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Comment on 'Strong reduction of AGO2 expression in melanoma and cellular consequences'

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Sir,

We would like to congratulate Völler *et al* (2013) on their recent study showing an unchanged mRNA AGO2 expression in melanoma and a strong reduction of AGO2 expression on protein level. This goes along with the findings in our study on the miRNA processing machinery performed in melanoma, which likewise has previously shown an unchanged mRNA AGO2 expression level in melanoma (Sand *et al*, 2012c). Interestingly, in contrast to melanoma skin cancer, mRNA AGO2 expression levels in epithelial skin cancer (both cutaneous squamous cell and basal cell carcinoma) were significantly higher ($P<0.05$) compared with healthy controls (Sand *et al*, 2010, 2012a, b). Although we do agree with the authors that a deregulation of microRNA (miRNA) was observed in several types of cancer and particularly in skin cancer, with reference to our previous studies we do not agree that changes in the miRNA processing enzymes have not been analysed until today as stated in their abstract (Sand *et al*, 2009, 2011, 2012d, e, 2013; 2014; Sand and Skrygan, 2014).

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Reply to comment on: strong reduction of AGO2 expression in melanoma and cellular consequences

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Sir,

We are grateful for the feedback regarding our article 'Strong reduction of AGO2 expression in melanoma and cellular consequences' (Völler *et al*, 2013b). In this study, we discovered a melanoma-specific modulation of AGO2, a member of the miRNA-processing cascade. Moreover, we demonstrated that AGO2 reduction is a direct trigger for the deregulated miRNA pattern in melanoma.

The reduced AGO2 protein amount was observed in melanoma cell lines as well as tissue samples of primary tumours and metastasis. Interestingly, AGO2 reduction was not detectable at mRNA expression level, which indicates a further processing of the AGO2 mRNA transcript in melanoma.

Previous studies analysing the enzymes of the miRNA-processing cascade in cancer were either focused on the mRNA level (e.g., Sand *et al*, 2012; Jafari *et al*, 2013) or did not connect the deregulation with a disordered miRNA pattern (e.g., Ma *et al*, 2011; Grund *et al*, 2012; Jafarnejad *et al*, 2013; Völler *et al*, 2013a). Therefore, we stated that 'Deregulation of miRNA expression was observed in several types of cancer, but changes in the miRNA-processing enzymes have not been analyzed until today'. However, this statement would have to be focused on the enzyme AGO2 and analysis on protein level in melanoma. We apologize that the current statement is too general as the authors of the previous comment correctly stated.

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