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PEER-REVIEW REPORT

Name of journal: *World Journal of Experimental Medicine*

Manuscript NO: 99239

Title: Melanocortin 4 receptor (M R) mutation in obesity

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05751232
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: India

Manuscript submission date: 2024-07-18
Reviewer chosen by: Jia-Lin Zhang
Reviewer accepted review: 2024-08-02 00:25
Reviewer performed review: 2024-08-14 10:39
Review time: 12 Days and 10 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

These were largely due to the complex intracellular signalling by Melanocortin 4 receptor, and the understanding by the Melanocortin 4 receptor receptor, its expression and downstream signalling enabled the identification of agonists which mimic its physiological actions. This article is very innovative and provides good ideas for the potential pathogenesis and intervention measures of obesity, which is worth learning for researchers. The article has a clear train of thought, abundant research literature included, and can closely analyze and discuss the relationship between MC4R and obesity--The hypothalamic leptin-melanocortin pathway is central to the regulation of appetite and weight, where leptin activates proopiomelanocortin (POMC) neurons, leading to the production of melanocortin peptides; these in turn act on melanocortin 4 Receptor to suppress appetite and increase energy expenditure. Melanocortin 4 receptor mutations are responsible for syndromic and non-syndromic obesity. as well as potential mechanisms of action. It has good logic and clear hierarchy， Setmelanotide, a Melanocortin 4 receptor agonist has been approved for use in the treatment of obesity due to Melanocortin 4 receptor mutations. It did not have adverse effects on heart and

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blood pressure in humans while having a substantial weight loss effect, with a favourable therapeutic indexSetmelanotide, a Melanocortin 4 receptor agonist has been approved for use in the treatment of obesity due to Melanocortin 4 receptor mutations. It did not have adverse effects on heart and blood pressure in humans while having a substantial weight loss effect, with a favourable therapeutic index. The same time ,In addition to MC4R agonists and antagonists, inverse agonists are potential areas for investigation; these include AgRP and its mimics for Melanocortin 4 receptor.