Characterization of the hA53T-Sud mouse model

Histological evaluation of colon tissue

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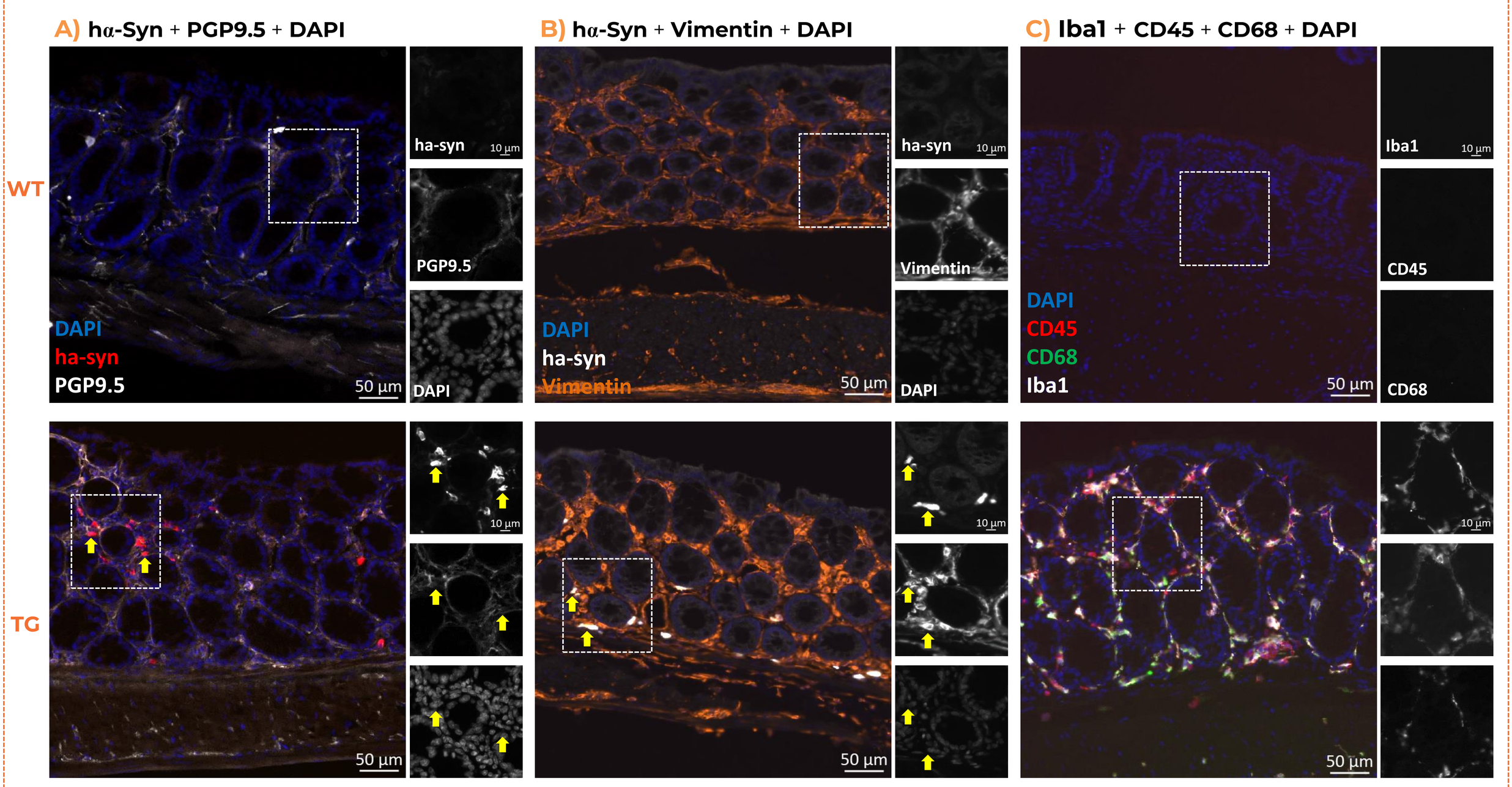
BACKGROUND

Parkinson´s disease (PD) is a multicentric neurodegenerative disorder characterized by the accumulation and aggregation of α-synuclein (α-syn). Point mutations in α-syn have been identified in rare forms of familial PD and are reported to accelerate α-syn oligomerization and aggregation. Recently, it has been recognized that the brain-gut-axis including autonomic nervous system (ANS) and the enteric nervous system (ENS) may be affected in PD. An excessive stimulation of the innate immune system may induce inflammation and contribute to the initiation of α-syn misfolding. Hence, in the current study, we histologically characterized colon samples of human α-syn transgenic mice with A53T mutation (hA53Ttg) developed by Sudhof and colleagues.

RESULTS

Histological analyses in colon tissue of hA53T

hA53Ttg hemizygous mice presented strong signal differences compared to wildtype controls. Qualitative analysis of the swiss roll revealed expression of hα-syn that seems to not be co-localize with PGP9.5-positive nervous tissue but connective tissue. Also, hA53Ttg hemizygous mice showed neuroinflammation as indicated by positive signal for CD45, CD68 and Iba1 which was absent in non-transgenic littermates.



▲Figure 1. Qualitative analyses of immunofluorescent labeling of PGP9.5, ha-Syn, vimentin, CD45, CD68 and Iba1 in the colon of a hA53Ttg hemizygous mouse and a non-transgenic littermate. (**A**) Analysis of hα-Syn co-labeled with PGP9.5 indicating neuronal tissue. (**B**) Labeling of hα-Syn and vimentin visualizing connective tissue. Note that hα-Syn-positive objects are in close proximity to vimentin-positive areas (yellow arrows). (**C**) Inflammatory processes presented by CD45 ,CD68 , and Iba1 staining.

MATERIALS and METHODS

Colon tissue of 5.5-month old male A53Ttg hemizygous mice and age- and sex-matched non-transgenic littermates was histologically evaluated. Briefly, swiss rolls of colon tissues were prepared, subsequently cut at 10 microns on a cryotome and immunofluorescently labeled for human alpha-synuclein (ha-syn) as well as the inflammation markers cluster of differentiation (CD) 45, CD 68 and ionized calcium-binding adapter molecule 1 (Iba1). Also, protein gene product 9.5 (PGP 9.5) and vimentin were labeled to visualize nervous and connective tissue, respectively. Finally, tissue sections were qualitatively evaluated.

SUMMARY and CONCLUSION

This preliminary study shows that hα-syn is not only expressed in peripheral tissue of hA53Ttg hemizygous mice, but also indicates that the hα-syn expression is not co-localized to nervous tissue but is available in close proximity vimentin-positive connective tissue.
Moreover, the presence of different inflammation markers in colon tissue states the bidirectional communication between the central nervous system and the gastrointestinal tract in PD.
In conclusion, this study reveals the importance of colon tissue of this PD mouse model and might subsequently indicate its potential use for efficacy studies targeting the observed pathologies

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