Review of: "Yorkie-Cactus (IκBα)-JNK axis promotes tumor growth and progression in Drosophila"

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In this paper, Snigdha *et al.* elucidated a previous unknown Yorkie-Cactus-JNK-MMP1 signaling, which links the Hippo, TLR, and JNK pathways, and plays a vital role during tumor growth and progression. Further genetic tests indicated that Cactus activates JNK and upregulates MMP1 via a non-canonical (TNFR-independent) mechanism. Overall, this is a coherent fly genetics paper. All of the data are substantial and presented clearly and logically. In my opinion, this paper's discovery will be appreciated in the Hippo, TLR, and JNK fields, although I am unsure of the relevance of the proposed mechanism beyond *Drosophila*. Beyond these, some unclear but interesting points listed below are worth to be further investigated in future studies.

1. Although Cactus is strongly induced and is required for JNK activation and MMP1 upregulation in the $Yki^{3SA};Scrib^{RNAi}$ and $Ras^{V12};scrib^{RNAi}$ tumors, it is still unknown if Cactus is sufficient to trigger the JNK activation and MMP1 upregulation in the wild-type background. Evaluating pJNK and MMP1 in *Cactus* overexpression clones would be a straightforward assay.
2. In figures 2J-J', 2P-P', 3C-C', and 3I-I', the apparent heterogeneity of pJNK and MMP1 levels between tumor cells inside the same clone was not acknowledged in the paper. This would be another interesting point for future study.