Proteogenomic characterization of hepatocellular carcinoma

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Features of the Sentence Audit:

The Sentence Audit combines two complementary proofreading approaches:

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- 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.

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- 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 | SUMMARY | 9 |
| Section: 2 | INTRODUCTION | 14 |
| N/A | | 0 |

Title Proteogenomic characterization of hepatocellular carcinoma

S1 [001] SUMMARY

S1 [002] We performed a proteogenomic analysis of hepatocellular carcinomas (HCCs) across clinical stages and etiologies.

We performed a proteogenomic analysis ...
... of hepatocellular carcinomas ...
... (HCCs) ...
... across clinical stages ...

S1 [003] We identified pathways differentially regulated on the genomic, transcriptomic, proteomic and phosphoproteomic levels.

We identified pathways differentially regulated ...

 \dots on the genomic, \dots

... and etiologies.

- ... transcriptomic, ...
- ... proteomic ...
- ... and phosphoproteomic levels.

S1 [004] These pathways are involved in the organization of cellular components, cell cycle control, signaling pathways, transcriptional and translational control and metabolism.

These pathways are involved ...

- ... in the organization ...
- ... of cellular components, ...
- ... cell cycle control, ...
- ... signaling pathways, ...
- ... transcriptional ...
- ... and translational control ...
- ... and metabolism.
- **S1 [005]** Analyses of CNA-mRNA and mRNA-protein correlations identified candidate driver genes involved in epithelial-to-mesenchymal transition, the Wnt-β-catenin pathway, transcriptional control, cholesterol biosynthesis and sphingolipid metabolism.

Analyses ...
... of CNA-mRNA ...
... and mRNA-protein correlations identified candidate driver genes involved ...
... in epithelial-to-mesenchymal transition, ...
... the Wnt-β-catenin pathway, ...
... transcriptional control, ...
... cholesterol biosynthesis ...

... and sphingolipid metabolism.

S1 [006] The activity of targetable kinases aurora kinase A and CDKs was upregulated.

```
The activity ...
... of targetable kinases aurora kinase A ...
... and CDKs was upregulated.
```

S1 [007] We found that CTNNB1 mutations are associated with altered phosphorylation of proteins involved in actin filament organization, whereas TP53 mutations are associated with elevated CDK1/2/5 activity and altered phosphorylation of proteins involved in lipid and mRNA metabolism.

We found ...
... that CTNNB1 mutations are associated ...
... with altered phosphorylation ...
... of proteins involved ...
... in actin filament organization, ...
... whereas TP53 mutations are associated ...
... with elevated CDK1/2/5 activity ...
... and altered phosphorylation ...
... of proteins involved ...
... in lipid ...
... and mRNA metabolism.

S1 [008] Integrative clustering identified HCC subgroups with distinct regulation of biological processes, metabolic reprogramming and kinase activation.

Integrative clustering identified HCC subgroups ...
... with distinct regulation ...
... of biological processes, ...
... metabolic reprogramming ...
... and kinase activation.

S1 [009] Our analysis provides insights into the molecular processes underlying HCCs.

Our analysis provides insights into the molecular processes underlying HCCs.

S2 [010] INTRODUCTION

S2 [011] Liver cancer was the sixth most commonly diagnosed cancer with 841,000 cases and the fourth leading cause of cancer death with 782,000 deaths globally in 2018 (Arnold et al., 2020).

```
Liver cancer was the sixth most commonly diagnosed cancer ...
... with 841,000 cases ...
... and the fourth leading cause ...
... of cancer death ...
... with 782,000 deaths globally ...
... in 2018 ...
... (Arnold et al., 2020).
```

S2 [012] Hepatocellular carcinoma (HCC) accounts for 75%-85% of all primary liver malignancies and has rising incidence and mortality in western countries (Arnold et al., 2020).

Hepatocellular carcinoma ...
... (HCC) ...
... accounts ...
... for 75%-85% ...
... of all primary liver malignancies ...
... and has rising incidence ...
... and mortality ...
... in western countries ...
... (Arnold et al., 2020).

S2 [013] The past decade has seen numerous studies characterizing the genomic and transcriptomic features and diversity of HCC.

The past decade has seen numerous studies characterizing the genomic and transcriptomic features and diversity of HCC.

S2 [014] Genomic analyses have revealed that TERT promoter, CTNNB1 (encoding β-catenin) and TP53 (encoding p53) are frequently mutated in HCC, while genes involved in other critical processes, such as oxidative stress response, chromatin remodeling and hepatocyte differentiation, are recurrently mutated but in <10% of HCC (Cancer Genome Atlas Research Network, 2017; Fujimoto et al., 2012, 2016).

Genomic analyses have revealed that TERT promoter, CTNNB1 (encoding β-catenin) and TP53 (encoding p53) are frequently mutated in HCC, while genes involved in other critical processes, such as oxidative stress response, chromatin remodeling and hepatocyte differentiation, are recurrently mutated but in <10% of HCC (Cancer Genome Atlas Research Network, 2017; Fujimoto et al., 2012, 2016).

S2 [015] Transcriptomic subtyping has revealed between 2 and 6 HCC subclasses that differ in the expression of genes related to proliferation, stemness, metabolism, hepatocyte differentiation and liver function (Bidkhori et al., 2018; Boyault et al., 2007; Désert et al., 2017; Hoshida et al., 2009; Lee et al., 2004; Makowska et al., 2016).

```
Transcriptomic subtyping has revealed ...
... between 2 ...
... and 6 HCC subclasses ...
```

```
... that differ ...
... in the expression ...
... of genes related ...
... to proliferation, ...
... stemness, ...
... metabolism, ...
... hepatocyte differentiation ...
... and liver function ...
... (Bidkhori et al., 2018; ...
... Boyault et al., 2007; ...
... Désert et al., 2017; ...
... Hoshida et al., 2009; ...
... Lee et al., 2004; ...
... Makowska et al., 2016).
```

S2 [016] More recently, global proteome and phosphoproteome profiling has been made possible by mass spectrometry-based methods.

```
More recently, ...
... global proteome ...
... and phosphoproteome profiling has been made possible ...
... by mass spectrometry-based methods.
```

S2 [017] Two proteogenomic studies of HCCs, both of hepatitis B virus (HBV)-associated HCCs, have been published (Gao et al., 2019; Jiang et al., 2019).

```
Two proteogenomic studies ...
... of HCCs, ...
... both ...
... of hepatitis B virus ...
... (HBV)-associated HCCs, ...
... have been published ...
... (Gao et al., 2019; ...
... Jiang et al., 2019).
```

S2 [018] In the first study, the proteome and phosphoproteome profiling of early-stage HBV-associated HCCs found that a subset of HCCs characterized by disrupted cholesterol homeostasis and overexpression of SOAT1 was associated with poor outcome (Jiang et al., 2019).

```
In the first study, ...
... the proteome ...
... and phosphoproteome profiling ...
... of early-stage HBV-associated HCCs found ...
... that a subset ...
... of HCCs characterized ...
... by disrupted cholesterol homeostasis ...
... and overexpression ...
... of SOAT1 was associated ...
... with poor outcome ...
... (Jiang et al., 2019).
```

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

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