Reviewer’s report

Title: Peripheral PDLIM5 expression in bipolar disorder and the effect of olanzapine administration

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Reviewer: Alessio Squassina

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In this paper the authors explored the correlation between PDLIM5 expression levels and response to olanzapine in whole blood cells derived from bipolar disorder (BD) patients before and after 4 and 8 weeks of treatment, and from a sample of healthy controls. PDLIM5 did not correlate with response, measured with the Young Mania Rating Scale (YMRS). However, gene expression was different when comparing naive BD patients with healthy controls. The authors also investigated the correlation between SNPs in the promoter region of PDLIM5 and mRNA levels, reporting negative findings.

As a whole, the manuscript is well written and the data clearly presented.

Data supporting the possible involvement of PDLIM5 in the mechanism of action of olanzapine are poor and, as such, the study is based on weak assumptions. However, considering the previous findings showing possible involvement of this gene in the pathophysiology of BD and in the mechanism of action of the most widely used mood stabilizer in the treatment of BD, lithium, the question raised by the authors might be worth of investigation.

Major Compulsory Revisions

1) As stated by the authors, the greatest limitation of this work is the sample size, especially in light of the different ethnic origin of the subjects included. It is very well known that the role of genetic variation in response to medications can hugely vary according to ethnicity. The authors adjusted the analysis of correlation between RQ levels and YMRS for ethnicity, but the small sample size does not allow to confidently interpreting the findings. For instance, the proportion of Malays, Chinese and Indians between Cases and Controls might be significantly different or the difference might disappear if tested in a larger dataset. The authors should consider ethnicity also in the comparison between cases and controls and discuss the data accordingly.

2) The authors should cite two other papers (Squassina et al 2008, Psychiatr Genet. 18(3):128-32.; Squassina et al 2008, Pharmacol Res. 57(5):369-73) and discuss findings in light of the negative results from these articles.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests