Promising new neuroimaging techniques for early detection of Alzheimer's disease

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Investigators from the International Center for Biomedicine and the University of Chile, in collaboration with the Center for Bioinformatics of the Universidad de Talca, have discovered that two drugs, the benzimidazole derivatives lanzoprazole and astemizole, may be suitable for use as PET (positron emission tomography) radiotracers and enable imaging for the early detection of Alzheimer's Disease. The study is published in the current issue of the *Journal of Alzheimer's Disease*.

Lanzoprazole and astemizole specifically tag pathological oligomers of tau which form the core of neurofibrillary tangles (NFTs), a pathognomonic brain lesion in Alzheimer´s patients. Prof. Dr. R.B. Maccioni and Dr. Leonel Rojo, authors of the study commented, "Since neurofibrillary tangles are positively correlated with cognitive impairment, we propose that these drugs have great potential in PET neuroimaging for in vivo early detection of AD and in reducing the formation of NFTs. These studies, based on advanced proteomics and databases of molecular interactions, may help to find potential new drugs for early diagnosis and treatment of Alzheimer´s disease. The findings are the result of a long-standing research program supported by the Alzheimer´s Association-USA and Fondecyt, Chile to evaluate new drug candidates." Technological applications of this discovery are being developed with the collaboration of VentureL@b of the Universidad Adolfo Ibañez.

Interestingly, lanzoprazole and astemizole, already approved for treatment of proton pump disorders and as an antihistamine respectively,

specifically bind directly to aggregated variants of <u>tau protein</u>, paired helical filaments (PHFs) and NFTs in Alzheimer´s brains. Until now it has not been possible to detect these pathological brain structures in living Alzheimer´s patients. The only confirmation of the disease has been attained by postmortem neuropathological evaluation.

Dr. Maccioni and Dr. Rojo postulate that "This important discovery will provide the stepping stone for the development of new specific neuroimaging technologies based on PET radiotracers that monitor the formation and growth of NFTs in patients during the course of their lives."

The interactions of lanzoprazole and astemizole with the anomalous tau aggregates were assessed by classical radioligand assays, combined with surface plasmon resonance, bioinformatic approaches and immunofluorescence studies on isolated PHFs and brain samples from Alzheimer's cases. The affinity of these for tau aggregates was significantly higher than that of polymers of the amyloid-☐ peptide according to SPR analysis. This is relevant since senile plaques are abundant but not pathognomonic in AD patients. Immunochemical studies on PHFs from brains of AD patients and SPR studies confirm these findings. The capacity of all these drugs to penetrate the blood-brain barrier was confirmed by either in vitro studies using parallel artificial membrane permeability assays or in vivo by pharmacokinetic studies comparing distribution profiles in blood and brain in mice.

More information: Rojo, Leonel E., Jans Alzate-Morales, Iván N. Saavedra, Peter Davies and Ricardo B. Maccioni. Selective Interaction of Lansoprazole and Astemizole with Tau Polymers: Potential New Clinical Use in Diagnosis of Alzheimer's Disease. *J Alzheimers Dis* 19:2 (January 2010).