

Response to Reviewers' Comments

Reviewer 1

1. The Reviewer states that “since Sp TF is a transcription factor and NR4A1 is a receptor their properties are considered to be different and it is unlikely that they have a common pathway as shown in Fig. 1”. Figure 1 has been completely revised to emphasize the separate modes of action of Sp TFs and NR4A1. However, both Sp TF and NR4A1 interact with individually and also with multiple proteins and there is strong evidence from ChIP, transactivation, promoter analysis and inhibitory studies that NR4A1/Sp complexes are formed. Moreover, there is extensive evidence that other nuclear receptors also interact with Sp TFs.

2. The Reviewer states that, “In Fig. 2, it is unclear which part of the graph the “blue” written in the text indicates. The genetic changes in the combination of Sp1,3,4 are shown, but there is no graph for each (the text states that there are individual results). What do you mean by different genes? The Figure Legend is also insufficiently explained and the contents cannot be fully understood. There are some parts where causal IPA is mistakenly written as casual IPA”. We have now clarified these issues in the revised manuscript. Figure 2 is a reanalysis of genomic studies on Sp1, Sp3 and Sp4 regulated genes in Panc1 cells and their functions. The results show that each Sp TF regulates unique genes but also many genes in common. This is now more extensively explained in the text and Figure caption.

Reviewer 2

Thank you for your positive comments.

Reviewer 3

As suggested by the Reviewer, we revised Figure 1 and have attached the “authors understanding of the role of transcription factor Sp and NR4A1” to the Conclusion section.