A Manuscript Microscope 'Sentence Audit' of:

Combined Inhibition of SHP2 and CXCR1/2 Promotes Anti-Tumor T Cell Response in NSCLC

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.

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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	10
Section: 2	Introduction	15
N/A	--- --- --- --- --- --- ---	0
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The Sentence Audit Of The Research Paper

Title **Combined Inhibition of SHP2 and CXCR1/2 Promotes Anti-Tumor T Cell Response in NSCLC**

S1 [001] Abstract

S1 [002] Clinical trials of SHP2 inhibitors (SHP2i) alone and in various combinations are ongoing for multiple tumors with over-activation of the RAS/ERK pathway.

Clinical trials ...
... of SHP2 inhibitors ...
... (SHP2i) ...
... alone ...
... and in various combinations are ongoing ...
... for multiple tumors ...
... with over-activation ...
... of the RAS/ERK pathway.

S1 [003] SHP2 plays critical roles in normal cell signaling; hence, SHP2is could influence the tumor microenvironment.

SHP2 plays critical roles ...
... in normal cell signaling; ...
... hence, ...
... SHP2is could influence the tumor microenvironment.

S1 [004] We found that SHP2i treatment depleted alveolar and M2-like macrophages and promoted B and T lymphocyte infiltration in Kras- and Egfr-mutant non-small cell lung cancer (NSCLC).

We found ...
... that SHP2i treatment depleted alveolar ...
... and M2-like macrophages ...
... and promoted B ...
... and T lymphocyte infiltration ...
... in Kras- ...
... and Egfr-mutant non-small cell lung cancer ...
... (NSCLC).

S1 [005] However, treatment also increased intratumor gMDSCs via tumor-intrinsic, NF-kB-dependent production of CXCR2 ligands.

However, ...
... treatment also increased intratumor gMDSCs ...
... via tumor-intrinsic, ...
... NF-kB-dependent production ...
... of CXCR2 ligands.

S1 [006] Other RAS/ERK pathway inhibitors also induced CXCR2 ligands and gMDSC influx in mice, and CXCR2 ligands were induced in tumors from patients on KRASG12C-inhibitor trials.

Other RAS/ERK pathway inhibitors also induced CXCR2 ligands ...
... and gMDSC influx ...
... in mice, ...
... and CXCR2 ligands were induced ...
... in tumors ...
... from patients ...
... on KRASG12C-inhibitor trials.

S1 [007] Combined SHP2(SHP099)/CXCR1/2(SX682) inhibition depleted a specific cluster of S100a8/9high gMDSCs, generated Klrg1+ CD8+ effector T cells with a strong cytotoxic phenotype but expressing the checkpoint receptor NKG2A, and enhanced survival in Kras-and Egfr-mutant models.

Combined SHP2(SHP099)/CXCR1/2(SX682) ...
... inhibition depleted a specific cluster ...
... of S100a8/9high gMDSCs, ...
... generated Klrg1+ CD8+ effector T cells ...
... with a strong cytotoxic phenotype ...
... but expressing the checkpoint receptor NKG2A, ...
... and enhanced survival ...
... in Kras-and Egfr-mutant models.

S1 [008] Our results argue for testing RAS/ERK pathway/CXCR1/2/NKG2A inhibitor combinations in NSCLC patients.

Our results argue ...
... for testing RAS/ERK pathway/CXCR1/2/NKG2A inhibitor combinations ...
... in NSCLC patients.

S1 [009] Statement of Significance Our study shows that inhibiting the SHP2/RAS/ERK pathway triggers NF-kB-dependent up-regulation of CXCR2 ligands and recruitment of S100A8high gMDSCs, which suppress T cells in NSCLC.

Statement ...
... of Significance Our study shows ...
... that inhibiting the SHP2/RAS/ERK pathway triggers NF-kB-dependent up-regulation ...
... of CXCR2 ligands ...
... and recruitment ...
... of S100A8high gMDSCs, ...
... which suppress T cells ...
... in NSCLC.

S1 [010] Combining SHP2 and CXCR2 inhibitors blocks this gMDSC immigration, resulting in enhanced Th1 polarization, induction of CD8+ KLRG1+ effector T cells with high cytotoxic activity and improved survival in multiple NSCLC models.

Combining SHP2 ...
... and CXCR2 inhibitors blocks this gMDSC immigration, ...
... resulting ...
... in enhanced Th1 polarization, ...
... induction ...

... of CD8+ KLRG1+ effector T cells ...
... with high cytotoxic activity ...
... and improved survival ...
... in multiple NSCLC models.

S2 [011] Introduction

S2 [012] SHP2, encoded by PTPN11, is required for activation of RAS upstream of the RAS guanine nucleotide exchange proteins SOS1/2.

SHP2, ...
... encoded ...
... by PTPN11, ...
... is required ...
... for activation ...
... of RAS upstream ...
... of the RAS guanine nucleotide exchange proteins SOS1/2.

S2 [013] Consequently, SHP2 inhibitors (SHP2i) can block downstream signaling by overactive receptor tyrosine kinases (RTKs) and so-called “cycling” RAS mutants (e.g., KRASG12C), which retain significant intrinsic RAS-GTPase activity and therefore rely on SOS1/2 activity (1).

Consequently, ...
... SHP2 inhibitors ...
... (SHP2i) ...
... can block downstream signaling ...
... by overactive receptor tyrosine kinases ...
... (RTKs) ...
... and so-called “cycling” ...
... RAS mutants ...
... (e.g., KRASG12C), ...
... which retain significant intrinsic RAS-GTPase activity ...
... and therefore rely ...
... on SOS1/2 activity ...
... (1).

S2 [014] In addition to its potential tumor cell-autonomous actions, SHP2 plays critical roles in normal RTK, cytokine, integrin, and immune checkpoint receptor signaling (2).

In addition ...
... to its potential tumor cell-autonomous actions, ...
... SHP2 plays critical roles ...
... in normal RTK, ...
... cytokine, ...
... integrin, ...
... and immune checkpoint receptor signaling ...
... (2).

S2 [015] “Driver” mutations (e.g., amplified or mutant RTKs, mutant KRAS) significantly—and differentially—also have tumor cell-intrinsic and -extrinsic effects and evoke distinct cellular and humoral responses in different tissues (3).

“Driver” ...
... mutations ...
... (e.g., amplified ...
... or mutant RTKs, ...
... mutant KRAS) ...
... significantly—and differentially—also have tumor cell-intrinsic ...
... and -extrinsic effects ...
... and evoke distinct cellular ...
... and humoral responses ...
... in different tissues ...
... (3).

S2 [016] Consequently, SHP2is have important, potentially driver-specific, effects on the tumor microenvironment (TME), including potentially complex effects on anti-tumor immunity (2,4-6).

Consequently, ...
... SHP2is have important, ...
... potentially driver-specific, ...
... effects ...
... on the tumor microenvironment ...
... (TME), ...
... including potentially complex effects ...
... on anti-tumor immunity ...
... (2,4-6).

S2 [017] Most pre-clinical studies of SHP2is have used cell-derived or patient-derived xenografts (CDXs, PDXs) established in immune-deficient mice or syngeneic tumor models implanted in the sub-cutaneous (SQ) space.

Most pre-clinical studies ...
... of SHP2is have used cell-derived ...
... or patient-derived xenografts ...
... (CDXs, ...
... PDXs) ...
... established ...
... in immune-deficient mice ...
... or syngeneic tumor models implanted ...
... in the sub-cutaneous ...
... (SQ) ...
... space.

S2 [018] The former models lack adaptive immune responses; the latter rarely harbor the mutational spectrum of the cognate human disease and fail to reproduce tissue-specific immunity (e.g., resident macrophages, T cells, etc.).

The former models lack adaptive immune responses; ...
... the latter rarely harbor the mutational spectrum ...
... of the cognate human disease ...
... and fail ...

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

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