A Manuscript Microscope 'Sentence Audit' of:

The E3 ubiquitin ligase RNF216/TRIAD3 is a central regulator of the hypothala mic-pituitary-gonadal axis

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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.

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Manuscript Source: https://www.biorxiv.org/content/10.1101/2021.03.21.436306v1

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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.

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

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• 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:

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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	14
Section: 2	Introduction	13
N/A	--- --- --- --- --- --- ---	0
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The Sentence Audit Of The Research Paper

Title # The E3 ubiquitin ligase RNF216/TRIAD3 is a central regulator of the hypothalamic-pituitary-gonadal axis

S1 [001] Summary

S1 [002] RNF216/TRIAD3 is an E3 ligase that ubiquitinates substrates in the nervous system.

RNF216/TRIAD3 is an E3 ligase ...

... that ubiquitinates substrates ...

... in the nervous system.

S1 [003] Recessive mutations in RNF216/TRIAD3 cause Gordon Holmes syndrome (GHS), where hypogonadotropic hypogonadism is a core phenotype.

Recessive mutations ...

... in RNF216/TRIAD3 cause Gordon Holmes syndrome ...

... (GHS), ...

... where hypogonadotropic hypogonadism is a core phenotype.

S1 [004] However, the functions of RNF216/TRIAD3 within the neuroendocrine system are not well-understood.

However, ...

... the functions ...

... of RNF216/TRIAD3 ...

... within the neuroendocrine system are not well-understood.

S1 [005] Here, we used the CRISPR-Cas9 system to knock out Rnf216/Triad3 in GT1-7 cells, a GnRH immortalized cell line derived from mouse hypothalamus.

Here, ...

... we used the CRISPR-Cas9 system ...

... to knock out Rnf216/Triad3 ...

... in GT1-7 cells, ...

... a GnRH immortalized cell line derived ...

... from mouse hypothalamus.

S1 [006] Rnf216/Triad3 knockout cells had decreased steady state Gnrh and reduced calcium transient frequency.

Rnf216/Triad3 knockout cells had decreased steady state Gnrh ...

... and reduced calcium transient frequency.

S1 [007] To address functions of RNF216/TRIAD3 in vivo, we generated a Rnf216/Triad3 constitutive knockout (KO) mouse.

To address functions ...

... of RNF216/TRIAD3 in vivo, ...

... we generated a Rnf216/Triad3 constitutive knockout ...

... (KO) ...

... mouse.

S1 [008] KO mice of both sexes showed reductions in GnRH and soma size.

KO mice ...

... of both sexes showed reductions ...

... in GnRH ...

... and soma size.

S1 [009] Furthermore, KO mice exhibited sex-specific phenotypes with males showing gonadal impairment and derangements in gonadotropin release compared to KO females, which only had irregular estrous cyclicity.

Furthermore, ...

... KO mice exhibited sex-specific phenotypes ...

... with males showing gonadal impairment ...

... and derangements ...

... in gonadotropin release compared ...

... to KO females, ...

... which ...

... only had irregular estrous cyclicity.

S1 [010] Our work shows that dysfunction of RNF216/TRIAD3 affects the HPG axis in a sex-dependent manner, implicating sex-specific therapeutic interventions for GHS.

Our work shows ...

... that dysfunction ...

... of RNF216/TRIAD3 affects the HPG axis ...

... in a sex-dependent manner, ...

... implicating sex-specific therapeutic interventions ...

... for GHS.

S1 [011] Highlights

Highlights

S1 [012] Rnf216/Triad3 controls Gnrh and intrinsic hypothalamic cell activity

Rnf216/Triad3 controls Gnrh ...

... and intrinsic hypothalamic cell activity

S1 [013] Rnf216/Triad3 knockout male mice have greater reproductive impairments than females

Rnf216/Triad3 knockout male mice have greater reproductive impairments ...

... than females

S1 [014] Rnf216/Triad3 controls the HPG axis at multiple levels

Rnf216/Triad3 controls the HPG axis ...

... at multiple levels

S2 [015] Introduction

S2 [016] The integrity of the hypothalamic-pituitary-gonadal (HPG) axis is necessary for neuroendocrine control of reproductive behavior that systemically allows for the secretion of hormones via tightly regulated neural networks (Harris, 1955).

The integrity ...
... of the hypothalamic-pituitary-gonadal ...
... (HPG) ...
... axis is necessary ...
... for neuroendocrine control ...
... of reproductive behavior ...
... that systemically allows ...
... for the secretion ...
... of hormones ...
... via tightly regulated neural networks ...
... (Harris, 1955).

S2 [017] Activation of the HPG axis is initiated by a population of kisspeptin neurons in the anteroventral periventricular nucleus (AVPV) and arcuate nucleus (ARN) that mediates the release of kisspeptin, which binds to G-protein coupled receptor 54 (GPR54) receptors located on the surface of gonadotropin-releasing hormone (GnRH) positive neurons in the preoptic area of the hypothalamus (Han et al., 2005; Herbison, 2016).

Activation ...
... of the HPG axis is initiated ...
... by a population ...
... of kisspeptin neurons ...
... in the anteroventral periventricular nucleus ...
... (AVPV) ...
... and arcuate nucleus ...
... (ARN) ...
... that mediates the release ...
... of kisspeptin, ...
... which binds ...
... to G-protein coupled receptor 54 ...
... (GPR54) ...
... receptors located ...
... on the surface ...
... of gonadotropin-releasing hormone ...
... (GnRH) ...
... positive neurons ...
... in the preoptic area ...
... of the hypothalamus ...
... (Han et al., 2005; ...
... Herbison, 2016).

S2 [018] The activation of these receptors facilitates calcium-dependent pathways that are critical for GnRH production and release (Armstrong et al., 2009; Kotani et al., 2001; Moenter et al., 2003).

The activation ...

... of these receptors facilitates calcium-dependent pathways ...
... that are critical ...
... for GnRH production ...
... and release ...
... (Armstrong et al., 2009; ...
... Kotani et al., 2001; ...
... Moenter et al., 2003).

S2 [019] GnRH then stimulates secretory gonadotropes located in the anterior pituitary to release the gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) to the gonads, which regulates the secretion of sex steroids (Plant, 2015).

GnRH then stimulates secretory gonadotropes located ...
... in the anterior pituitary ...
... to release the gonadotropins, ...
... luteinizing hormone ...
... (LH) ...
... and follicle-stimulating hormone ...
... (FSH) ...
... to the gonads, ...
... which regulates the secretion ...
... of sex steroids ...
... (Plant, 2015).

S2 [020] Loss-of-function mutations in HPG axis neuropeptides, gonadotropins, and receptor genes cause hypogonadotropic hypogonadism (HH) (Achrekar et al., 2010; Bramble et al., 2016; Bruysters et al., 2008; de Roux et al., 2003; de Roux et al., 1997; Seminara et al., 2003).

Loss-of-function mutations ...
... in HPG axis neuropeptides, ...
... gonadotropins, ...
... and receptor genes cause hypogonadotropic hypogonadism ...
... (HH) ...
... (Achrekar et al., 2010; ...
... Bramble et al., 2016; ...
... Bruysters et al., 2008; ...
... de Roux et al., 2003; ...
... de Roux et al., 1997; ...
... Seminara et al., 2003).

S2 [021] HH is a condition that is defined by gonadal impairments with decreased levels of sex steroids due to HPG axis defects (de Roux et al., 1997; Kalantaridou and Chrousos, 2002).

HH is a condition ...
... that is defined ...
... by gonadal impairments ...
... with decreased levels ...
... of sex steroids ...
... due to HPG axis defects ...
... (de Roux et al., 1997; ...
... Kalantaridou ...
... and Chrousos, 2002).

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

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