BAT Molecular Imaging with PET-CT, SPECT-CT, PET-MRI and PET-FI: A Systematic Review of the Literature Data

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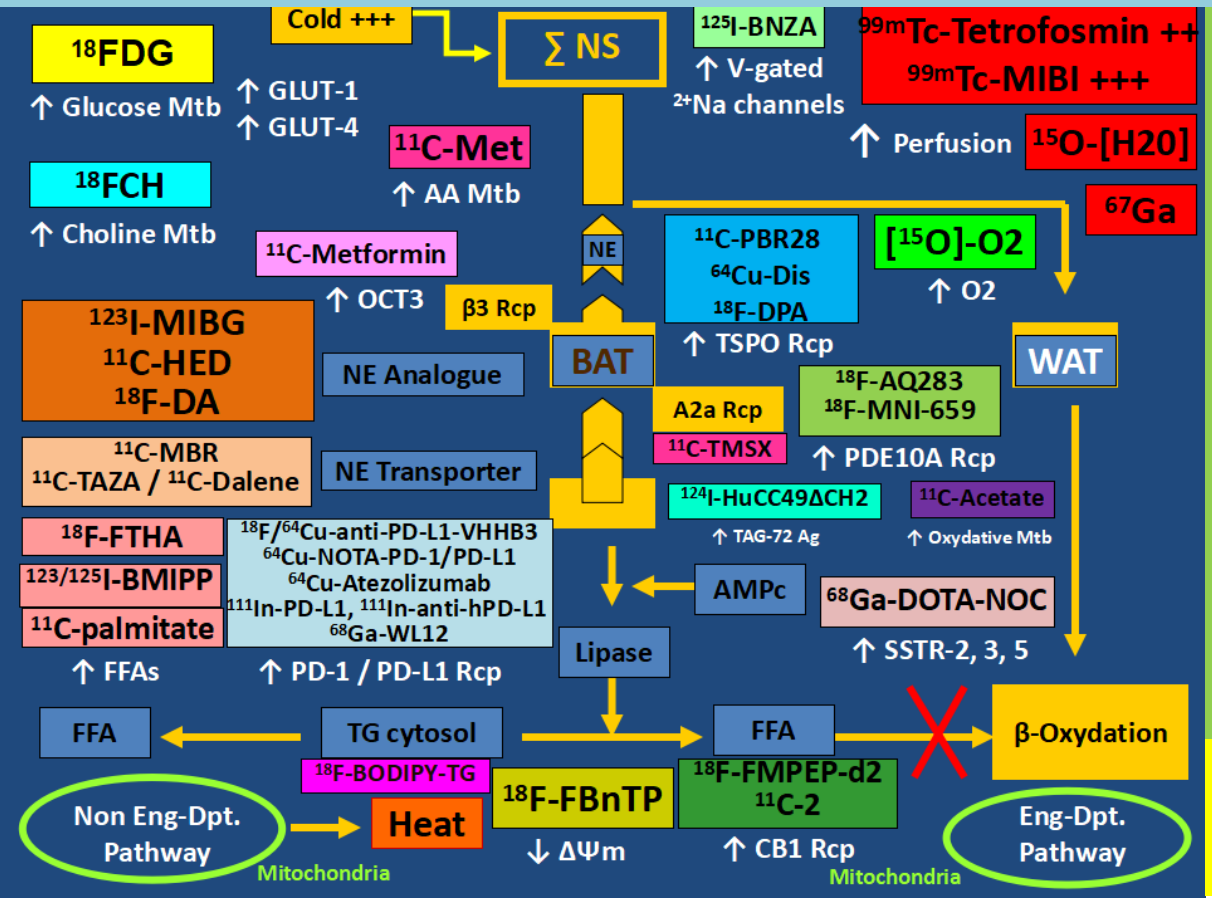
Purpose: Brown adipose tissue (BAT), a mitochondria-rich and richly perfused organ, is a major determinant of the body temperature maintenance. The human body thermoregulation is a physiological condition for the non-shivering and uncoupling non-energy dependent production of heat under the sympathetic nervous system (SNS) stimulation. BAT function has also been documented in pathological conditions including metabolic diseases (diabetes mellitus and obesity), cardio-vascular diseases (heart disease and atherosclerosis), endocrine diseases (hyperthyroidism), SNS derived tumors (pheochromocytoma, paraganglioma, neuroblastoma), benign tumor (hibernoma) and cancer (breast cancer, lymphoma), and also in anorexia/cachexia. A systematic review of the literature data was performed on the hybrid imaging of BAT with nuclear medicine molecular probes.

Subjects and Methods: A literature search was performed on Medline/PubMed using the following key-words: " BAT ", " brown adipose tissue ", " brown fat ", " PET-CT ", " SPECT-CT ", " PET-MRI ", " Fluorescence-PET ". Only articles on nuclear medicine radiolabeled tracers used in the BAT imaging were included in the systematic review.



Results: In nuclear medicine, BAT imaging with PET-CT, SPECT-CT, PET-MRI and fluorescence-PET has been reported in preclinical studies and in clinical studies. Molecular targets for the visualization of BAT included the β3 norepinephrine (NE) receptor and transporter, the adenosine A2a receptor, the GLUT-1/GLUT-4 glucose transporters, the choline transporter, the LAT1 transporter, the FFA substrate, the TG substrate, the PDE10A receptor, the PD-1/PD-L1 receptors, the SSTR 2-3-5 receptors, the OCT3 transporter, the mitochondrial CB1 and TSPO receptors, the mitochondria and transmembrane voltages, and the TAG-72 antigen. BAT radiolabeled probes were reported for the targeting of perfusion (^{99m}Tc-MIBI, ^{99m}Tc-tetrofosmin, ^{15}O-H2O, ^{67}Ga), glucose metabolism (^{18}FDG), phosphatidylcholine metabolism (^{18}F-fluorocholine), FFA metabolism (^{18}F-FTHA, $^{123/125}$I-BMIPP, ^{11}C-palmitate), TG metabolism (^{18}F-BODIPY-TG), oxidative metabolism (^{11}C-acetate), amino acid transport (^{11}C-methionine), oxygen consumption ([^{15}O]O2), sympathetic system/NE receptor (^{123}I-MIBG, ^{11}C-*meta*-HED, ^{18}F-fluorodopamine), sympathetic system/NE transport (^{11}C-MBR, ^{11}C-TAZA, ^{11}C-Dalene), sympathetic/NE regulation (^{11}C-metformin), G-protein pathway (^{11}C-MTSX), somatostatin receptors (^{68}Ga-DOTA-NOC), programed cell death pathway (^{18}F/^{64}Cu-anti-PD-L1-VHHB3, ^{64}Cu-NOTA-PD-1/PD-L1, ^{64}Cu-atezolizumab, ^{111}In-PD-L1, 111In-anti-hPD-L1, ^{68}Ga-WL12), benzodiazepine receptor (^{11}C-PBR28, ^{64}Cu-Dis, ^{18}F-DPA), phosphodiesterase receptor (^{18}F-AQ283,^{18}F-MNI-659), cannabinoid receptor (^{18}F-FMPEP-d2,^{11}C-2), mitochondrial membrane potential ΔΨm (^{18}F-FBnTP) and voltage-gated $^{2+}$Na channels (^{125}I-BNZA), and tumor-associated glycoprotein 72 (^{124}I-HuCC49ΔCH2).

Conclusion: BAT plays a critical role in the body thermostasis, immunity and metabolism. Molecular hybrid imaging with radiolabeled probes may help for the visualization, characterization and quantification of BAT in pathophysiological conditions. BAT's various molecular targets may also be imaged for preclinical and clinical research.