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Response to “Comparison of Gene Expression Profiling and Chromosome 3 Analysis by Fluorescent in situ Hybridization and Multiplex Ligation Probe Amplification in Fine-Needle Aspiration Biopsy Specimens of Uveal Melanoma”

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Dear Drs. Grossniklaus and Singh,

We would like to thank Drs. Plasseraud and Monzon for their interest in our recent publication “Comparison of Gene Expression Profiling and Chromosome 3 Analysis by Fluorescent in situ Hybridization and Multiplex Ligation Probe Amplification in Fine-Needle Aspiration Biopsy Specimens of Uveal Melanoma.” Their summary of biologic properties of gene expression profiling (GEP) testing and its differences from chromosome 3 analysis are important to understand. The goal of our study was to report the “real world” rate of discordance between GEP, multiplex ligation probe amplification (MLPA), and fluorescent in situ hybridization (FISH) testing results in uveal melanoma biopsy specimens.

In their letter to the editor [1], Drs. Plasseraud and Monzon write that we “erroneously suggest that DNA testing (FISH or MLPA) is ‘more sensitive at detecting high risk for metastasis patients.’” However, the full statement in the printed manuscript reads “Perhaps DNA testing is more sensitive at detecting high risk for metastasis patients” which is a possible consideration in our paper to help explain the discordance we have demonstrated, but not one that we have actual data to support. Furthermore, in their letter to the editor, the authors state we conclude GEP is an “inherently inaccurate test”; however, the statement, in its entirety, reads “RNA and its inherent instability compared to DNA may be more

prone to handling error and perhaps this may be the source of an inherently inaccurate test in the setting of gene expression profiling.” We feel that it is important that our thoughtfully written discussion points not be misrepresented by inaccurate misinterpretation by the authors.

Drs. Plasseraud and Monzon refer to the technical success of GEP testing being shown to be 97% in one clinical study. Our “real world” results suggest that GEP provides a test result in nearly all tissue samples, despite the fact that we and others have reported that non-melanoma tissue may also result in a Class designation by GEP. Therefore, a high “technical success” with GEP does not imply increased accuracy or even necessarily relevant patient information. In fact, high “technical success,” in lieu of a “no test result” response, may confer a false sense of security to patients with monosomy 3 who receive a Class 1A GEP result. In other words, no information may be better than wrong information regarding metastatic prognosis for patients.

We agree that the results of this paper must be taken in light of the limited follow-up time, as we clearly acknowledge in the discussion. We look forward to reporting on the accuracy of different tissue prognostication methods in this cohort as the follow-up time increases and the data reveal itself.

Conflict of Interest

Dr. Tara A. McCannel is an uncompensated member of the Advisory Board of Impact Genetics. All other authors report no relevant conflicts of interest.

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Reference

- 1 Plasseraud KM, Monzon FA: Response to “Comparison of Gene Expression Profiling and Chromosome 3 Analysis by Fluorescent in situ Hybridization and Multiplex Ligation Probe Amplification in Fine-Needle Aspiration Biopsy Specimens of Uveal Melanoma”. *Ocul Oncol Pathol* 2018;4:129.