

# Alpha-synuclein immunoreactivity in the enteric nervous system of human small intestine

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Alpha-synuclein ( $\alpha$ -syn) is a 140 amino acid protein, belonging to the synuclein family, expressed in mammalian neurons. Structural alterations of  $\alpha$ -syn as well as its overexpression have been related to the onset and the progression of several human neurodegenerative diseases, as Parkinson's diseases (PD). Indeed,  $\alpha$ -syn aggregates are the main component of the Lewy bodies (Lbs), considered as pathological hallmarks of neurodegenerative diseases [1-2], known as synucleinopathies. PD is a multicentric neurodegenerative process that affects several neuronal structures in the central and peripheral nervous system, among which is the enteric nervous system (ENS). Remarkably, recent reports have shown that the lesions in the ENS occurred at very early stage of the disease, even before the involvement of the central nervous system. So, the ENS could be critical in the pathophysiology of PD [3] and the pathological alterations within the ENS could be involved in the gastrointestinal dysfunction frequently encountered by parkinsonian patients. Although at present Lbs, as well as  $\alpha$ -syn pathological aggregates, have been evidenced throughout the autonomic nervous system projecting to the gut of patients affected by PD or other neurodegenerative diseases, however data on the distribution of  $\alpha$ -syn in human normal ENS are lacking. Our study focused on the immunohistochemical distribution of  $\alpha$ -syn in the ENS of proximal tract of human normal small intestine. Surgical specimens of duodenum and proximal jejunum, collected from patients submitted to a pancreaticoduodenectomy, were fixed and paraffin embedded. Intestinal slices underwent immunohistochemical procedure using monoclonal anti  $\alpha$ -syn antibody. Alpha-syn immunoreactive (ir) structures were detected along both myenteric and submucosal plexuses as well as in the circular and longitudinal muscular layers. We found perivascular  $\alpha$ -syn-ir fibers in the submucosa and a dense ir periglandular network projecting up to the axis of the villi in the mucosa. The immunohistochemical distribution pattern of  $\alpha$ -syn has been compared with that of major enteric neurotransmitters. Our preliminary observations confirm a physiological role of  $\alpha$ -syn in the ENS, and may contribute to clarify its role in the peripheral nervous system.

## References

- [1] Spillantini et al, Nature 1997; 388:839-40.
- [2] Arima et al, Brain Res 1998; 808:93-100.
- [3] Braak et al, Neurosci Lett 2006; 396:67-72.
- [4] Wakabayashi et al, Acta Neuropathol 2010; 120:1-12.