Reviewer’s report

Title: Expression of TLR3 and its correlation with apoptosis, proliferation, angiogenesis and prognostic in HCC

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Reviewer: Jinsheng Zhang

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Toll-like receptors (TLRs) recognize pathogen-associated molecular patterns (PAMPS) leading to the activation of the innate immune response and subsequently to the shaping of the adaptive immune response. TLR3 signaling is induced by double-stranded (ds)RNA, a molecular signature of viruses, and is mediated by the TRIF (TIR domain-containing adaptor-inducing IFNbeta) adaptor molecule. Thus, TLR3 plays an important role in the host response to viral infections. TLR3 was also documented involving in pathogenesis of a variety of tumors, such as cancers of lung, breast, stomach, colorectum, etc.

In about 20 published papers, TLR3 has been studied in hepatocellular carcinoma both in patients’ samples and in animal models. Some of their data indicated that TLR3 expression in HCC plays an important role with regard to cell survival and proapoptotic activity, as well as that TLR3 mediates both anti-angiogenic and anti-tumor responses.

In the manuscript, authors studied the expression of TLR3 in 85 patients’ HCC tissues by immunohistochemical staining and went in pursuit of its correlations with the cell proliferation, apoptosis and angiogenesis in the tumor tissue. The clinical data were reviewed and its correlation with the expression of TLR3 was investigated. The research expands acknowledgement of role TLR3 may play in hepatocarcinogenesis and provide a clue for further investigation of TLR3 in liver cancers.

Major comments:

1. All the data authors presented are subjective and descriptive, therefore, it is necessary to add some material data, such as computer-aided image assessment for semi-quantitative assay of positive staining area in the slides.

2. Most of the coefficients of correlation are less than ±0.5, indicating that expression of TLR3 has weak correlations with the parameters of cellular apoptosis and proliferation, etc. These may be improved by dual immunohistochemical stainings, such as TLR3 + TUNEL, TLR3+Ki-67 and TLR3+NFkB, etc.

3. In HCC cells, It was found that cell surface stimulation of TLR3 with Poly I:C did not affect cell viability, in contrast, cytoplasmic stimulation with transfected Poly I:C significantly induced apoptosis accompanied by the down-regulation of anti-apoptotic protein. The question is that did authors find some differences in correlations of TLR3 with apoptosis between membrane and cytoplasm staining.
Minor comment:
In all microscopic figures, authors only provided high magnificent (X400) views, in order to understand more global views of distribution of positive stainings, less magnificent view pictures should be showed.