Poeciliid Research

Transposable elements in melanoma progression: Insights from *Xiphophorus* fish

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Abstract. This critical analysis examines the findings of Münch et al (2024), which highlight the role of transposable elements (TEs) in the progression of melanoma in *Xiphophorus* fish. The study provides evidence linking increased TE expression with genomic instability and tumor progression, from benign pigment lesions to malignant melanomas. By analyzing transcriptomic data across hybrid fish models, the researchers demonstrated that TEs disrupt the regulation of critical genes and are influenced by hybrid genomic interactions and epigenetic factors such as DNA methylation. These findings underscore the importance of TEs in cancer biology, offering a framework to explore their role in human cancers while presenting diagnostic and therapeutic potential in oncology.
Key Words: transposable elements, melanoma, *Xiphophorus*, genomic instability, hybridization, epigenetics, cancer progression, tumor markers, RNA sequencing, DNA methylation.

The purpose of this scientific critical work of the "news and views" type is to highlight the role of transposable elements (TEs) in the progression of melanoma in *Xiphophorus* fish by critically analyzing a recent study, while contextualizing its findings within the broader implications for cancer research and genomic instability mechanisms.

A new research was conducted by Luca Münch, Frederik Helmprobst, Jean-Nicolas Volff, Domitille Chalopin, Manfred Schartl, and Susanne Kneitz, representing institutions such as Neurology Asklepios Klinik Barmbek in Hamburg, the University of Würzburg, Philipps-University Marburg, Institut de Génomique Fonctionnelle de Lyon, and the University of Bordeaux. Münch et al (2024) focused on exploring the role of transposable elements (TEs) in the progression of melanoma in *Xiphophorus* fish (Figure 1), a model organism known for its genetic predisposition to pigment cell tumors (Petrescu-Mag & Proorocu 2022; Schartl & Lu 2024). The study aimed to understand how TEs contribute to tumor development by analyzing their expression profiles in different stages of melanoma progression, from benign lesions to malignant tumors, within hybrids of *Xiphophorus* species. Researchers particularly investigated the influence of TE activity on genomic instability, a hallmark of cancer, and sought to uncover the regulatory mechanisms underlying this phenomenon. They utilized RNA sequencing to profile TE expression across tissues with varying stages of tumor development, identifying specific patterns linked to malignancy (Münch et al 2024). Furthermore, the study explored the interactions between parental genomes in hybrids, particularly focusing on the tumor-promoting gene xmrk and associated regulatory loci.

Figure 1. *Xiphophorus spp* (source: Ioan Valentin Petrescu-Mag, photo by Daniel Cocan).

The results of Münch et al (2024) showed a progressive increase in TE expression from healthy skin to benign lesions and ultimately to malignant melanomas, suggesting a strong correlation between TE activity and tumor progression. The study identified significant upregulation of class I transposons in malignant tissue, alongside notable changes in uncharacterized TE families (Münch et al 2024). Transcriptomic data revealed that TEs derived from the parental genomes of *Xiphophorus maculatus* (Günther 1866) and *Xiphophorus hellerii* Heckel, 1848 displayed differential expression patterns, influenced by hybrid genetic interactions. Regions on chromosomes LG5 and LG21 were particularly enriched with active TEs, which appeared to disrupt the normal regulation of critical genes such as rab3d, cdkn2ab, and adgre5 (Münch et al 2024). These findings highlighted the role of TEs in destabilizing the genome and driving the progression of melanoma through increased genetic instability. Additionally, the study confirmed that epigenetic factors, such as DNA methylation inherited from parental species, contributed to the regulation of TE activity in hybrids, further influencing tumor development (Münch et al 2024).

The observations and discoveries from this study have significant implications for understanding the role of TEs in cancer biology. By demonstrating that TE activity is associated with tumor progression, the research emphasizes the importance of studying these elements as potential drivers of genomic instability in cancer. While the findings are specific to *Xiphophorus*, they provide a valuable framework for exploring similar mechanisms in human cancers. This research contributes to a deeper understanding of how hybridization and epigenetic factors influence TE activity, opening avenues for investigating their regulatory roles in other species. Additionally, the identification of TEs as markers of tumor progression may inform the development of diagnostic tools or therapeutic strategies for melanoma and other cancers.

References

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