

Investigation of the intestinal inflammatory status in a Parkinson's disease mouse model reveals distinct changes at an early disease stage

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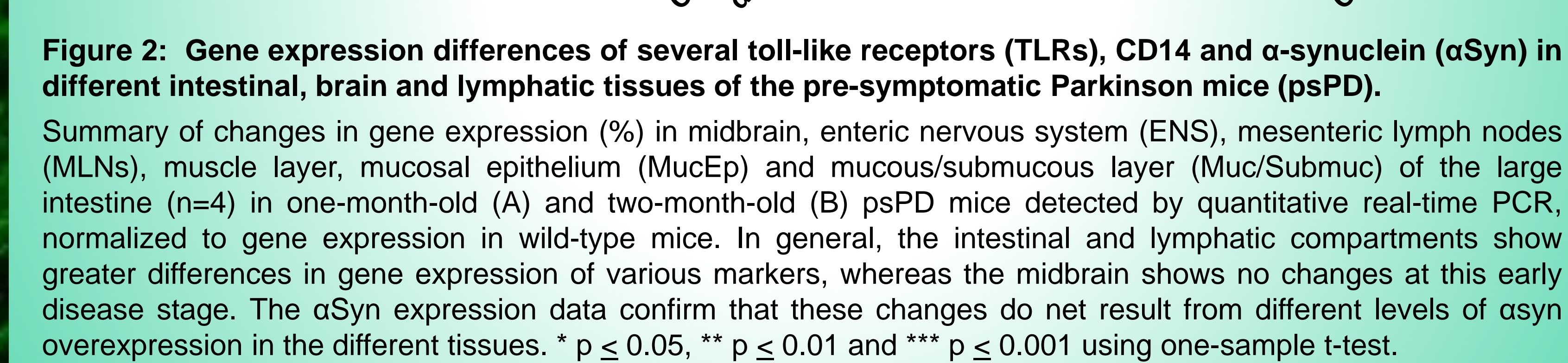
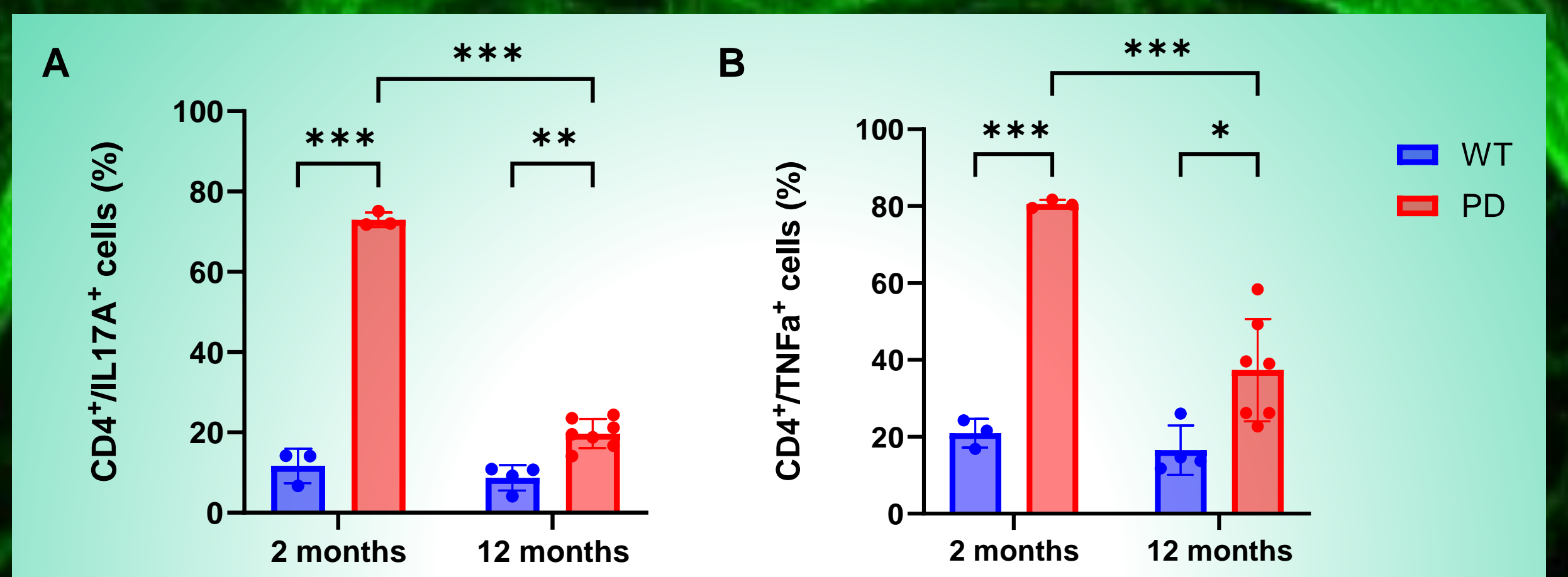
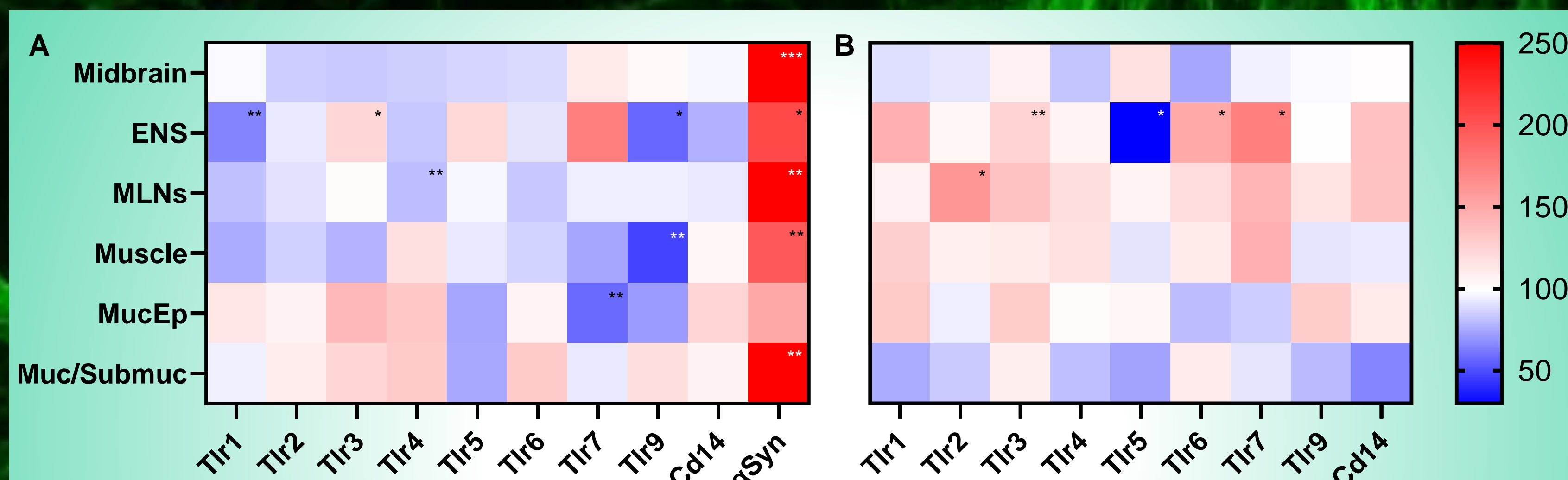
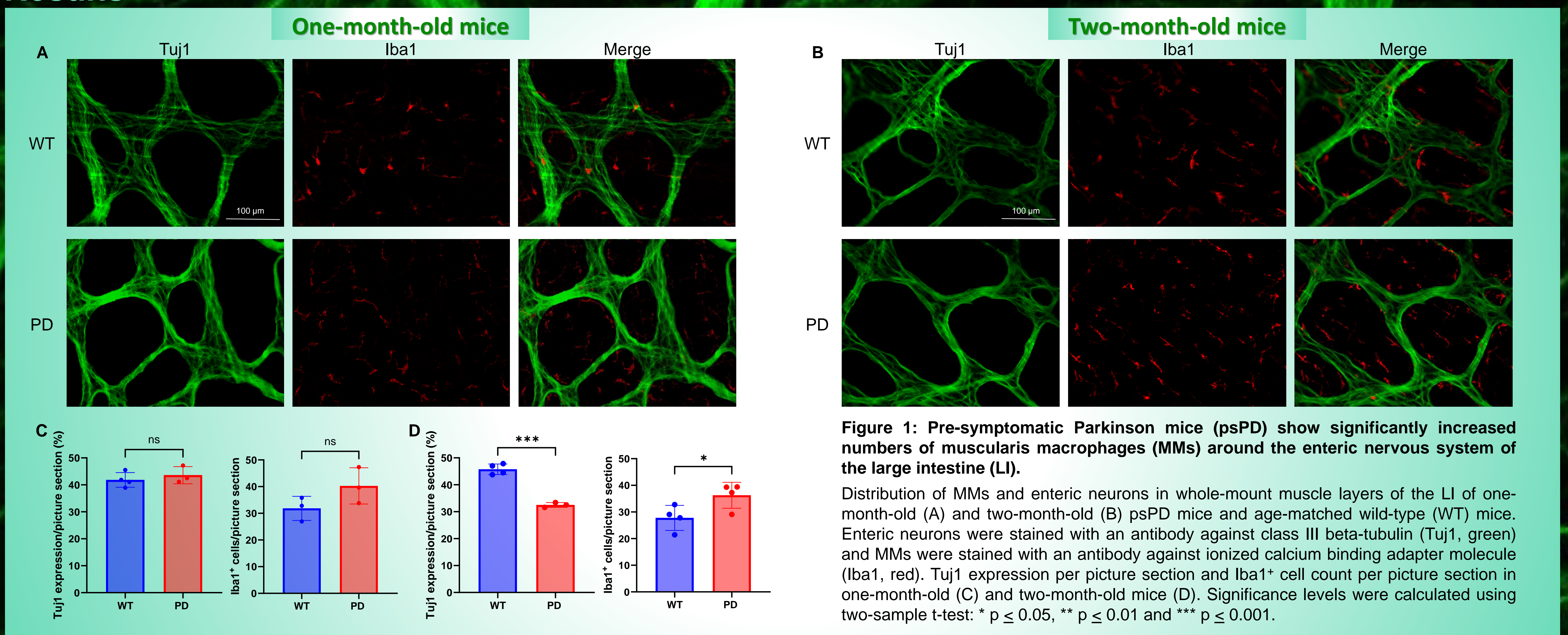
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Abstract

Parkinson's disease (PD) is the fastest growing neurological disorder in the world. However, the exact cause of the disease is still unknown. In addition to the classic motor symptoms such as bradykinesia, resting tremor and rigidity, PD patients also suffer from various non-motor symptoms like gastrointestinal complaints, which can even occur up to 20 years before motor disturbances. The neuropathological hallmark of PD is a misfolding of the protein α -synuclein (α Syn), which then aggregates with other proteins to form intraneuronal Lewy bodies causing neuronal death. The identification of α Syn aggregates in the vagus nerve and in the enteric nervous system (ENS) in early disease stages, as well as the early onset of gastrointestinal symptoms, led to the gut being considered a potential initiation site for PD. Intestinal inflammatory processes and immune responses may initiate aggregation of α Syn in the ENS. From there, pathology can spread via the vagus nerve to the midbrain and other brain areas. Thus, the intestine and in particular the ENS and its neuroimmune interactions are the focus of scientific interest playing a central role in the PD pathogenesis. This study aims to investigate the earliest inflammatory events in the gut and enteric nervous system of a Parkinson's disease mouse model in order to gain more insight into the pathogenesis. Pre-symptomatic PD mice (psPD, one- and two-month-old) were used to identify early pathological changes and in addition, older mice (one-year-old) with proven motor symptoms were examined. We investigated the abundance of immune cell infiltrates throughout the gut and around the ENS, as well as the expression of various inflammatory markers in lymphatic, gastrointestinal and brain compartments.

Results



Conclusion

In summary, our study shows that inflammation in the gut occurs at a very early stage of the disease, while the brain is not yet affected. These data support the idea that PD originates in the gut and that the pathogenesis is triggered by an initial intestinal inflammation. Our findings offer an interesting and novel approach to identify suitable biomarkers in humans. The ENS as one of the earliest affected structures could be an ideal target for early diagnosis of the disease. This could allow earlier identification of at-risk individuals to prevent, delay and treat the disease more effectively.

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