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Letter

THE IMPORTANCE OF SPECIFIC ANTIBODIES IN VIM-3 RESEARCH: ADDRESSING A KEY METHODOLOGICAL FLAW

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We read with great interest the recent publication by Teoman et al. 2025[1], which examines the role of vimentin 3 as a new potential biomarker in oral squamous cell carcinomas. While the study contributes valuable insights, we must highlight a critical methodological flaw that undermines the validity of its conclusions.

The authors utilized the VIM-3B4 antibody to detect Vim3 expression in their study. However, as clearly demonstrated by von Brandenstein et al.[2,3], this antibody binds exclusively to the rod domain of vimentin, a region that is present in both the full-length vimentin and the truncated Vim3 isoform. Consequently, the VIM-3B4 antibody is incapable of distinguishing between these two forms. This limitation renders the authors' claim, that their detected signals are specific to Vim3, scientifically unsupported.

The authors conclude that the detected signals are specific to Vim3. However, given that full-length vimentin is widely expressed in various cell types and tissues, it is highly plausible that the observed signals originate from full-length vimentin rather than the truncated Vim3 isoform[4]. Without the ability to differentiate between these isoforms, the conclusions drawn by the authors are not supported by the data presented. The truncated Vim3 variant is characterized by a unique C-terminal end that is absent in full-length vimentin. A specific antibody targeting this C-terminal region, developed and characterized by the von Brandenstein research group at the University Hospital Cologne, is the only tool currently capable of distinguishing between Vim3 and full-length vimentin (EP2784510A1). Without the use of this specific antibody the specific detection of Vim3 is not achievable.

Furthermore, the findings of von Brandenstein et al.[2,3] clearly demonstrate that Vim3 is a tumor associated isoform that is minimally expressed, if at all, in healthy tissues. The use of the VIM-3B4 antibody without additional validation leads to an overlap with full-length vimentin, thereby compromising the accuracy of the results. This methodological flaw calls into question the authors' assertion that Vim3 was specifically detected in their study.

Given these considerations, we must conclude that the data provided in the publication are insufficient to specifically demonstrate the expression of Vim3

To accurately analyze Vim3 expression in future studies, we recommend the use of the specific antibody against the C-terminal end of Vim3, which is only available through the von Brandenstein research group. Further validation of results through methods such as Western blotting with specific antibodies or mass spectrometry would also be essential to definitively confirm the identity of the detected isoform.

These observations align with well-established evidence that the VIM-3B4 antibody lacks the specificity required to distinguish between the truncated Vim3 isoform and full-length vimentin, as demonstrated by von Brandenstein et al.[2]. In this context, it has been shown that accurate detection of Vim3 necessitates the use of

antibodies targeting its unique C-terminal end, which is absent in full-length vimentin. Without this specificity, the conclusions regarding Vim3 expression are not substantiated.

In conclusion, we agree with the authors that the potential role of Vim3 in tumor biology and associated pathways warrants further investigation. However, based on the current methodological limitations, we emphasize that the use of the VIM-3B4 antibody alone is insufficient to specifically detect Vim3. Therefore, the findings presented in the study should be reconsidered in light of these critical concerns, and future research should prioritize the use of specific antibodies to ensure accurate and reliable results.

References

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