Discovery and evaluation of a novel tau PET tracer [18F]THK-5562 for Alzheimer's disease

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Tau is one of the characteristic deposits in Alzheimer's Disease which occurs in neurofibrillary tangles within neurons. Positron-emission tomography (PET) is a nuclear imaging technique, making it possible to detect tau aggregation in AD in vivo, thereby helping to pre-diagnose and trace disease progression. Up to now, many tau tracers have been developed. For example, the first generation tau tracer [18F]AV-1451 and [18F]THK-5351 developed by our group displayed strong uptake in patients' brains. Although they were promising, considerable off-target binding has been observed, especially to MAO-B and other non-tau protein deposits. This led to the optimization of binding characteristics and discovery of novel tau tracers.

More than 200 candidates synthesized by our group were screened through binding assay for tau, amyloid β, monoamine oxidase A and B. Among these compounds, [18F]THK-5562 was identified with high affinity and selectivity for tau aggregation without off target bindings, followed by further evaluation. As a result, [18F]THK-5562 displayed excellent in vivo pharmacokinetics characteristics in mice. Besides, [18F]THK-5562 seemed to be specific for 3R/4R tau in AD by autoradiography and immunohistochemistry.

In conclusion, preclinical validation suggested the potential usefulness of [18F]THK-5562 in imaging tau aggregation in Alzheimer's disease.