Author's response to reviews

Title: TrkA is amplified in malignant melanoma patients and induces an anti-proliferative response in cell lines

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Dear Professor Solera,

Please find attached the research article entitled “TrkA is amplified in malignant melanoma patients and induces an anti-proliferative response in cell lines”.

There is a growing body of literature indicating the amplification of genomic region 1q as a hotspot of tumorigenic rearrangements and amplification. In this study we used a dataset of genomic alterations in primary cutaneous melanoma we developed to identify genomic amplification of TrkA, located in the 1q23.1 region, in association with primary tumor progression and outcome of patients. We also demonstrated with several cell-based experiments that induction of the NGF-TrkA signaling may mediate a phenotype that is typical of oncogene-induced proliferation arrest, through MAPK activation and via the up-regulation of p21, potentially counteracting the AKT pro-proliferative function.

Our findings reinforce the importance of TrkA in melanoma biology, and suggest the existence of a dual mechanism involving the NGF-TrkA signaling in cancer progression: a pro-oncogenic action, observed in patients, that may be balanced by an anti-proliferative response, revealed by cellular experiments, with consequent clinical implications.

We think that the significance of questions addressed and the novel insights we found in the NGF-TrkA pathway could be of particular interest to the readers of *BMC Cancer*.

All the authors contributed to the work described in this paper and all take responsibility for it. None of the data presented in this paper have been published elsewhere.

Thank you for considering our work for publication in *BMC Cancer*. We look forward to hearing from you at your best convenience.

Yours faithfully,

Luigi Pasini

Alessandro Quattrone