TAF1 AS A THERAPEUTIC TARGET AND BIOMARKER IN PROGRESSIVE MULTIPLE SCLEROSIS

A research group from CSIC and CIBERNED has made the first identification of a molecular alteration in multiple sclerosis (MS) brain tissue able to trigger disease progression. This rendered a genetic mouse model of MS with construct and face validity, useful to explore ways to treat the progressive phase of the disease.

The Need

Multiple sclerosis (MS) affects 2.8 million people worldwide and is characterized by CNS neuroinflammation and demyelination leading to disablility. Genetic risk variants implicate genes involved in immune function, while MS severity is associated with variation in genes preferentially expressed within the CNS. This probably explains why the currently available immunological therapies are effective solely in preventing relapses in the initial phase and no treatment is available to prevent or halt the progression that seems to forge within the CNS. To date, the molecular events able to trigger progressive MS have remained unknown.

The Solution

Through a detailed research in normal-appearing cerebral cortex samples (i.e., free of demyelinating lesions) from control and case individuals, we found lower immunodetection of the C-terminus of TAF1 from patients with progressive MS. These results point to changes in TAF1 and its modifiers as potential biomarkers of progressive MS.

Likewise, the possibility of TAF1 as a therapeutic target for progressive MS is raised since the alteration observed in the brain of individuals with MS could have a causal relationship with the disease, being sufficient to generate the demyelinating condition in an animal model, and no other target is known in the progressive phase of this disease.

Innovative Aspects

- We have created, using CRISPR technology, a mouse line in which the C-terminal region encoded by exon 38 has been deleted. This animal model, called Taf1del38 mouse, develops a progressive motor phenotype and massive demyelination of the CNS, accompanied by neuroinflammation mediated by resident glia, without infiltration of the CNS by cells of the immune system. Therefore, the Taf1d38 mouse model demonstrates that the elimination of the C-terminal end of TAF1 alone is capable of triggering a symptomatic, histopathological and molecular picture very similar to progressive MS.
- The Taf1d38 mouse is emerging as the first genetic model of progressive MS, useful for further investigating the etiopathogenic mechanisms of the disease, and also as a test bed for the preclinical analysis of new therapies.
- We first discovered that the C-terminal end (encoded by exon38) of TAF1 is altered in MS brains.

Intellectual Property:

- Priority European patent application filed (August 14, 2024)
- Suitable for international extension (PCT application)

Aims

Looking for a partner interested in a license and/or a collaboration agreement to develop and exploit this asset.

Contact details

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