Reviewer’s report

Title: A systems biology approach to understand the pathophysiological mechanisms of cardiac pathological hypertrophy associated with rosiglitazone

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Reviewer: Nanping Wang

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In this study, Verschuren and colleagues analyzed the RNA profiles of heart tissue of rosiglitazone or pioglitazone treated pre-diabetic mice. 16 samples in total (n=5-6 hearts per experimental group) were analyzed. They uncovered that a shift in energy metabolism by rosiglitazone may impact cardiac pathological hypertrophy.

- Major Compulsory Revisions
Since this is a systems biology approach, the part of genome-wide transcriptome analysis is a little simple. Please provide further information such as clustering analysis results and table of differentially expressed genes in the text or in supplemental data.

In microarray data analysis (Fig. 4C, 4D), the author states that down regulation of PPAR# and PGC-1# target genes (such as CPT1, ACADVL, FATP1, UCP3) by rosiglitazone but not pioglitazone may contribute to cardiac pathological hypertrophy. But they didn’t validate expression of these genes by qPCR or other approaches.

- Minor Essential Revisions
In Study design and diets: What is the dose of rosiglitazone and pioglitazone given by mg/kg/day?

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 have nothing to disclose.