responses were noted for each model as they exhibited differential sensitivities to DNA-damaging agents, microtubule stabilizers, and c-KIT targeting kinase inhibitors mirroring the diversity of clinical outcomes. KIY-A-PREDICT™ also identified drugs and drug-like compounds that uniformly inhibited viability. This is significant because there is currently no standard of care drugs for ACC, as few, if any, have demonstrated homogenous responses in test populations. Monensin has been shown to inhibit activity of the MYB transcription factor, making it an attractive candidate drug for the treatment of ACCs which have a high prevalence of MYB activating alterations. In our study, monensin was effective in all three models with IC50 concentrations in the low micromolar range. These results correlate well with immunohistochemical staining of MYB in ACC 3D-\textit{XPDX}™ and 3D-\textit{XPDX-m™}. Taken together, this data represents a new ex vivo 3D cell culture platform for the study of ACC biology and potential therapies.

# Conclusions

- ACC PDX cultured ex vivo in KIYATEC’s 3D-\textit{XPDX}™ platform are viable and express disease-relevant biomarkers up to 14 days.
- ACC PDX cultured ex vivo in KIYATEC’s 3D-\textit{XPDX-m™} are viable long term, express disease relevant biomarkers, and recapitulate complex tissue morphology.
- ACC 3D-\textit{XPDX}™ models screened against a diverse panel of drugs and drug-like compounds in KIYATEC’s KIY-A-PREDICT™ drug response profile platform identified actionable drug “hits” in less than 7 days.