A Manuscript Microscope 'Sentence Audit' of:

Replicative senescence dictates the emergence of disease-associated microglia and contributes to Aβ pathology

What is the Manuscript Microscope Sentence Audit?

The Manuscript Microscope Sentence Audit is a research paper introspection system that parses the text of your manuscript into minimal sentence components for faster, more accurate, enhanced proofreading.

Why use a Sentence Audit to proofread your manuscript?

- Accelerated Proofreading: Examine long technical texts in a fraction of the usual time.
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Manuscript Source: https://www.biorxiv.org/content/10.1101/2021.03.22.436174v1

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Features of the Sentence Audit:

The Sentence Audit combines two complementary proofreading approaches:

1. Each sentence of your text is parsed and displayed in isolation for focused inspection.
2. Each individual sentence is further parsed into Minimal Sentence Components for a deeper review of the clarity, composition and consistency of the language you used.

The Minimal Sentence Components shown are the smallest coherent elements of each sentence of your text as derived from it's conjunctions, prepositions and selected punctuation symbols (i.e. commas, semicolons, round and square brackets).

The combined approaches ensure easier, faster, more effective proofreading.

Comments and Caveats:

• The sentence parsing is achieved using a prototype natural language processing pipeline written in Python and may include occasional errors in sentence segmentation.

• Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").

• Always consult the original research paper as the true reference source for the text.

Contact Information:

To get a Manuscript Microscope Sentence Audit of any other research paper, simply forward any copy of the text to John.James@OxfordResearchServices.com.

All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

Section No.	Headings	Sentences
Section: 1	ABSTRACT	6
Section: 2	INTRODUCTION	21
N/A	--- --- --- --- --- --- ---	0
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The Sentence Audit Of The Research Paper

Title # Replicative senescence dictates the emergence of disease-associated microglia and contributes to Aβ pathology

S1 [001] ABSTRACT

S1 [002] The sustained proliferation of microglia is a key hallmark of Alzheimer's disease (AD), accelerating its progression.

The sustained proliferation ...
... of microglia is a key hallmark ...
... of Alzheimer's disease ...
... (AD), ...
... accelerating its progression.

S1 [003] Here, we sought to understand the long-term impact of the early and prolonged microglial proliferation observed in AD, hypothesising that extensive and repeated cycling would engender a distinct transcriptional and phenotypic trajectory.

Here, ...
... we sought ...
... to understand the long-term impact ...
... of the early ...
... and prolonged microglial proliferation observed ...
... in AD, ...
... hypothesising ...
... that extensive ...
... and repeated cycling would engender a distinct transcriptional ...
... and phenotypic trajectory.

S1 [004] We found that the early and sustained microglial proliferation seen in an AD-like model promotes replicative senescence, characterised by increased βgal activity, a senescence-associated transcriptional signature and telomere shortening, correlating with the appearance of disease-associated microglia (DAM) and senescent microglial profiles in human post-mortem AD cases.

We found ...
... that the early ...
... and sustained microglial proliferation seen ...
... in an AD-like model promotes replicative senescence, ...
... characterised ...
... by increased βgal activity, ...
... a senescence-associated transcriptional signature ...
... and telomere shortening, ...
... correlating ...
... with the appearance ...
... of disease-associated microglia ...
... (DAM) ...
... and senescent microglial profiles ...

... in human post-mortem AD cases.

S1 [005] Prevention of early microglial proliferation hindered the development of senescence and DAM, impairing the accumulation of Aβ and associated neuritic damage.

Prevention ...
... of early microglial proliferation hindered the development ...
... of senescence ...
... and DAM, ...
... impairing the accumulation ...
... of Aβ ...
... and associated neuritic damage.

S1 [006] Overall, our results support that excessive microglial proliferation leads to the generation of senescent DAM, which contribute to early Aβ pathology in AD.

Overall, ...
... our results support ...
... that excessive microglial proliferation leads ...
... to the generation ...
... of senescent DAM, ...
... which contribute ...
... to early Aβ pathology ...
... in AD.

S2 [007] INTRODUCTION

S2 [008] Microglia, the brain's main resident macrophages, originate from yolk-sac progenitors that invade the brain primordium during early embryonic development 1.

Microglia, ...
... the brain's main resident macrophages, ...
... originate ...
... from yolk-sac progenitors ...
... that invade the brain primordium ...
... during early embryonic development 1.

S2 [009] These founders undergo several cycles of proliferation during embryonic and early postnatal development to achieve the numbers and distribution observed in the adult brain 2–4.

These founders undergo several cycles ...
... of proliferation ...
... during embryonic ...
... and early postnatal development ...
... to achieve the numbers ...
... and distribution observed ...
... in the adult brain 2–4.

S2 [010] In the adult steady state, the microglial population undergoes several rounds of renewal, through a slow turnover mechanism of proliferation being temporally and spatially coupled to intrinsic apoptosis 5.

In the adult steady state, ...
... the microglial population undergoes several rounds ...
... of renewal, ...
... through a slow turnover mechanism ...
... of proliferation being temporally ...
... and spatially coupled ...
... to intrinsic apoptosis 5.

S2 [011] The re-activation of microglial proliferative programmes is the earliest response to pre-pathological events in chronic neurodegenerative diseases, with microglial proliferation increased in Alzheimer's disease (AD)6,7.

The re-activation ...
... of microglial proliferative programmes is the earliest response ...
... to pre-pathological events ...
... in chronic neurodegenerative diseases, ...
... with microglial proliferation increased ...
... in Alzheimer's disease ...
... (AD)6,7.

S2 [012] Microglia have a very rapid proliferative response to the incipient accumulation of Aβ 8, during the onset of Tau pathology9, and in several other related models of neurodegeneration 10,11.

Microglia have a very rapid proliferative response ...
... to the incipient accumulation ...
... of Aβ 8, ...
... during the onset ...
... of Tau pathology9, ...
... and in several other related models ...
... of neurodegeneration 10,11.

S2 [013] This rapid response is observed by the fast transition to a proliferative transcriptional state triggered shortly after disease onset in the CK-p25 model of neurodegeneration 12.

This rapid response is observed ...
... by the fast transition ...
... to a proliferative transcriptional state triggered shortly ...
... after disease onset ...
... in the CK-p25 model ...
... of neurodegeneration 12.

S2 [014] We, and others, have demonstrated that the proliferation of microglia is a central contributor to disease progression.

We, ...
... and others, ...
... have demonstrated ...
... that the proliferation ...
... of microglia is a central contributor ...

... to disease progression.

S2 [015] Inhibition of microglial proliferation, using CSF1R inhibitors, ameliorates amyloid 6,13,14 and tau pathology 9, and has emerged as a promising target for clinical investigation.

Inhibition ...
... of microglial proliferation, ...
... using CSF1R inhibitors, ...
... ameliorates amyloid 6,13,14 ...
... and tau pathology 9, ...
... and has emerged ...
... as a promising target ...
... for clinical investigation.

S2 [016] Interestingly, microglial cells entering early proliferation in disease, later undergo phenotypic specification into a disease-associated microglia (DAM)12, by unknown mechanisms.

Interestingly, ...
... microglial cells entering early proliferation ...
... in disease, ...
... later undergo phenotypic specification ...
... into a disease-associated microglia ...
... (DAM)12, ...
... by unknown mechanisms.

S2 [017] DAM represent a key microglial subpopulation present across several brain disorders, and is dependent on TREM2-APOE signalling 15,16.

DAM represent a key microglial subpopulation present ...
... across several brain disorders, ...
... and is dependent ...
... on TREM2-APOE signalling 15,16.

S2 [018] However, the specific mechanisms by which microglial proliferation evokes the DAM phenotype, and how this is related to synaptic and neuronal degeneration is yet to be defined.

However, ...
... the specific mechanisms ...
... by which microglial proliferation evokes the DAM phenotype, ...
... and how this is related ...
... to synaptic ...
... and neuronal degeneration is ...
... yet to be defined.

S2 [019] Integrating our knowledge of microglial population dynamics renders an interesting hypothesis.

Integrating our knowledge ...
... of microglial population dynamics renders an interesting hypothesis.

S2 [020] When combined, the cycling events accumulated in microglia from development to disease would put these cells on a trajectory towards cellular senescence.

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

To get the full audit of this text (or any other research paper),
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John.James@OxfordResearchServices.com
