

**PROJECT:** PREVENTIVE  
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CtrlAQUA

# Using molecular biomarkers in the kidney for early detection of nephrocalcinosis in Atlantic salmon

## HYPOTHESIS:

Molecular changes reveal functional and structural disturbances during development of nephrocalcinosis in Atlantic salmon

**DURATION:** November 2022 - March 2023

**FISH SIZE TESTED:** 400-600 grams (commercial settings Trovåg, Bremnes)

**SALINITIES TESTED:** Brackish water (15 ppt) and Salt feed (SuperSmoltFeedOnly)

**PHOTOPERIOD PROTOCOL:** Continuous light (24 hour light)

## HIGHLIGHTS:

- The etiology of nephrocalcinosis is unknown. Transcriptome responses indicate presence of an intracellular pathogen, but only in kidneys with high scores.
- Nephrocalcinosis may impair excretory and osmoregulatory functions of kidney. The ion pumps located basolateral in the cell of several parts of the nephron tubule (figure 1A) play key part in secondary transport of ions and water. The “trunk kidney” (urine producing part) consists of several thousand nephron tubules that transport salts containing the major components of kidney stones (calcium, phosphate, magnesium, and bicarbonate).
- Histological analysis revealed development of sub-epithelial changes in several parts of the nephron tubule at an early phase of nephrocalcinosis. This indicates regulatory disturbances, which may be corrected or slowed down by timely preventive measures (adjustments in production environment, feed, salinity, temperature and pH).
- Gene expression of Nka subunits is significantly reduced in mild nephrocalcinosis (score 0-1) while the downregulation of these genes is almost undetectable in severe nephrocalcinosis (score 3), see figure 1B. Similar trends were observed for Nka enzyme activity although significant reduction in activity does not occur before severe nephrocalcinosis (2-3: complete loss of pumping capacity), see figure 1B. These changes are consistent with the morphological changes (figure 1C).
- Transcriptome analysis showed downregulation of several Nka isoforms and many transporters of inorganic and organic substances. Overall, nephrocalcinosis suppressed kidney metabolism, especially biotransformation and detoxification.
- Upregulation of genes involved in the development of cartilage and bone indicated substitution of nephrons with inert tissues.
- Combined with blood chemistry and diagnostic tools (x-ray and histology), molecular analyses improve understanding the risks associated with nephrocalcinosis, and may help to prevent and reduce incidences of this disorder in commercial production settings.



## RECOMMENDATION:

- The biomarkers described have been tested in commercial settings and can be recommended for practical use. New candidate biomarkers were discovered.
- It is necessary to further investigate if the biomarkers can predict nephrocalcinosis before development of other symptoms. Research is also needed to link changes in biomarkers to feeds, water quality, transport/handling stress and other conditions in salmon farming.
- Diagnosis of known pathogens and unknown microorganisms in kidneys with nephrocalcinosis is recommended.

The factsheet is ready for implementation, but with the note that the testing has not been done for all industrial relevant conditions.

for diagnostics (x-ray and histological analysis).

Takvam, M., Sundell, K., Sundh, H., Gharbi, N., Kryvi, H., and Nilsen, T.O., (2023; submitted). New wine in old bottles: Modification of the Na<sup>+</sup>;K<sup>+</sup> ATPase enzyme activity assay and its application in aquaculture. *Reviews in Aquaculture*

Takvam et al., 2021. <https://doi.org/10.3389/fphys.2021.664588>

Takvam et al., 2021. <https://doi.org/10.14814/phy2.15059>

## READ MORE:

The reader is also referred to other related Factsheets in PREVENTIVE

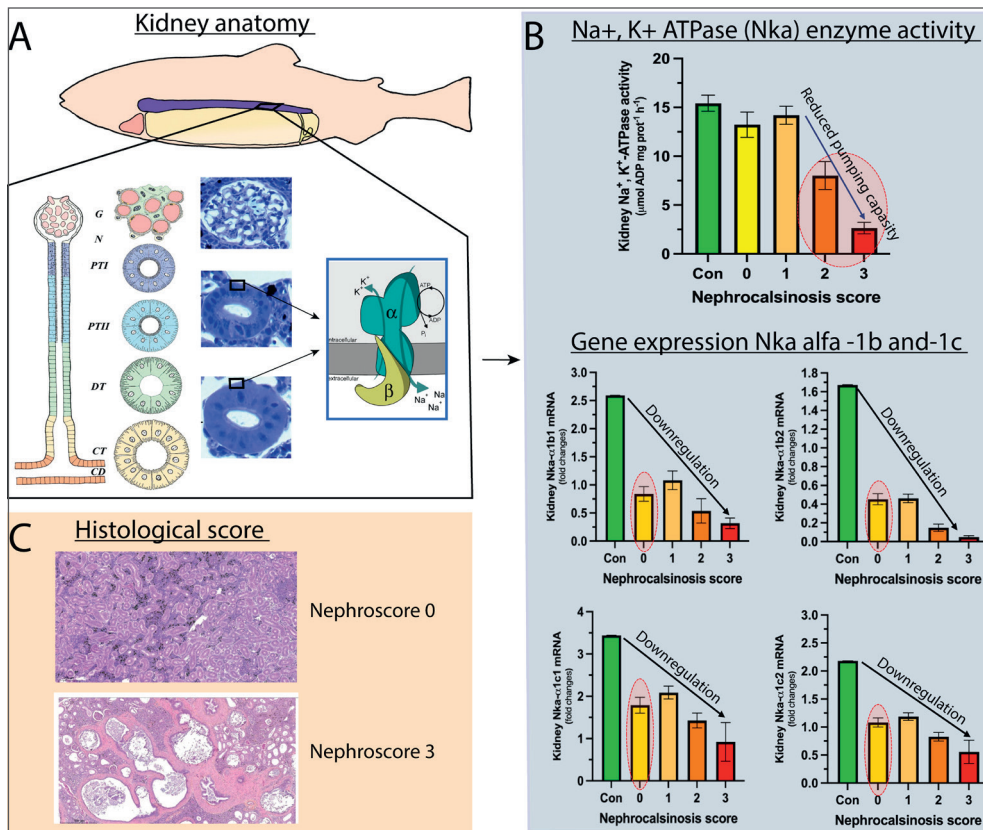


Figure 1: Overview - molecular biomarkers in the kidney of Atlantic salmon: Overview of kidney anatomy, histological score and molecular markers in different severities of nephrocalcinosis in Atlantic salmon. Sources: Takvam et al., 2021a; 2021b; Takvam et al., 2023. Histology: Patogen; Alf Dalum