Reviewer's report

Title: FOXA1 promotes tumor cell proliferation through AR involving the Notch pathway in endometrial cancer

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Reviewer: Antimo Migliaccio

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The paper by Qiu et al shows that the expression of FOXA1 and androgen receptor (AR) in endometrial carcinomas (EC) is significantly higher than in normal tissue or atypical hyperplasia. FOXA1 expression is significantly correlated with AR expression in pathological tissue specimens and high levels of both FOXA1 and AR positively correlate with pathological grade in EC. Furthermore, expression of downstream AR targets such as XBP1, MYC, ZBTB16 and UHRF1 is promoted by FOXA1 up regulation. The data reported also indicate that over expression of Notch1 and Hes1 induced by FOXA1 can be reversed by AR depletion, which also attenuates FOXA1 stimulated cell proliferation. This apparently is mediated by an interaction between FOXA1 and AR. The AR seems involved only in proliferative effects of FOXA1 whereas seems not involved in FOXA1 induced cell migration. On this basis the Authors suggest that FOXA1 and AR could represent potential target in EC therapy.

This paper is rather interesting but as it stands it is predominantly descriptive. The Authors suggest that FOXA1/AR interaction could play a main role in the cooperative effect of these proteins but they do not provide molecular insight into the mechanism of this cooperation. If the Authors hypothesize that it occurs at transcriptional level a ChIP assay on the promoters of AR target genes could provide useful informations.

The role of FOXA1 is rather debated as this protein has been reported to act in many cases as a tumor suppressor. The Authors should better discuss this issue. Similarly the effect of AR and FOXA1 alone or in combination on Notch pathway should be investigated in deeper detail.

Level of interest: An article of importance in its field

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