Author's response to reviews

Title: Fas Activated Serine-Threonine Kinase Domains 2 (FASTKD2) mediates apoptosis of breast and prostate cancer cells through its novel FAST2 domain

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Cover Letter and Response to the Reviewer’s Comments

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We thank the Reviewers for their constructive comments and are delighted that they feel that the manuscript is an article of importance in its field. As per the Editor’s comments we have submitted the revised manuscript with line numbers and Figure 4C is now included as part of Figure 4. As per the BMC Cancer instructions the figures are now submitted as PNG files.

Reviewer 1

1. The Reviewer asks that Figures 1,2,3,5 and 6 have size markers. We are not sure why this is necessary since the DAPI stained nuclei serve to provide an assessment of the size of the cell.

2. We have gone back to the original image and redid the figure. The Zeiss fluorescent microscope we have cannot precisely image mitochondria. However, in the AIF-GFP +DD1(S28A) panel in the new figure, the green fluorescence is now more delineated in perinuclear organelles and not just as a uniform extranuclear green fluorescence. Importantly, AIF-GFP has been established to localize to mitochondria and then shift to the nucleus as a result of increased mitochondrial permeability in apoptosis (Reference 16).

3. We have previously documented that breast cancer cells undergoing NRIF3/DD1-mediated apoptosis (which we have shown is mediated by FASTKD2) exhibit a bystander effect (Reference 3). NRIF3/DD1 expression leads to apoptosis of breast cancer cells but not HeLa cells. However, if the medium of breast cancer cells transfected to express NRIF3/DD1 is transferred to HeLa cells 5 hours after transfection, the HeLa cells undergo apoptosis. This bystander effect can be blocked by inhibiting ROS production in the breast cancer cells (Reference 3).

4. P values – We have included the p values for Fig. 4B and 4C (lines 294, 295, 313 and 314).

5. We have corrected typos and grammar.

Reviewer 2

1. We have corrected the double sentence in the INTRODUCTION and now spelled caspase-2 correctly in the RESULTS and have used ensure instead of insure in
manuscript. We thank the Reviewer for pointing out these problems. We read over the manuscript many times and missed these errors.

In summary we thank the reviewers for their suggestions and comments and hope the manuscript is now acceptable for publication in BMC Cancer.