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Transgenic mice brain imaging studies of Alzheimer's disease

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Lipophilicity is one of the major brain radiopharmaceutical design criteria. Alzheimer disease PET imaging agents based on lipophilicity modification are [18F]RO6958948 [1] and [18F]Florbetapir, design by replacing with a Nitrogen element either in the aromatic ring of [18F]Flortaucipir or [18F]Florbetaben. The structure of [18F]FEONM (Figure 1) is designed to provide higher lipophilicity than [18F]FDDNP. Structure modification on a certain bioactive molecule in order to increase its lipophilicity will be also possibly increasing the percentage of penetrating blood brain barrier. Increasing the blood brain barrier crossing ratio, the specificity of this active biomolecule targeting effect might be decreased. Therefore, we design an ethyl oxide modified naphthol based Alzheimer disease positron emission tomography imaging agent [18F]FEONM, in order to compare the uptake effect of Tau tangle and Beta amyloid. PET radiopharmaceiticals for brain imaging are based on very short half-life radionuclides, most of them will be decayed in one day. One of the longest half-life organic radionuclides is fluorine-18, therefore critical step to producing PET radiopharmaceuticals online is radiofluorination reaction. The highest radiofluorination reaction yield can be made from carboxy glass reactor [2]. In carboxy glass reactor, the function of gap area (FG) [3] curve of radiofluorination yield can be approached with Gauss distribution, Gauss or Welch apodization function. After determine the radiofluorination rate constant, the length of microfluidic plug flow reactor can be designed with an analytical form based on Welch apodization function [4]. Brain hippocampus imaging relative specific binding ratio of [18F]FEONM on a Tau tangle P301S/PS19 transgenic mouse model is two time higher than cerebellum [3], Beta amyloid Tg2576 transgenic mouse model is less than two. On a triple transgenic 3xTg mouse model with both Tau tangle and Beta amyloid formed, the uptake ratio of hippocampus is fifty percent higher than cerebellum. Therefore, [18F]FEONM is a new Alzheimer PET imaging agent. Besides, other than transgenic mouse model, streptozotocin induced Tau tangle mouse model [5] also shows higher brain hippocampus [18F]FEONM uptake than control mouse. From the transgenic mouse model imaging study, we found [18F]FEONM will uptake on both Tau tangle and Beta amyloid transgenic mouse. In comparison to [18F]FDDNP, it shows no Beta amyloid transgenic mice uptake in brain hippocampus [6]. This result represents part of the specific binding of Tau tangle transgenic mouse of [18F]FDDNP has shift to Beta amyloid. Therefore, Tau tangle and Beta amyloid uptake status can be done by [18F]FEONM in the same time for diagnosis Alzheimer disease. Radiation exposure will be half dosage compared to taking both imaging. These findings based on a new design conclude that a new PET radiopharmaceutical design has the same concept like a new radiofluorination microfluidic reactor design. Either a new chemical structure or a new mathematical model contributes an achievement.

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Biography

Jenn-Tzong Chen is a PhD student of Institute of Polymer Science and Engineering, and Chemical Engineering of National Taiwan University. He is also an associate researcher of Isotope Application Department of Institute of Nuclear Energy Research. After graduated from the Chemical Engineering Department of Ming-Chi Institute of Technology, he studied Chemical Engineering in National Taiwan Institute Technology for one year. Then he graduated from Chemical Engineering Department of National Taiwan University with master degree. He has been trained in Forschungszentrum Jülich, Germany and Washington University in St. Louis, US and so on. At present he works for cyclotron produced radioisotope process development and application. He has published some papers and owned some patterns.

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