



SDI Review Form 1.6

Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	2014_IJBcRR_14873
Title of the Manuscript:	The E1 Copper Binding Domain of Full-length Amyloid Precursor Protein Promotes Epithelial to Mesenchymal Transition in DU145 Cells in an Isoform-specific Manner
Type of the Article	Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	- lines 108-117: For the sake of clarity, the authors should provide information regarding the APP isoform specificity/epitopes/domains targeted by the antibodies. For a reader not aquanted with this subject it is difficult to follow the probing of the APP protein isoforms / cleaving variants since the antibodies are not properly introduced. Figure 2B: Inadequate resolution of the Vimentine immunoblotting image.	We have inserted text between lines 123 and 133 in order to clarify this point. We have inserted a better resolution blot.
Minor REVISION comments	-lines 130-131: Using t-test statistics on only 3 biological repeats of each experimental condition is not recommended, as homoscedasticity of the data is hard to validate. Normal distribution can not be validated of so few data points. A non-parametric method would be recommended. -Figure 1A: I would suggest some discussion regarding the induced APP₇₇₀ and APP₇₇₁ upregulation by the APP₆₉₅ exogenous over-expression .	This is a standard and adequate statistical test for data of this nature used as a matter of routine in the vast majority of papers published each year in the field. Although this is not a central result we have commented on this already in the text beginning on line 166: 'Note that slight increases in the larger APP isoform products were also observed in APP₆₉₅-transfected cells; we believe that this is due to the weak ability of transfected APP₆₉₅ to self-regulate the expression of the endogenous protein as observed previously [15].'



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<u>Optional/General</u> comments	The study address very interesting phenomenon of amyloid precursor protein (APP) and its maturation forms involvement in prostate cancer progression. Notably, the pathogenic pathway involved in Alzheimer's disease was found involved in prostate cancer and targeted in this study. The paper is well structured and well written, representing a further continuation of previous study of the role of APP in cancer progression utilizing a DU145 cell line model. The authors have investigated the predominant isoform of APP in DU145 cells both on mRNA and protein level and selected the lest abundant as target for exogenous over-expression. Authors show APP₆₉₅ isoform as responsible for EMT demonstrating altered E-cadherin and Vimentine expression as well as morphological criteria as dendricity. APP₆₉₅ was found the one producing the cancer progression associated sAPPβ. They show mechanistically, which domain of the APP is responsible for this <i>in vitro</i> phenomenon using several domain mutagenesis. Significant contribution is the finding that Thyrosin 687 is responsible for the EMT effects, related to APP internalization. The produced beta secretase cleaved was found rather as a bypass product related to, but not required for the EMT.	Thank you for your comments.
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