

Scientific Editing report

Paper title: DE2300c5: a potential therapeutic treatment for hyponatremia

SUMMARY

A prolonged decrease in serum sodium concentration can cause chronic hyponatremia, a condition that is frequent among the elderly and that, in spite of a reputation for being asymptomatic, is increasingly recognized as being potentially harmful. This paper proposes the inhibition of 11 β -hydroxysteroid dehydrogenase type 2 (11 β -HSD2) as a novel means of treating chronic hyponatremia. They identify DE2300c5 as a potent and specific inhibitor of 11 β -HSD2, and describe a marked increase in intracellular sodium in renal cortical cells treated with this agent.

These findings appear to be novel, and we expect them to be of interest to researchers working in a range of fields, including endocrinology, pharmacology and, to a lesser extent, receptor biology. Although the article does not include clinical data, the implications might also be of some interest to clinicians involved in geriatric care. However, we feel that the paper would be even more attractive to these audiences with a more careful presentation of the main argument. In particular, more work on guiding the reader through the main argument in the Introduction and Discussion would help editors and readers recognize the study's potential impact.

Essential issues

- The abstract and introduction would both benefit from the inclusion of additional background information on hyponatremia (causes, symptoms, underlying biology, treatment options), to help establish the main question of the article.
- The article contains insufficient reference to the literature – no source is provided for some statements. Furthermore, in the Discussion it is often unclear whether statements relate to the present paper or to previous papers, so it is unnecessarily hard to assess their novelty/impact.
- The methods section does not appear to provide sufficient detail for a competent person to repeat the study and reproduce the results.
- The identity and properties of DE2300c5 are not well described. For example, is it (or is one with similar properties) already used as a treatment for a related disease?
- The role of miR-401 in sodium homeostasis is not clearly established, which makes the significance of these data difficult to evaluate. If they are not directly relevant to the main argument, they should be moved to Supplementary Information (or if truly irrelevant, removed).

Other important issues

- The title mentions the agent, but the *action* of this agent is more important, and is more likely to engage readers. We have suggested an alternative.
- Standard nomenclature for genes and proteins is not adhered to. See our in-text comments.

Possible journals for submission

Given the novel findings and the areas of interest in the paper, we suggest one of the following journals. They have all published papers on hyponatremia in the past.

- *The Journal of Clinical Endocrinology and Metabolism*. An official journal of the Endocrine Society; publishes original research on new developments that enhance understanding, diagnosis and treatment of endocrine and metabolic disorders.
- *Kidney International*. An official journal of the International Society of Nephrology; publishes original research on all aspects of renal research.
- *Hypertension*. An official journal of the American Heart Association that publishes scientific

- investigations in the broad field of blood pressure regulation and pathophysiology, clinical treatment and prevention of hypertension.
- Otherwise, you might like to consider *PLOS ONE*. This journal would have the advantage of being accessible to the entire target audience for the paper, as it is cross-functional and open access. Furthermore, it has a rapid turnaround time from submission to publication.

FEATURES OF THE PAPER

Organisation and flow

In general, a paper communicates the scientific results in three stages: it raises a question, it discusses it, and it makes a point. This applies to the paper as a whole: the central issue is established in the introduction (as well as title and abstract), the discussion is presented in the results and discussion sections, and the point is made in the discussion and conclusion paragraphs. It also applies to individual paragraphs: the sentences and their order should be carefully crafted to establish these three key ingredients and to create a coherent and logical flow. Another crucial means of helping text to flow is to make use of suitable transitions, to link sentences to each other, particularly between paragraphs.

The paper was generally written quite well, but in the most detailed sections, particularly the Methods and Results, the narrative was quite hard to follow. In particular, often ideas were introduced suddenly, with their relevance to the surrounding text unclear. It is important to add a few words to clarify your logical argument/rationale for the sake of the reader. We have suggested several ways of addressing this in the text.

Title and abstract

Most readers only read the title and the abstract of a paper. Therefore, these sections should be concise and enticing, yet specific enough to clearly communicate what the paper is about. The abstract should provide a concise and self-contained description of the background of the field, problem/question to be addressed in the paper, the main result/findings of the paper and the significance thereof, to address the paper's main objectives.

See our comments above on a suggested revision to the title – it is important to emphasise the scientific findings, which will interest a wider range of scientists than the agent. The name of the agent will be meaningless to your target audience until they have read the paper.

The abstract is well structured, but the content in some places was incomplete and/or vague. The start, for example, could be improved by better establishing the need for your study and by describing previous work on HSD inhibitors. Otherwise, although finishing the abstract with a forward-looking sentence is often very effective, in our opinion the original claims were a little too far-reaching, so we have edited them – please check our edits and comments here carefully.

Introduction

The aim of the introductory paragraphs is to clearly and concisely establish the context of the main question that the paper is trying to answer, how the paper relates to previous research in the field, and why it is important – the 'hook' that shows the readers why they should care.

Although the background information present in the Introduction is relevant to your study and to

[Rest of the section-by-section breakdown of the paper deleted. Typical report length is 4-7 pages.]