Integrated approach based on transcriptomic and proteomic platforms to identify the biological mechanisms underlying the ALS disease

ALS is a neurodegenerative disease, without therapies that alter its course, with fatal outcome. In Lombardy, there are about 1000 affected patients and an expected incidence of 0.8 new cases per day. The biological mechanisms underlying the disease remain largely unknown as well as the factors determining clinical and course variability. INTERSLA (Innovazione, nuovi modelli Tecnologici e Reti per curare la SLA) is an interdiscplinary project of integrated research for ALS treatment. The IRCCS Fondazione Istituto Neurologico “C. Besta” is the Principal Investigator together with other partners such as Avantea S.r.l., Ist. Zooprofilattico di Piemonte, Liguria e Valle d’Aosta, CNR (IBFM, IGM, IN, IRGB, ITB, SCITEC Institutes), Istituto Ricerche Farmacologiche IRCCS Mario Negri. Specifically, INTERSLA project aims to broaden the knowledge of the pathogenesis of ALS using high-tech platforms for the discovery of potential biomarkers and big data analysis, which will draw information from a clinical, genetic, tissue, cell, biochemical-molecular and immunological characterization of patients and animal model systems.

The main goal of ITB is the development of an integrated approach based on transcriptomic and proteomic platforms to discover potential biomarkers for more effective therapeutic strategies thanks to the analysis of big data.

The experimental set up will consist in the molecular characterization of patients and animal models, because SOD1-mutated pigs show multiple analogies with the same type of SLA in humans. In details, by RNA-seq analysis in “bulk”, ITB will investigate the transcriptional profile starting from spinal cord of pigs at various stages of disease development in comparison to healthy ones. However, to fully understand the underlying mechanisms for progression of ALS, a more comprehensive catalog of cell types affected within the CNS is necessary. Single cell RNA-seq (scRNA-seq) methodology provides this opportunity and it will be used in SOD1-mutated and wild-type pig brains to analyze both known and novel cell types, cell-cell interactions, as well as, the causal genes and cellular pathways altered during ALS progression (1).

Then, the innovative proteomics platform, based on the coupling of nano-LC and high resolution mass spectrometry (nLC-hrMS), will allow to obtain the untargeted proteomic profile of extracellular vesicles, extracted from serum of ALS patients and from “SLA model” porcine, before and after disease onset (2). The analysis of circulating biomarkers will be correlated with ALS severity to identify early disease biomarkers. Moreover, protein differential expression and their evaluation by systems biology will be useful to investigate which molecular pathways could be related to ALS. Finally, the integration of the “omics” data will allow a more complete molecular characterization of the examined biological phenomenon. In this way, it becomes easier to identify different subclasses of patients or biological markers that play a fundamental role in the ALS pathogenesis, in order to be able to improve diagnostic and prognostic skills and identify targeted pharmacological interventions.

References:

Keywords: transcriptomics, proteomics, ALS.

Contacts: roberta.bordoni@itb.cnr.it, pierluigi.mauri@itb.cnr.it, antonella.depalma@itb.cnr.it

Website(s): https://www.openinnovation.regione.lombardia.it/it/b/17088/innovazione-nuovi-modelli-tecnologici-e-reti-per-curare-la-sla

Authors: Bordoni Roberta, Clarissa Consolandi, Eleonora Mangano (Genomic Unit), Antonella De Palma, Rossana Rossi, Pierluigi Mauri (Proteomic Unit).