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Letter

Ultrasound guided generation of PDOX models of adenoid cystic carcinoma

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Adenoid cystic carcinomas (ACC) represent a rare type of head and neck cancer that remain clinically persistent for decades despite aggressive multimodal intervention [1]. Successful development of clinically-relevant animal models of ACC is critical to improve our understanding of the mechanisms of salivary tumourigenesis and to develop novel therapies against this disease. To this end, Cornett et al. [2] have recently shown that patient-derived orthotopic xenograft (PDOX) models of ACC maintain high fidelity to human tumours and exhibit several hallmarks of human disease including innervation since ACCs are notorious for perineural invasion. This elegant body of work is significant and serves to remind us of the well-recognized contribution of the microenvironment to disease phenotype and therapeutic response that is often unaccounted for in animal models of cancer.

In this regard, non-invasive imaging methods can play a valuable role in credentialing PDOX models of cancer and maximizing their translational value. In the study published in *EBioMedicine* [2], building on earlier work by Dr. Moskaluk and colleagues [3], PDOX models of ACC were established by surgical opening of the necks in mice to expose the submandibular glands, followed by injection of ACC cells into the glands. Given the superficial location of the salivary glands, the surgical access to glandular tissue and establish orthotopic tumours was likely straight-forward and well-tolerated by the animals. Nevertheless, an alternative strategy to reliably establish orthotopic tumours in mice without the need for invasive surgery involves the use of ultrasound (US). US is a non-invasive imaging method that is routinely used in the clinical assessment of salivary gland pathology, guidance of salivary gland biopsies and for localized injection of agents to treat salivary gland disorders [4]. Given these advantages, we have been previously demonstrated the potential of US-guided injections to establish PDOX models of ACC [5]. High-frequency US allows for easy identification of murine salivary gland tissue and injection of tumour cells into the salivary gland can be readily performed under US-guidance. While the procedure requires anesthesia, it is minimally invasive and alleviates the need for surgical exposure of the glands. The resultant orthotopic tumours can also be visualized and quantified using 3D-US. The procedure is safe, well-tolerated by animals and can be completed in ~10 min. Compared to advanced imaging techniques such as MRI, CT or PET, US is cost-effective, less technically-demanding and user-friendly. Furthermore, due to its short image acquisition times, US enables near real-time tracking of needle position that facilitates timely and accurate delivery of cells into the salivary gland. We therefore submit that US can serve as a valuable tool that can enhance the translational utility of PDOX models of ACC by providing a non-surgical, minimally-invasive approach for establishment of orthotopic tumours and allowing for accurate, longitudinal measurement of tumour volume following treatment. The conduct of imaging-guided preclinical trials using PDOX models of ACC as reported by Cornett and colleagues can accelerate evaluation and clinical translation of novel targeted therapies for these rare but aggressive neoplasms.

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Conflicts of interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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