

TTR amyloidosis: a scientific journey

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Mário Corino de Andrade described in 1952 in the journal “Brain” the first form of an hereditary amyloidosis, Familial Amyloidotic Polyneuropathy, FAP - affecting the peripheral nervous system, also known as Andrade’s disease. In 1939 , Andrade observed different patients complaining of loss of sensitivity to temperature and pain and suspected the clinical symptoms were peculiar and belonged to a rare hereditary disease. To understand in depth what he considered a new endemic clinical entity, he asked the collaboration of experts in different fields, such as biochemistry, genetics, pathology, who confirmed the genetic nature of the disease and the presence of systemic amyloid deposits, that we know since 1984 to be constituted by mutant transthyretin (TTRV30M), particularly in the peripheral nervous system. Explosion of molecular biology tools provided identification worldwide of more than 100 TTR mutations, most of them associated with amyloid neuropathies and cardiopathies as well as perspectives for their clinical improvement.

Molecular and cellular in-depth studies are underway in several laboratories to dissect underlying etiopathogenic mechanisms in TTR related amyloidoses; in particular: (1) consequences of protein aggregation on peripheral nerve and other organs and tissues; (2) development of improved/alternative therapies in pre-clinical models; (3) biomarker identification for therapy follow-up.