

A study, "Genomic Signatures Predict Migration and Spawning Failure in Wild Canadian Salmon" published in the prestigious journal "Science" in January 2011 has created a lot of public and media interest. This research is particularly timely given the large fluctuations in Fraser River sockeye salmon populations seen during the last few years. To learn more about the research, staff at the BC Centre for Aquatic Health Sciences asked Dr. Kristina Miller, who is the primary author of the paper, to provide information on the study's results and implications. Her responses, in question and answer, format are below.

What is the study about?

In the past decade, Fraser sockeye salmon have experienced massive (40-95%), highly fluctuating premature mortalities both in the Fraser River en route to spawning areas and on spawning areas. The aim of the study was to determine the role of salmon condition on these premature mortality events. Ultimately, we were interested in developing tools that would enable accurate predictions of the fate of salmon in the river. The approach was to track fate of individual salmon using biotelemetry (radio tracking) and to assess a broad range of physiological processes using genomics. Our study contrasted gene expression profiles between fish that made it to spawning grounds and those that went missing en route in the river. We identified in three separate experiments the same signature associated with premature mortality of adult salmon, whether fish were physiologically sampled in the ocean, upon entry into the river, or at spawning grounds. Within this gene signature, we observed an immune response similar to that which would be seen in an animal fighting an intracellular pathogen infection. The stimulation of genes we observed have been associated with viruses. This led us to the hypothesis that the signature associated with mortality was of viral origin. An actual disease agent was not identified in this study.

Did it show there is a virus in farmed salmon?

No. First of all, the involvement of a virus in eliciting the mortality-related signature (MRS) was only a hypothesis, as no specific disease agent was identified in this study. Second, this study was based solely on wild sockeye salmon returning to spawn in the Fraser River, not farmed salmon. Importantly, the MRS was observed in fish tagged both in Johnstone Strait and in Juan de Fuca Strait, and unpublished data shows the signature is also present in salmon migrating through the Haida Gwaii, before they would have encountered salmon farms.

Can farmed salmon be tested for this virus?

Farmed salmon could be tested to see if they carry the genomic signature, but again, the study did not identify a specific virus (disease agent). Research aiming to identify whether a viral pathogen is involved in eliciting this signature is underway. If a specific virus is identified using the molecular sequencing approaches being applied, it could be tested on farmed salmon.

Why aren't farmers testing?

The farmers have not specifically been asked to provide samples to test for the genomic signature, nor have the farmers asked that their fish be tested, although there has been some discussion about this. If a specific pathogen is isolated in association with this signature, it would be prudent to test for the presence of the pathogen in farmed salmon. If farmed salmon are positive for the pathogen, it could be insightful to conduct the genomic analysis to assess the degree to which they respond to gauge whether there is resultant disease, or the pathogen is benign. Histological analysis to contrast fish that do and do not contain the MRS is underway in sockeye salmon, and would also be important to assess in farmed fish if they carry the pathogen.

Where could the virus have come from?

Again, at the present time, there is not a specific virus identified, so we simply can't answer this question. However, if a specific virus is identified, molecular epidemiological approaches could be applied to answer these questions.

Are enhancement facilities testing for this virus?

The MRS is present in Cultus Lake sockeye leaving the hatchery, but we do not have sufficient data to determine whether the prevalence is any higher for these enhanced fish than for other populations in the Fraser River sampled in the same year. This is something we are looking into. We are also running a microarray experiment contrasting hatchery and wild coho salmon, and we will be assessing this signature in these fish.

What is a genomic signature?

Humans carry over 30,000 distinct genes within their genome, and salmon are estimated to contain potentially twice this amount due to residual tetraploidy. In functional genomic analyses, we assess the transcriptional activity (which genes are being turned on and off to make proteins) of a large portion of these genes simultaneously using microarrays-- slides that have printed on their surface 10's of thousands of salmon genes. In our study, we used two different slides, one which contained 16,000 salmon genes, and another with 32,000 salmon genes. A genomic signature is derived statistically as a sub-set of the genetic messages that are turned on/off in association with a specific biological or environmental phenomenon; in our Science study, elevated mortality was the phenomenon. Once the genes associated with a signature are differentiated statistically, statistical approaches can be applied to determine what biological processes those genes are involved in are over-represented, providing a "functional signature" of the data. It is on the basis of this functional signature that mechanisms associated with individual signatures can be postulated. As well, there is a large body genomic data from controlled laboratory studies that can be mined for similarity to genomic signatures obtained.

When in the salmon's life cycle do they pick up the virus?

Sockeye salmon smolts leaving the river carry the highest prevalence of the MRS. Parr sampled in November, 5 months before they will smolt and migrate to the ocean, already carry the signature. In the two years for which there are full life-cycle data, it appears that the prevalence in brain and liver is highest in smolts leaving the river, and is substantially lower in returning adults. We have observed this signature in varying proportions of sockeye salmon each year with samples dating back to 2003.

Did a virus actually cause the signature? If so, what virus?

Research is underway to answer this question. Results are promising, but we do not yet have sufficient information to fully answer this question.

Thank you to Dr. Miller for her clarification of the research results and their relevance to coastal British Columbia.

The paper's complete reference is:

Miller K.M., Li S., Kaukinen K.H., Ginther N., Hammill E., Curtis, J.M.R., Patterson D.A., Sierocinski T., Donnison L., Pavlidis P., Hinch S.G., Hruska K.A., Cooke S.J., English K.K., and Farrell A.P. (2011) "Genomic Signatures Predict Migration and Spawning Failure in Wild Canadian Salmon" *Science* 331:214-217.