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Response to Esgueva *et al*

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In Reply: It is with great interest and appreciation that we read the comments by Esgueva *et al*[1] in relation to our paper titled '*TMPRSS2-ERG* gene fusions are infrequent in prostatic ductal adenocarcinomas' published in the March 2009 issue of the journal of *Modern Pathology*.[2]

We agree with the authors' statement that studies assessing the relationship between *ERG* fusion and clinical outcome have so far yielded conflicting results.[3–9] The main objective of our study was to evaluate the previously not-assessed incidence of *TMPRSS2-ERG* fusion in a well-characterized cohort of prostatic ductal carcinoma. Considering the well-documented aggressive behavior of prostatic ductal carcinoma, our finding of a relatively low incidence of *TMPRSS2-ERG* fusion in such tumors could be seen as indirect evidence arguing for its lack of association with aggressive outcome.

A comprehensive review of the previous literature on the relationship of fusion with outcome was neither attempted nor implied in our discussion, given the above well-defined focus of our study. In this regard, the omission of the study by Attard *et al*[4] was definitely unintentional. By citing examples from two groups of studies showing conflicting evidence on the association of *TMPRSS2-ERG* fusion with aggressive outcome, we simply attempted to illustrate the controversy rather than to provide a comprehensive categorization of the end points and cohort details of all previous studies.

The authors' speculation regarding the possibility of symptomatic presentation as a potential common denominator between our cohort and the expectant management cohort of patients diagnosed on TURP in the report by Demichelis *et al*[3] is intriguing but unlikely to be relevant in our cohort. As we detail in the 'Materials and methods' section of our paper, our cohort was diagnosed through PSA screening and/or through digital rectal examination. Furthermore, despite earlier reports, it is now well recognized that only a minority of prostatic ductal adenocarcinomas are completely limited to the central location, and similar to acinar prostatic carcinomas they are more likely to be discovered during PSA screening, as certainly was the case in our cohort.[10]

Finally, the break-apart FISH strategy that we adopted in our study is identical to the one used by two of the authors on the above commentary,

in several of their previous *TMPRSS2-ERG* fusion reports.[11,12] Therefore, it is somewhat surprising that the authors have chosen to raise doubts about the validity of this methodology as they have previously documented its utility using quantitative PCR analysis.[12]

We thank the letter authors for their comments and for the opportunity to clarify some of the issues they raised.

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