Reviewer’s report

Title: Early over expression of messenger RNA for multiple genes, including insulin, in the Pancreatic Lymph Nodes of NOD mice is associated with Islet Autoimmunity

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Reviewer: Taku Okazaki

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Discretionary Revisions

Based on their former finding that the presence of insulin autoantibodies (E-IAA) predicts early diabetes onset in NOD mice, Regnault et al. analyzed gene expression profiles in pancreatic lymph nodes (PLNs) of E-IAA(+) and E-IAA(-) 5 weeks old NOD mice to identify genes implicated in the early steps of the autoimmune process. They found gene expression profiles in PLNs are quite different between E-IAA(+) and E-IAA(-) mice. They also found genes coding for insulin and for proteins known to be implicated in tissue remodeling and Th1 immunity are highly expressed in PLNs from E-IAA(+) mice. Most of the experiments are properly designed and current findings provide useful information for the understanding of the initial steps of type I diabetes. This reviewer has only minor concerns.

(1) One of the future prospectives of the current study is to identify non-invasive marker that can predict the onset of diabetes more precisely or earlier than E-IAA. Authors are recommended to list genes that encode soluble proteins and discuss their possible predictive value.

(2) One of the six E-IAA(-) samples showed gene expression profile similar to E-IAA(+) samples. Although this reviewer agrees with authors’ explanation, annotations in Fig.2 and 6 are misleading. Authors are recommended to label each lane as either “E-IAA neg” or “E-IAA pos” based on the presence of IAA but not the results of clustering.

(3) The number of genes coding for extracellular proteins among modulated genes are different between text (p.13, 62 genes) and Figure 4a (60 genes). Authors are asked to explain this discrepancy.

(4) The magnifications of Fig.3F and G are different. In addition, the insulin(+) area in PLN (paracortex~medulla) is out of frame in inguinal LN. Authors are recommended to show similar area with the same magnification.

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.