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Classification and prediction of clinical Alzheimer's diagnosis based on plasma signaling proteins

Ray S, Britschgi M, Herbert C, Takeda-Uchimura Y, Boxer A, Blennow K, Friedman LF, Galasko DR, Jutel M, Karydas A, Kaye JA, Leszek J, Miller BL, Minthon L, Quinn JF, Rabinovici GD, Robinson WH, Sabbagh MN, So YT, Sparks DL, Tabaton M, Tinklenberg J, Yesavage JA, Tibshirani R, Wyss-Coray T. Nat Med. 2007 Nov;13(11):1359-62. Epub 2007 Oct 14.

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17934472&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

An international team of scientists led by Tony Wyss-Coray of Stanford University has identified an Alzheimer's-specific plasma biomarker signature that not only identifies patients with the disease, but is also effective in predicting the onset of Alzheimer's years before patients become symptomatic. Notably, biological analysis of the 18-protein signature using IPA generated insights into the molecular mechanisms underlying the development of Alzheimer's disease. IPA networks centered on several of the proteins in the signature, including TNF- α , M-CSF, and EGF, and indicated disruptions to hematopoiesis, immune response pathways, and apoptosis. This work may eventually result in the first noninvasive clinical test for Alzheimer's disease and presents a viable strategy for discovery of novel biomarker signatures for other neurodegenerative disorders. Future clinical studies employing this signature may also prove useful for monitoring individual patient response to novel Alzheimer's treatments.

One of the key strategies that the Stanford team employed in their hunt for molecular biomarkers of Alzheimers was to first identify a set of signaling proteins that may carry messages of neurodegeneration from the brain to readily accessible peripheral tissues like the blood. This so-called "cellular communicome" was then used as the basis for designing an ELISA that assayed blood samples from 259 individuals: normal, with mild cognitive impairment (MCI), or with Alzheimer's. Statistical analysis of the assay results identified a signature of 18-signaling proteins with highly significant differences in expression between individuals with Alzheimer's disease and nondemented controls. IPA provided a critical biological link between the highly specific disease signature and the pathways and processes that underlie the development of the disease itself.