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Evaluation of tumor metabolic pattern of two nasopharyngeal carcinoma (NPC) mice models using small animal PET/MR system

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Introduction

Nasopharyngeal carcinoma (NPC) is highly prevalent among southern Chinese, particularly the ethnic Cantonese population. Patient-derived xenografts (PDXs) have been used as important models in preclinical evaluation for novel therapeutic drugs. In order to select the best model for treatment studies, it is important to understand the longitudinal changes of these tumors, such as tumor growth, metabolism and necrosis. In this study, two NPC models will be included: C666-1 is one of the most widely used NPC models and C17 is the newly established NPC cell line.

Purpose

Longitudinally describe and compare the metabolic pattern of two NPC models: C666-1 and C17, using ^{18}F-FDG microPET/MR.

Methods

- Mice model establishment: 10^7 tumor cells were injected (C666-1) or small tumor fragments were subcutaneously implanted (C17) into right loin of each NOD/SCID mouse (n=5 for each model).
- MicroPET/MR imaging: Mice were scanned with ^{18}F-FDG PET/MR (3T, Mediso) twice a week for consecutive 4 weeks using a standard protocol. T1W and T2W MRI images were obtained. 20-minute static PET images were acquired 60 minutes after injection of radiotracer.
- Image processing and analysis: Gross tumor volume was measured manually by MRI and metabolic tumor volume (MTV) was measured semi-automatically using threshold value determined by mouse liver SUV. The volume of necrosis was determined by subtracting the MTV from the gross tumor volume.
- Histology: Animals were sacrificed after imaging and tumors were explanted and fixed. H&E and Ki67 staining were performed to confirm necrosis and viable tumor cells.

Results

Figure 1: Comparison of tumor volume and SUV between C666-1 and C17

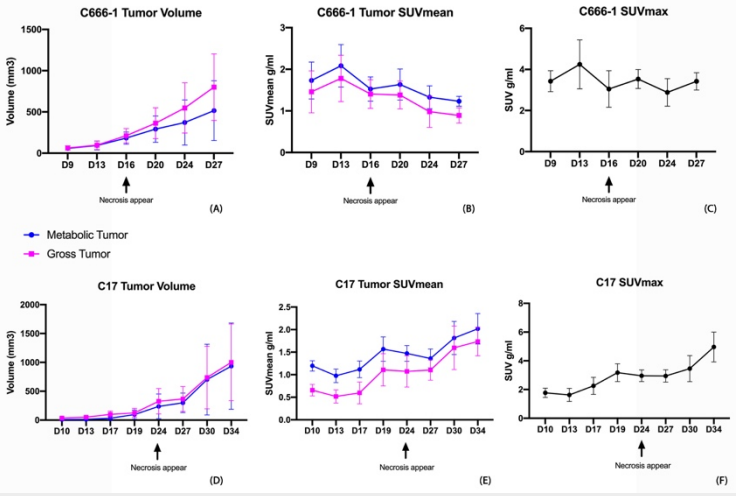
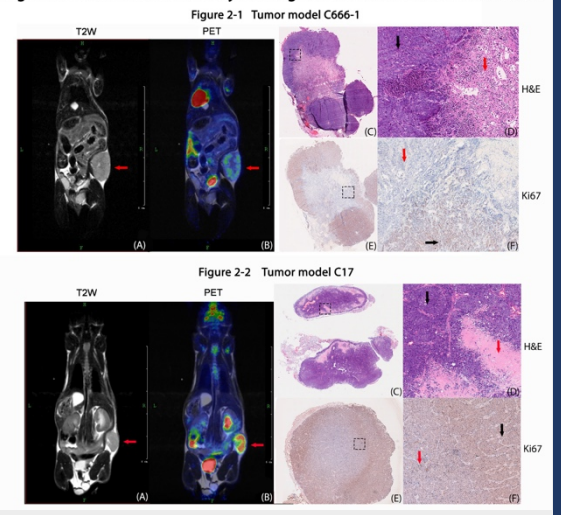


Figure 2: Necrosis is confirmed by histological studies for both C666-1 and C17



- Liver ^{18}F-FDG uptake value is a reliable parameter for internal standardization on the microPET/MR system.
- Longitudinally, the tumor metabolic patterns were different between C666-1 and C17. Fig.1(A,D) show the graphs of the MTV (blue) and gross tumor volume (red), with the difference representing the necrosis. Necrosis was observed progressively on PET images, and this was more evident in the C666-1 model.
- In model C666-1, tumor SUVmean (Fig.1B) and SUVmax (Fig.1C) reached the peak on D13 before necrosis appeared on D16, then declined as the necrotic region became larger. In model C17, tumor SUVmean (Fig.1E) and SUVmax (Fig.1F) increased till D34.
- Compared with C17, tumor volume increased at an earlier time point for C666-1 (D13 vs D19) and tumor necrosis was more extensive for C666-1. By D30, the necrotic region comprised up to 42% of the total tumor volume for C666-1 compared to 13% for C17.
- Subcutaneously implanted tumors were shown on T2W images (Fig.2-1A, Fig.2-2A, arrow). Central necrotic region can be clearly observed on PET images in both C666-1 (Fig.2-1B) and C17 (Fig.2-2B).
- Necrosis was confirmed by H&E and Ki67 staining (Fig.2C-F).

C666-1: Center of the tumor becomes completely necrotic (Fig.2-1D/F, red arrow) with proliferating cells barely observed.

C17: Proliferating cells (Fig.2-2D/F, black arrow) can be observed in the center and outer region of the tumor. Central region has fewer proliferating cells compared with outer region. Necrosis can be observed in the tumor, but in less extensive compared with C666-1.

Conclusion

Longitudinal microPET/MR studies can describe the diversity of tumor metabolic patterns between different NPC models. Since C17 demonstrated a lower necrosis rate and a slower tumor progression, we suggest C17 model may be more suitable for longitudinal studies of NPC cancer treatment.