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Integrative machine learning approach for characterizing a blood-based redox profile and identifying a lead biomarker for Alzheimer disease diagnosis

Diagnosis of Alzheimer's disease (AD) early in its course is a crucial starting point in the management of the disease, allowing early interventions in the at-risk individuals when cognitive symptoms are absent or only minimally compromised. Blood-based biomarkers could represent a considerable advantage in providing information about diagnosis and disease progression. They could be an ideal choice in the first step of the multistage diagnostics, to determine which individuals should be referred for further specialist examinations. A profiling approach followed by multivariate data analysis and machine learning techniques has been aspirational in the discovery of specific AD signatures. Here, applying a sequential integrative machine learning approach, 733 blood samples derived from pre-symptomatic to late stage AD, cognitive normal subjects (CN) and patients affected by Parkinson's and others dementia (OD), were used to identify a blood-based redox-related biomarker for AD risk. We started by examining a panel of 10 redox-related variables in both intra- and extracellular blood compartments, for discriminating AD from healthy subjects and patients with mild cognitive impairment (MCI). Then applying Random Forest and ROC analysis, we identified in plasma_Up53^{2D3A8+} the lead variable that best correlated with AD. The high performance of plasma_Up53^{2D3A8+} in identifying AD at preclinical and prodromal stages was confirmed in samples derived from a longitudinal population study (InveCe.Ab), and from PharmaCog/E-ADNI cohort. In addition, SRM-MS preceded by 2D3A8 antibody immunoprecipitation performed on 88 samples derived from AIBL cohort allowed identifying a select p53 quantotypic peptide, thus validating Up53^{2D3A8+} as a promising biomarker for AD timely diagnosis.

This integrative disease modelling allowed reducing ad minimum the number of profiling biomarkers to be tested, moving towards lead biomarkers to stratify AD risk, and to pursue the idea of multiplex-biomarker signatures for a personalized AD diagnosis.

Biography

Daniela Uberti is a Professor of Pharmacology, at the University of Brescia. She is a co-author of more than 70 peer-reviewed publications (H- Index 27), and 3 patents related to an early biomarker for Alzheimer's Disease (AD), and the 2D3A8 antibody against a criptic epitope of p53 with a diagnostic and prognostic value for AD. On 2012 she co-founded the University Spin off Diadem, that in 2017 raised €1.5 million in its A Round led by Panakes Partners and more recently an additional €1 million for taking the company towards EU & US regulatory approval of the 2D3A8-related blood test. Her researches are mainly focused on the identification of a specific blood based profile in Alzheimer's disease. She heads a REDOX Biology laboratory involved in studying the regulation and dysregulation of redox homeostasis in ageing and aged-related disease. She also involves in proteomics and redox-proteomics studies in neurodegenerative disease, electrochemical sensors development for biomarkers detection, natural compounds identification/characterization as redox homeostasis modulators.

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