Multi-modal Functional Imaging of Brown Adipose Tissue

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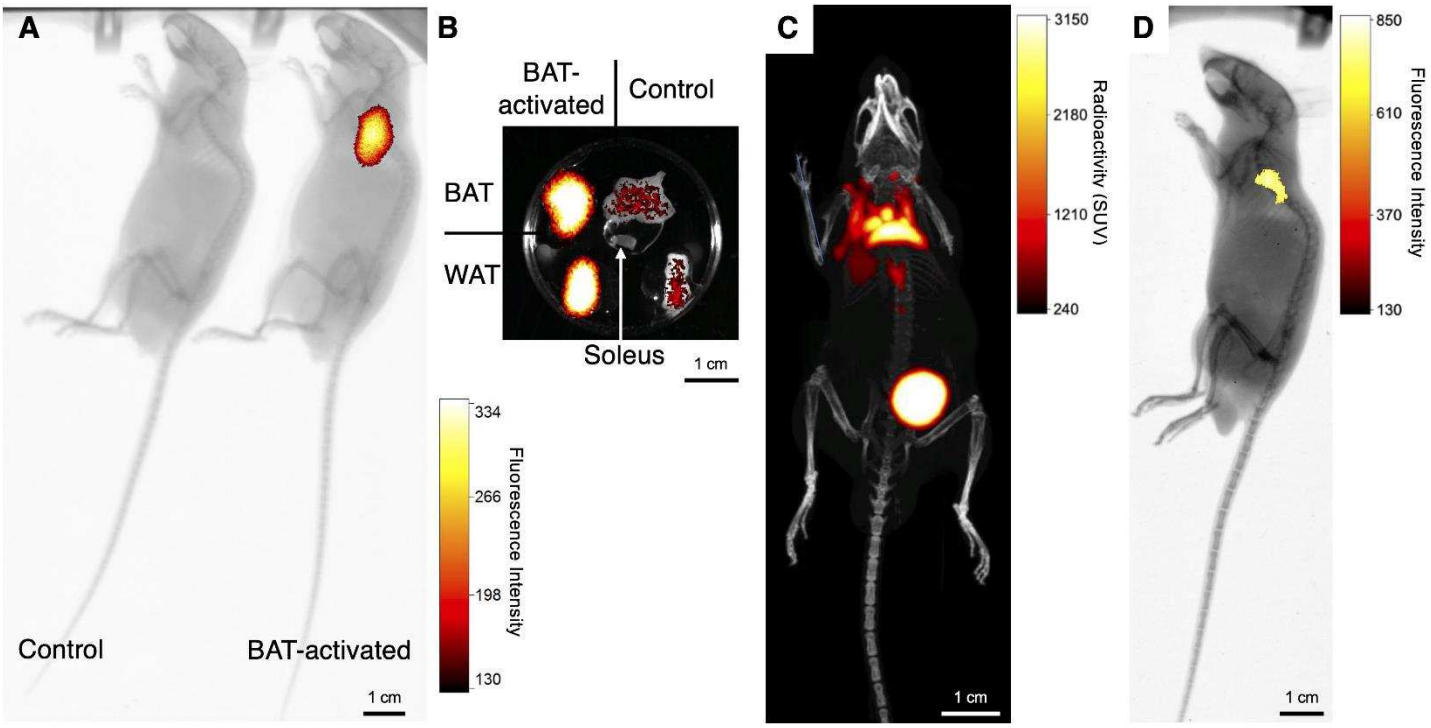

Brown adipose tissue (BAT) is a mitochondrial dense tissue capable of regulating body temperature and energy balance (1). BAT exhibits high rates of glucose and fatty acid oxidation to drive thermogenesis. BAT is a potential therapeutic target for metabolic diseases including obesity and type 2 diabetes (1). Determining in vivo BAT metabolic activity is a powerful tool in translational research. Positron Emission Tomography (PET) using ^{18}F-fluorodeoxyglucose (FDG) is the standard technique for imaging BAT glucose uptake as a proxy for thermogenic activity (2). However PET is limited by the requirement for radio isotope tracers, associated costs, and a lack of functionality to detect concurrent metabolic processes within the same animal. Multi-modal imaging can overcome these limitations. We combined FDG PET with fluorescence optical imaging, a promising technique, not yet widely used in BAT studies (3). We induced BAT activity in C57BL6 mice with CL316,243, a highly specific beta 3-adrenoreceptor agonist (β3-AR), with 1 mg/kg subcutaneous injection for 3 days. We intravenously injected a commercially available fluorescent probe, RediJect 2-DG (100 µl) 3h before imaging with an Xtreme II optical imaging system (Bruker, Ettlingen) in CL316,243-treated BAT-activated animals or saline injected controls (panel A). Anatomical regions of interest were used in analysis of fluorescence optical imaging. Animals treated with β3-AR had higher uptake of RediJect 2-DG in BAT, which we confirmed with ex vivo optical imaging of harvested tissues including BAT, subcutaneous white adipose tissue (sWAT) and soleus muscle (panel B). Increased sWAT signal is not detectable in vivo due its proximity to the saturating signal from the bladder, a limitation also observed in PET/CT (4). Next, we compared RediJect 2-DG to FDG to determine if RediJect 2-DG was a suitable alternative to FDG and to establish the impact of co-injection. We co-injected RediJect 2-DG and FDG into a mouse with induced BAT activity. In succession, we imaged the same mouse with PET/CT to detect the FDG (panel C) and then used optical imaging to detect the RediJect 2-DG (panel D). Rediject 2-DG optical imaging identifies increased activity in the BAT anatomical region as was observed with PET and validated ex vivo using optical imaging and gamma-counter biodistribution analysis. This study is an important step to progress onto wider multi-tracer work. Simultaneous co-injection of a radioisotope and fluorescent probe

could expand current BAT in vivo imaging modalities and facilitate the future detection of multiple concurrent metabolic processes in a single animal.

Equipment: Albira Si PET/SPECT/CT (Bruker), Xtreme II optical imaging system (Bruker)
Reagents: XenoLight RediJect 2-DeoxyGlucosone (DG) (PerkinElmer), CL316,243 (Sigma)

References

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