A Manuscript Microscope 'Sentence Audit' of:

From atoms to cells: bridging the gap between potency, efficacy, and safety of small molecules directed at a membrane protein

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.
- Superior Proofreading: Detect subtle errors that are invisible to traditional methods.
- Focused Proofreading: Inspect each individual sentence component in isolation.
- Reliable Proofreading: Ensure every single word of your manuscript is correct.
- Easier Proofreading: Take the hardship out of crafting academic papers.

Bonus 1: Improved Productivity: Rapidly refine rough drafts to polished papers.
Bonus 2: Improved Authorship: Cultivate a clear, concise, consistent, writing style.
Bonus 3: Improved Reputation: Become known for rigorously precise publications.

Manuscript Source: https://www.biorxiv.org/content/10.1101/2021.03.19.432117v1

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Audit Date: 31/03/21 **Audit Identifier:** 73F4U74Q8WBHQEG **Code Version:** 3.6

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	9
Section: 2	Introduction	18
N/A	--- --- --- --- --- --- ---	0
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The Sentence Audit Of The Research Paper

Title # From atoms to cells: bridging the gap between potency, efficacy, and safety of small molecules directed at a membrane protein

S1 [001] Abstract

S1 [002] Membrane proteins constitute a substantial fraction of the human proteome, thus representing a vast source of therapeutic drug targets.

Membrane proteins constitute a substantial fraction ...
... of the human proteome, ...
... thus representing a vast source ...
... of therapeutic drug targets.

S1 [003] Indeed, newly devised technologies now allow targeting “undruggable” regions of membrane proteins to modulate protein function in the cell.

Indeed, ...
... newly devised technologies now allow targeting “undruggable” ...
... regions ...
... of membrane proteins ...
... to modulate protein function ...
... in the cell.

S1 [004] Despite the advances in technology, the rapid translation of basic science discoveries into potential drug candidates targeting transmembrane protein domains remains challenging.

Despite the advances ...
... in technology, ...
... the rapid translation ...
... of basic science discoveries ...
... into potential drug candidates targeting transmembrane protein domains remains challenging.

S1 [005] We address this issue by harmonizing single molecule-based and ensemble-based atomistic simulations of ligand–membrane interactions with patient-derived induced pluripotent stem cell (iPSC)-based experiments to gain insights into drug delivery, cellular efficacy, and safety of molecules directed at membrane proteins.

We address this issue ...
... by harmonizing single molecule-based ...
... and ensemble-based atomistic simulations ...
... of ligand–membrane interactions ...
... with patient-derived induced pluripotent stem cell ...
... (iPSC)-based experiments ...
... to gain insights ...
... into drug delivery, ...
... cellular efficacy, ...
... and safety ...
... of molecules directed ...

... at membrane proteins.

S1 [006] In this study, we interrogated the pharmacological activation of the cardiac Ca2+ pump (Sarcoplasmic reticulum Ca2+-ATPase, SERCA2a) in human iPSC-derived cardiac cells as a proof-of-concept model.

In this study, ...
... we interrogated the pharmacological activation ...
... of the cardiac Ca2+ pump ...
... (Sarcoplasmic reticulum Ca2+-ATPase, ...
... SERCA2a) ...
... in human iPSC-derived cardiac cells ...
... as a proof-of-concept model.

S1 [007] The combined computational-experimental approach serves as a platform to explain the differences in the cell-based activity of candidates with similar functional profiles, thus streamlining the identification of drug-like candidates that directly target SERCA2a activation in human cardiac cells.

The combined computational-experimental approach serves ...
... as a platform ...
... to explain the differences ...
... in the cell-based activity ...
... of candidates ...
... with similar functional profiles, ...
... thus streamlining the identification ...
... of drug-like candidates ...
... that directly target SERCA2a activation ...
... in human cardiac cells.

S1 [008] Systematic cell-based studies further showed that a direct SERCA2a activator does not induce cardiotoxic pro-arrhythmogenic events in human cardiac cells, demonstrating that pharmacological stimulation of SERCA2a activity is a safe therapeutic approach targeting the heart.

Systematic cell-based studies further showed ...
... that a direct SERCA2a activator does not induce cardiotoxic pro-arrhythmogenic events ...
... in human cardiac cells, ...
... demonstrating ...
... that pharmacological stimulation ...
... of SERCA2a activity is a safe therapeutic approach targeting the heart.

S1 [009] Overall, this novel platform encompasses organ-specific drug potency, efficacy, and safety, and opens new avenues to accelerate the bench-to-patient research aimed at designing effective therapies directed at membrane protein domains.

Overall, ...
... this novel platform encompasses organ-specific drug potency, ...
... efficacy, ...
... and safety, ...
... and opens new avenues ...
... to accelerate the bench-to-patient research aimed ...
... at designing effective therapies directed ...
... at membrane protein domains.

S2 [010] Introduction

S2 [011] Membrane proteins are pivotal players in the cell, playing essential biological roles in a variety of functions vital to the survival of organisms, including transport ions and molecules, signal transduction across cells, serve as scaffolds to help bind the cell to a surface or substrate, and catalyze reactions in biological membranes 1,2.

Membrane proteins are pivotal players ...
... in the cell, ...
... playing essential biological roles ...
... in a variety ...
... of functions vital ...
... to the survival ...
... of organisms, ...
... including transport ions ...
... and molecules, ...
... signal transduction ...
... across cells, ...
... serve ...
... as scaffolds ...
... to help bind the cell ...
... to a surface ...
... or substrate, ...
... and catalyze reactions ...
... in biological membranes 1,2.

S2 [012] Membrane proteins constitute a significant fraction (about 20-30%) of the human proteome 3, and these proteins represent more than 60% of the current drug targets 4; enzymes, transporters, ion channels, and receptors are all common drug targets.

Membrane proteins constitute a significant fraction ...
... (about 20-30%) ...
... of the human proteome 3, ...
... and these proteins represent more than 60% ...
... of the current drug targets 4; ...
... enzymes, ...
... transporters, ...
... ion channels, ...
... and receptors are all common drug targets.

S2 [013] Molecules directed at solvent-accessible pockets have been the primary strategy used to target membrane proteins 5; indeed, virtually all therapeutics targeting membrane proteins bind to solvated regions outside the lipid bilayer 6.

Molecules directed ...
... at solvent-accessible pockets have been the primary strategy used ...
... to target membrane proteins 5; ...
... indeed, ...
... virtually all therapeutics targeting membrane proteins bind ...

... to solvated regions outside the lipid bilayer 6.

S2 [014] Therefore, membrane protein-based drug discovery has rested on the primary assumptions that transmembrane domains are simply passive structural domains required to anchor membrane proteins to the lipid bilayer and that there are no specific sites and interactions within the transmembrane domains that can be effectively used for drug development.

Therefore, ...
... membrane protein-based drug discovery has rested ...
... on the primary assumptions ...
... that transmembrane domains are simply passive structural domains required ...
... to anchor membrane proteins ...
... to the lipid bilayer ...
... and that there are no specific sites ...
... and interactions ...
... within the transmembrane domains ...
... that can be effectively used ...
... for drug development.

S2 [015] Recent advances in crystallography, spectroscopy and, computational biophysics now challenge this conventional view and show that transmembrane domains actively mediate functional protein-protein interactions and exert modulatory roles in membrane proteins 7.

Recent advances ...
... in crystallography, ...
... spectroscopy and, ...
... computational biophysics now challenge this conventional view ...
... and show ...
... that transmembrane domains actively mediate functional protein-protein interactions ...
... and exert modulatory roles ...
... in membrane proteins 7.

S2 [016] The paradigm shift from traditional structural biology to a dynamic view of membrane proteins has enabled the discovery of effector sites located in conventionally undruggable transmembrane regions to modulate protein function 6,8,9.

The paradigm shift ...
... from traditional structural biology ...
... to a dynamic view ...
... of membrane proteins has enabled the discovery ...
... of effector sites located ...
... in conventionally undruggable transmembrane regions ...
... to modulate protein function 6,8,9.

S2 [017] Indeed, a prime example of a druggable transmembrane protein is the cardiac sarcoplasmic reticulum Ca2+-ATPase (SERCA2a).

Indeed, ...
... a prime example ...
... of a druggable transmembrane protein is the cardiac sarcoplasmic reticulum Ca2+-ATPase ...
... (SERCA2a).

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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