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Assessment of lipid metabolism involvement inALSusing G86R mouse model

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Amyotrophic lateral sclerosis (ALS)is a progressive neurodegenerative disease affecting the initiation and control of muscle movement with littletherapeutic options. Transgenic mice with mutated Cu/Zn superoxide dismutase ($SOD1^{G86R}$) develop an age-related loss of motor neurons that strongly resembles human ALS.Impairment of energy metabolism is a well-known phenomenon in ALS. Dyslipidemia in ALS was also found as a protective factor and thus a lipid profiling approachwasperformed in an attempt to measure metabolic disruption associated with this disease.

Motor neuron loss in the spinal cord and subsequentmuscle denervationare the major features of the pathological process leading to ALS.We thereforemeasured lipid profiles in muscles (soleus and tibialis anterior), lumbar spinal cord. Plasma was also sampled and analyzed.A UPLC/ToF-MSlipidomic method was used to follow lipids from pre-symptomatic and symptomatic mice (77 and 105 days old,respectively). Lipid analysis included triacylglycerols (TAG), ceramides and phosphatidylcholines (PC) among other lipid families.

Principal component analysis allowedthe discrimination between groups. Subsequent orthogonal partial least square discriminant analysis, as implemented inthe SIMCA-P® v12 analysis software, was carried out to highlight significant features that led to group separation.Soleus muscle and spinal cord had their lipid content disrupted at both stages while the plasma lipid profile was most altered at the symptomatic stage, with major depletion of triglycerides.Our results suggestphingolipid and phospholipid metabolismare critically modified in early stages of theALS physiopathological process.

Biography

Vincent Croixmarie has completed his Ph.D. in physical-chemistry at University Orsay France with the unfolding analysis of prion protein, using in silicotechinques in 2005. He joined metabolomic teamof Servier in 2006. Since then he is working as team leader in metabolomics in pre-clinical and clinical fields.

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