

## Melanoma in Platies and Swordtails

Will my black pigmented fish develop melanoma? It is a question asked by many hobbyists and breeders who raise platies and swordtails. Melanoma is a highly invasive and destructive cancer in humans. In *Xiphophorus*, melanoma can "eat away" at the body and fins and ultimately kill the fish either by metastasizing and disrupting the functioning of vital organs, or by enabling infections by opportunistic pathogens. Melanoma occurs spontaneously in wild and domesticated fish at a very low frequency. A more common, heritable form of melanoma is found in *Xiphophorus* interspecies hybrids and is of greater concern for the hobbyist and breeder.



Figure 1: This intensely black lyretail swordtail expresses *X. helleri* and *X. variatus* genes, but is melanoma free.

### Genetics of Melanoma

The pioneering work of Gordon and Kosswig in the 1920s, established that certain hybrids between *X. maculatus* that carry the sex-linked spotted dorsal (Sd) gene, and *X. helleri* are prone to developing melanoma. They and others showed that when the F1 hybrids were backcrossed to *X. helleri*, 25% of the offspring developed melanomas. Other sex-linked genes (e.g. spotted (Sp) and nigra (N)), which specify black pigment patterns, have subsequently been associated with melanoma in *Xiphophorus* hybrids. Several models were proposed to explain the genetic interactions that resulted in tumor formation. The most widely accepted view is that platies contain a gene, at the chromosomal locus Tu, which stimulates the abnormal proliferation of melanocytes, resulting in a melanoma. Additionally, the expression of this gene and consequently, the formation of tumors, are normally suppressed in platies by another gene located at the R locus (also known as Diff). Neither of these genes is present in *X. helleri*. In the F2 hybrids, the expression of the Tu locus gene (from the platy) in the absence of the suppressing R locus gene, results in melanoma.

Black pigmentation patterns in fish are specified by the distribution of non-proliferating cells called melanophores. Melanophores contain the black/brown pigment, eumelanin which is synthesized from the amino acid tyrosine. Fish and other animals deficient in the enzyme tyrosinase, cannot make eumelanin and are phenotypically albino. It is important to note that melanophores can be relatively small (micromelanophores) or large (macromelanophores). The cells that produce melanomas in platy-swordtail hybrids are proliferating melanocytes that give rise to macromelanophores, and not micromelanophores.

Cancer, whether it is melanoma in fish or colon cancer in people, is associated with the activation of growth-promoting genes (oncogenes) and the inactivation of growth-suppressing genes (tumor suppressors). It was therefore proposed that the Tu and R loci encode an oncogene and tumor suppressor gene, respectively. In 1989, the Tu locus gene was identified by Schartl and his

collaborators. The *Xiphophorus* melanoma receptor tyrosine kinase-2 (Xmrk-2) oncogene is a member of a growth factor receptor family that is activated in human breast cancer.

## Melanoma and the Hobbyist

Melanoma in *Xiphophorus* interspecies hybrids is a serious, mutilating disease that almost always kills the fish. Many of the colorful, commercially available platies and swordtails were developed by crossing *X. helleri* with either *X. maculatus* or *X. variatus*. Given that both *X. maculatus* and *X. variatus* express the Xmrk-2 oncogene and *X. helleri* does not express the R locus suppressor gene, the melanoma threat might seem substantial. However, there are several reasons why commercially available black pigmented fish do not develop melanoma very often. First, pigmented hybrids that look like maculatus or variatus platies (the hybrids have been repeatedly backcrossed to *X. maculatus* or *X. variatus*) are more likely to contain the suppressing R locus gene, therefore reducing melanoma risk. Second, all black and partially black swordtails are not routinely available in most pet stores, but the ones that I have seen, do not contain areas of intense black pigmentation that are associated with increased melanoma risk. This may be because fish with melanoma are generally not as healthy or active as unaffected fish and would likely be selected against in large breeding tanks or pools used by commercial breeders. Finally, many of the available black pigmented varieties of swordtails, such as those exhibiting a moon, comet or wag pattern (Fig. 2)\*, have a reduced risk of melanoma because the cells responsible for these black pigment patterns are micromelanophores and not the larger macromelanophores associated with melanoma. For all of these reasons, melanoma risk for fish purchased at a pet store is relatively low.



Figure 2: Swordtails with uniformly black dorsal and caudal fins (wag trait) rarely if ever develop melanoma.

Breeders trying to maintain or improve established strains, or develop new strains of black pigmented swordtails, are more likely to have (and potentially sell) fish that develop melanoma. Interbreeding black pigmented swordtails and platies will increase the melanoma risk in the offspring, but the greater concern is that many of the most popular and beautiful black pigmented swordtails which breeders maintain and sell today, are already at risk of developing melanoma because they were developed from hybrids. As a breeder, I know how difficult it is to cull a black pigmented melanoma prone swordtail, especially if it has other desirable traits such as a spectacular hifin. I'm also reluctant, as I'm sure that most breeders are, to eliminate an entire line of exceptional fish when only a small percentage of them will eventually develop melanoma as adults. This is the dilemma that many breeders face and one that makes completely eliminating melanoma from our swordtails and platies very difficult.

\* I don't have any first-hand experience with fish expressing the Arnoldi factor (black pigmentation between the fin rays), but I do not believe that they are prone to developing melanoma.

Melanoma can occur in babies, immature fish and in older fish as they age. Melanoma can also develop following sexual maturation in response to the increased production of sex hormones such as testosterone. In general, melanomas that occur in younger fish tend to be more invasive, resulting in rapid spread, fin destruction, and death (Fig. 3). Late onset melanomas may or may not be as destructive, but unfortunately, these melanoma prone fish are often used as breeders and the offspring sold, before melanoma is detected. Consequently, fish purchased from a breeder may develop melanoma as they age. It is therefore important to carefully inspect all black pigmented fish before obtaining them and on a regular basis thereafter (see below).



Figure 3: This five week old, black pigmented swordtail baby has early onset melanoma. The melanoma has spread throughout the posterior region of the body and the caudal fin.

Melanomas commonly arise in stocks of painted and black-bodied (e.g. Berlin/Hamburg and tuxedo) swordtails. A small percentage of my Berlin swordtails develop melanoma as they age, primarily at the base of the caudal fin (caudal peduncle) (Fig. 4). It is important to identify tumor prone fish as early as possible to eliminate them as breeders.

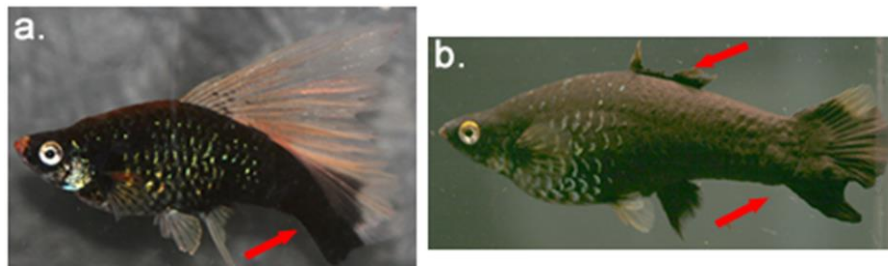


Figure 4: (a) This Berlin swordtail has intense black pigmentation at the base of the caudal fin that extends into the fin and is at great risk of developing melanomas as it ages. (b) This swordtail has a rapidly growing melanoma that has spread over the body, obscuring the blue iridescence, destroying the dorsal and caudal fins and producing multiple cancerous nodules throughout the caudal peduncle and caudal fin.

Albino fish can also develop melanomas. This may seem counterintuitive because melanoma is associated with black pigmentation and generally, albinos lack black pigment. However, in some cases, albino fish can make some eumelanin resulting in areas of light black or brown pigmentation. If these fish also express the Xmrk-2 oncogene and lack the R suppressor gene, they will develop melanoma at a high frequency (Fig. 5a). Furthermore, even non-pigmented albinos can develop melanoma. Non-pigmented albinos expressing the N, Sp, or Sd genes still produce macromelanophores, but they will not be black or brown because they do not contain eumelanin. Melanocytes in these white, or sometimes yellow, areas of the fish can become cancerous, resulting in an amelanotic melanoma (Fig. 5b).

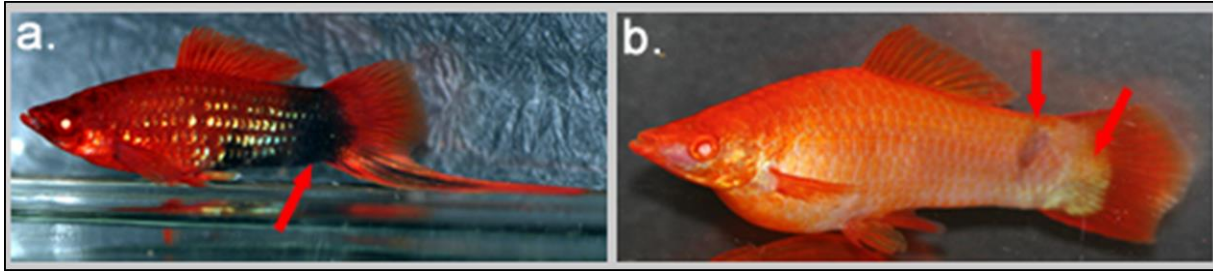


Figure 5: (a) This albino swordtail has a melanoma at the base of the caudal fin that continues to spread as the fish ages. (b) This albino swordtail has black pigmented and non-pigmented areas, which have a high likelihood of becoming cancerous.

Not all heavily pigmented livebearers are prone to developing melanoma. The black molly is a striking example of an all black fish, containing densely packed macromelanophores, which does not develop melanoma. As you might guess, black mollies do not express the *Xmrk-2* oncogene. It may therefore be possible to develop melanoma-free strains of *Xiphophorus* that no longer express the *Xmrk-2* oncogene, by selective breeding.

## Conclusion

Melanoma in platies and swordtails is a serious disease and one that should not be taken lightly. All hobbyists should be aware that many varieties of black pigmented platies and especially swordtails, which were developed by interbreeding these species, have the potential to develop melanoma. When obtaining a black pigmented fish from a pet store or a breeder, inspect it carefully. Look for areas of intense black pigmentation that are irregularly shaped. Make sure that black pigmented fins are intact and not abnormal in appearance. Inspect the black pigmented body of the fish, especially at the base of the caudal fin, to be sure that it is not thicker than non-pigmented areas and that "bumps" or other surface irregularities are not evident. Regardless of whether you are a casual or serious breeder, inspect your fish on a regular basis and eliminate melanoma prone fish from your breeding stocks if possible. It may be difficult to completely eliminate melanoma from platies and swordtails, but by becoming knowledgeable hobbyists and breeders, we can all help to achieve this goal.

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