

The present manuscript deserves to be published. It is conclusive and provides interesting insights into the restorative processes after TBI. I only recommend that the authors deal with the above minor observations which will strengthen the manuscript.

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**RAIN-2012-00410**

**Complement proteins C1q and C3a promote migration and astroglial differentiation of human neural stem cells**

**Hooshmand, Mitra; nguyen, hal; Hong, Samuel; Uchida, Nobuko; Tamaki, Stan; Cummings, Brian; Anderson, Aileen**

Dear Dr. Ibarra,

I would like to invite you to act as a referee on the above Original Article recently submitted to Brain.

The abstract is provided below for your information. If you are willing to review the manuscript and can do so within 2 weeks, please click the 'AGREED' link below. You will then be sent a message enabling direct access to the paper - without the need for a User ID or password.

If you cannot meet that timeline, please contact the editorial office and we will make arrangements to extend the review process.

It may be helpful for you to know that our current overall acceptance rate is less than 20% of all manuscripts submitted. Therefore, although many are rejected without seeking advice from independent experts, only a minority of those sent out for review can be accepted.

Apart from scientific authority, we are keen to ensure that original papers published in Brain represent more than just an increment in knowledge and are likely to be definitive articles of lasting value in their field. We pay attention to the style of writing and presentation of text and figures as well as the scientific details in order to make published papers of fully accessible to our readers. We do not accept papers which are so laden with abbreviations and jargon as to be difficult to understand for the general reader.

It is particularly helpful to receive comments addressed only to the Editors that are not passed on to authors since these often place the formal review in perspective. And we would be grateful if you were to score the paper in the categories listed in order to guide us in assessing its overall priority for inclusion in the journal.

If you are unable to act as a referee please click the 'DECLINE' link and we will not re-contact you in connection with this manuscript. However, there is an option to suggest alternative referees, and we would be grateful for the names of experts (and their email contact addresses if known to you) who would be well placed to participate in the review process.

Yours sincerely,

Angela Vincent

Associate Editor

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## REVISIÓN

The manuscript entitled “Complement proteins C1q and C3a promote migration and astroglial differentiation of human neural stem cells” by Hooshmand *et al.* attempted to demonstrate that hCNS-SCns transplantation after spinal cord injury (SCI) results in predominant migration toward the injury epicenter and astrocytic differentiation. As well, they show that complement proteins C1q and C3a mediate migration and astroglial differentiation of hCNS-SCns. Authors first showed that even though hCNS-SCns survive, engraft and migrate toward the injury epicenter they do not promote or impair locomotor recovery after acute SCI. Furthermore, they demonstrated that hCNS-SCns differentiate into astrocytes. In subsequent *in vitro* studies, Hooshmand and co-workers showed that conditioned media collected from neutrophils, but not from macrophages, promotes astrocytic differentiation and migration of hCNS-SCns. Further studies, showed that complement proteins C1q and C3a promoted astrocytic differentiation via a co-dependent mechanism and stimulated migration independently of one another. The following experiments demonstrated that the blockade of C1q and /or C3a promotes migration of hCNS-SCns away from the injury epicenter and inhibits their differentiation into astrocytes. In fact, blockade of these proteins shifts hCNS-SCns towards a neuronal lineage, restoring the beneficial effects of hCNS-SCns transplantation on motor recovery after an acute SCI.

The manuscript is well written and designed in a very detailed and logical manner. I consider that after some minor corrections the manuscript could be published.

Minor issues:

1. hCNS-SCns, NSC or hNSCs abbreviations are used interchangeably throughout the manuscript. Please use only hCNS-SCns when appropriate.
2. Section: Material and Methods, page 4 lines 15-17: In studies utilizing Abs directed against....; provide references.
3. Section: Material and Methods, page 5 lines 16-19: Immunostaining was performed as previously described....; provide reference.
4. Section: Material and Methods, page 6, lines 1-4: Uniform random sampling of the tissue...; although the authors provide additional data in the complementary information section, a reference should be cited within the main text.
5. Section: Material and methods, statistics, page 7 lines 7-8: BMS results were analyzed using repeated.....; provide the post-hoc test.
6. Section: Discussion, thinking about the possible therapeutic utility of this strategy (inhibition of C1q and C3a), authors should discuss more benefits and disadvantages of avoiding hCNS-SCns differentiation towards astrocytes (i.e. scar formation, etc.).
7. Section: Figure legend 2, hCNS-SCns migrating away form....change form by from