

*Response to the reviewer's comments*

Reviewer 1: The title of the review may need some revision because it should state clearly the core of the review which is the biologic role of CA125 in ovarian cancer pathobiology.

Response: As requested by the reviewer, we have change the title for the following: The role of MUC16 mucin (CA125) in the pathogenesis of ovarian cancer: much more than a tumor biomarker.

Reviewer 1: The factor(s) that control the proteolytic cleavage of MUC16 extracellular domain to appear as CA125 should be focused on and discussed if any.

Response: As requested by the reviewer, we have extended our discussion regarding this important topic. Our comprehension of the mechanisms involved in the release of MUC16 ectodomain and the factors that controlled this release is highly incomplete. This is reflected in the text. See MUC16 structure section, page 8 and 9.

Reviewer 1: The interchangeability of MUC16 and CA125 as nomenclature and biochemical entities should be made clear in text.

Response: As requested by the reviewer, we have clearly defined the terms MUC16 and CA125 in the text. See Introduction section, first paragraph, lines 6-8.