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miR-8 modulates cytoskeletal regulators to influence cell survival and epithelial organization in *Drosophila* wings

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Summary

The miR-200 microRNA family plays important tumor suppressive roles. The sole *Drosophila* miR-200 ortholog, miR-8 plays conserved roles in Wingless, Notch and Insulin signaling – pathways linked to tumorigenesis, yet homozygous null animals are viable and often appear morphologically normal. We observed that wing tissues mosaic for miR-8 levels by genetic loss or gain of function exhibited patterns of cell death consistent with a role for miR-8 in modulating cell survival *in vivo*. Here we show that miR-8 levels impact several actin cytoskeletal regulators that can affect cell survival and epithelial organization. We show that loss of miR-8 can confer resistance to apoptosis independent of an epithelial to mesenchymal transition while the persistence of cells expressing high levels of miR-8 in the wing epithelium leads to increased JNK signaling, aberrant expression of extracellular matrix remodeling proteins and disruption of proper wing epithelial organization. Altogether our results suggest that very low as well as very high levels of miR-8 can contribute to hallmarks associated with cancer, suggesting approaches to increase miR-200 microRNAs in cancer treatment should be moderate.