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**SUMMARY**

In October 2017, the “traffic light system” for Norwegian aquaculture was initiated and each of the 13 production zones were given a colour by the Ministry of Fisheries. Two zones were given red, three yellow, and the remaining eight zones green. In 2017, the salmon louse was the only factor considered in the traffic light system. The key point for the given colours is to what extent salmon lice produced on farmed fish induce additional mortality on wild Atlantic salmon smolts. The conclusion (i.e. colour) is based on an assessment made by an expert group which has been led by me. This was a challenging process, with short deadlines, and where all relevant data and information was integrated to make conclusions on salmon lice induced mortality in the 13 different production zones. There is a large variation in salmon lice impact in the different production zones, and a good scientific assessment is important so that the conclusions are robust. The report from the expert group also highlights scientific areas where more knowledge is required to increase the accuracy of the assessment in the future. The consequence if a zone is red will be reduction in aquaculture production, and, all measures that can reduce transfer of lice larvae originating on farmed fish to wild fish in that zone should then be implemented. This is in order to shift red zones to green.

Treatment has been the main strategy to keep lice levels low on farmed fish, and with the exception of the last year or so, this has primarily been achieved through medicines. Due to decreased efficacy of the available medicines, mechanical and or environmental-based treatments have taken over during the last 1–2 years. In the future, it will also be important to implement measures to continue to reduced dispersal of lice larvae from farmed to wild salmonids. More research is necessary including prophylactic measures on farmed fish (e.g. vaccines), infection dynamics of lice larvae (e.g. optimal localisation of farms to reduce lice dispersal to wild fish) and studies on wild salmonids to facilitate management (e.g. smolt migration, lice tolerance in different wild salmonid stocks).

In the past year, the SLRC board has paid increasing attention on the exit-strategy for the centre when its primary financing from the research council terminates in 2019. All partners have stated an interest to continue the SLRC and the process is called a continuation strategy. We also had a meeting with the SAB in September 2017 to discuss the SLRC exit-strategy, and to get their input on scientific topics and other relevant issues. There are three questions in the exit-strategy that need to be resolved: What main areas should we work on, what partners are required, and how should it be funded? The SLRC has an
annual budget of ~30 mNOKs. It is unlikely that we are able to secure this much funds in a continued form of SLRC. Less funding will result in reduced activity most likely by the removal of some topics. The introduction of the traffic light system to regulate Norwegian aquaculture highlights the need for high quality research on the salmon louse and interactions between farming and wild stocks. Although a large proportion of the management related research on the salmon louse is carried out by the institute sector in Norway, other institutions like the SLRC contribute with highly relevant knowledge, research infrastructure and competence. Some of the tools developed within the centre (e.g. production of genetic traceable lice) may be used to validate dispersal models as well as understand how lice from one farm interact with other farms or wild fish. I am confident that if the SLRC continues, high quality research will be a hallmark of the centre, and in turn, this will contribute to the industry, management, as well as basic science sectors.

Frank Nilsen

Director SLRC
Sea lice (Lepeophtheirus salmonis and Caligus spp.) are the major pathogens affecting the global salmon farming industry and have a significant impact in many regions. The annual loss has recently been estimated to €300 million and the aquaculture industry relies heavily on a few medicines for lice control. Widespread resistance to these medicines has increased the need to develop new treatment methods (biological, prophylactic and new medicines) and tools to avoid increased losses due to sea lice and to ensure a sustainable salmon farming industry in the future.

Research conducted at the centre will focus on methods and tools to facilitate the development of new medicines, develop new tools for resistance monitoring, reduce attachment in infective stages, improve host response to infection, identification and evaluation of new targets for a future sea lice vaccine, and to explore the possibilities to utilize RNAi as a novel method in lice control. By using the salmon louse genome sequence as a starting point, functional genomics methods will be utilized to identify molecular markers for drug resistance to facilitate monitoring and prolong the life time for valuable anti sea lice drugs. The Sea Lice Research Centre (SLRC) consists of the leading scientists within the field together with the major industrial players, represents a strong consortium to develop short and long term solutions for one of the most significant problems for the salmon farming industry world-wide. This will be achieved through state of the art research in relevant fields (parasitology, molecular biology and genomics, pharmacology, host parasite interactions) and establishment of an integrated database resource for the salmon louse genome in addition to state of the art wet-lab facilities for sea lice research. Results from the SLRC will enable an integrated control system to be established, based on key features in sea lice biology, to improve sustainability of the salmon farming industry.
CENTRE VISION AND GOALS

SLRC aims to be the world leader for research on the salmon louse and similar parasites. The nature of the centre will facilitate development of new methods for lice control and shorten the time from basic research to new products and tools for parasite control in the aquaculture sector to achieve a true integrated pest management in the future.

SLRC objectives

• New medicines and resistance monitoring & control methods (WP1)
• Anti-attachment diets (WP2)
• Immune controls (specific & nonspecific) (WP3, WP4)
• RNAi gene techniques for research tool development and future controls (WP4)
• In depth knowledge of the molecular biology of growth, reproduction and endocrine systems in sea lice (WP4)
• Annotated genome sequence linked into an integrated database containing experimental data (WP5, LiceBase)
• Updated microarray and other molecular tools (WP3, 4, and 5)
• Larval detection and assessment techniques (WP4)
• Sea lice facility (naïve lice population, challenge facility, etc.) (WP6, LiceLab)
• Development of true integrated pest management techniques for industry (Part V)
The SLRC Chairman’s comments – yearly report 2017

The deliberations of the Board in 2017 has emphasized the importance of establishing the exit strategy for the SLRC. This is substantiated by the persistent importance of gaining more genetic and biological understanding to find new ways to fight sea lice. The steady flow of results and publications from the centre demonstrates that there is still far more knowledge to be captured and dispersed. The Board thus recognises the need to continue the SFI as a permanently established sea lice centre to further propagate the basic and applied research and development needed for sustainable development of the industrialised fish farming industry in Norway.

The SLRC has through the centre director Professor Frank Nilsen, contributed to the authorities’ new “traffic light system” regulations of the Norwegian aquaculture industry. It is important that the regulators are given advice that is based on thorough biological and epidemiological competence from different, possibly also competing, research institutions. The centre has an active policy to protect intellectual property rights (IPR), to the benefit of the SLRC partners. Without proper IP protection, the commercial value of the results obtained are limited, and puts product development based on new research at risk. Notwithstanding this, to publish studies and to propagate the knowledge obtained are the key activities for the centre.

The Board had the good intentions of establishing best practice for Integrated Pest Management (IPM) for sea lice, and a task force was established. Over time, it became clear that the massive resistance to chemotherapeutants, increased use of cleaner fish, and use of mechanical treatments and equipment to prevent infestation, meant that the SLRC with its biological focus was not the right environment to present guidelines on IPM. The ever-changing world of mergers and acquisitions, spin offs, infrastructure and new strategies within the fish farming, pharma and feed businesses, has also affected the SLRC. Activities have had to be amended, and the fields of interest are changing. A detailed consortium agreement has been a valuable tool for maintaining good relations and a clear understanding among the partners.

Going forward, the exit strategy is one of the main issues for the Board. As an SFI, the centre is financed until the autumn of 2019 with funds from the partners and the Norwegian Research Council. The employed PhDs, post docs and technicians represents the true value of the SLRC, and the Board is grateful for their continued contribution. We soon need to be able to convey that they have an exciting and stable workplace also in the future.

The Board has received a clear statement from the host institution, the University of Bergen, that the University will support a permanent establishment of the sea lice centre at the university. Likewise, the NMBU and HI also states their support to such an initiative. The Norwegian Research Council will also be pleased to see this SFI developing into a permanent operation and will support research projects according to their regular support schemes. We believe that these commitments ensure an adequate number of research scientists in a future centre. Nevertheless, scientists need more than their salary to provide unprecedented knowledge. It is estimated that a yearly funding of about 15 MNOK is required for the centre going forward.
The Board considers support of basic research to be a public obligation whereas it expects the fish farming industry and its supporting industry to finance applied research. Fish farming is an important industry for Norway, and its continued sustainability and profitable growth is dependent on controlling sea lice infestation. The current mechanical methods constitute parts of a future solution, but they are costly and evaluation regarding fish welfare. We need a permanent lice centre with predictable financing on the two levels, basic and applied research. The Board and management believes that the future centre should concentrate its efforts on a few areas in order to attract the necessary funding. These areas will most probably include research to facilitate development of vaccines as well as host modulation. The opportunity within new methods in biotechnology, e.g. RNAi or CRISPR combined with further knowledge on the lice, represents exciting possibilities. International as well as national regulators seem to open up for products made from such techniques, providing new, approved, effective clinical measures for the fish farming industry. In addition, exiting possibilities lay within further exploration of functional feeds, new medicines, epidemiology and immunological and biological research. A task force has been established to investigate and advise the Board on all the important exit initiatives and decisions the coming months.

Last but definitely not least, I would like to present my thanks to Frank (Nilsen) and Ingunn (Wergeland) for all their efforts in being the centre of the Centre. These two steadily propagate its progress, dealing with excellent research as well as the insecure future and all the nitty gritty reporting and daily frustrations and happy moments. Your energy and enthusiasm are contagious – the SLRC would not be without you.

Oslo/Bergen, 2. Mars 2018

Benedicte H. Fossum
Chairman of the Board
**ORGANISATION**

The SLRC has both academic and industrial partners outside Bergen, and the main scientific activity in the centre is located in Bergen and Oslo. People working for the SLRC at IMR and UiB are co-located in the SLRC facilities at UiB at Marineholmen.

The industrial partners are complementary to each other and linked together by the academic partners. The eight SLRC partners in 2017 are:

**University of Bergen (UiB)** is the host institution for SLRC. Senior scientists from three departments at the faculty of mathematics and natural sciences are the base for the research in the SLRC. Senior scientists within biology, molecular biology and bioinformatics use their knowledge in the SLRC. The main wet-lab activities take place at UiB, where lice strains are kept. PhDs and Postdocs are educated within the center.

**The Norwegian University of Life Sciences (NMBU)** is represented in the SLRC with senior researchers from the Department of Food Safety and Infection Biology and the Department of Basic Sciences and Aquatic Medicine. PhDs and Postdocs are hired to work with the research in the SLRC. This partner is responsible for WP1 and WP3 and has close connections to WP2 and WP4. Until now, the main cooperating partners have been PatoGen Analyse, Elanco, EWOS and UiB.

**Institute of Marine Research** is represented in the SLRC with one senior researcher (80%), 1 post doc, 1 PhD student and one wet lab technician (50%). Major wet-lab activities, mainly RNAi trial takes place in the laboratories in Bergen. The Post doc and the PhD work in WP4, whereas the researcher works in both WP4 and WP6, where the technician also is connected.

Cargill is one of the world’s largest private held companies and with the acquisition of EWOS in 2015 they became a global leader in aqua nutrition. Cargill’s animal feed business is divided onto three business segments; Cargill Feed and Nutrition, Cargill Premix & Nutrition and Cargill Aqua Nutrition. Cargill Aqua Nutrition develops and produces feed and feed solutions for 3 key species – salmon, tilapia and shrimp – in 18 countries around the world. In addition to this, Cargill Aqua Nutrition also consist of Innovation centers and Technology application centers. **EWOS Innovation AS** is a user Partner in the SLRC with a long history of sea lice research. Scientists are based in Bergen, Dirdal, and Colaco in Chile, where research facilities have been expanded the last years. In the SLRC, development of compounds that reduce the settlement and survival of lice will be the focus. EWOS Innovation is the leader of WP2 and is involved in several of the projects in the other WPs.
**Lerøy Seafood Group ASA** is one of the world leading salmon farming companies with more than 100 farming licenses in Norway, in addition to slaughterhouses and processing factories. In the SLRC, the company is a supplier of raw materials and facilities for field trials. Lerøy has also been an important contributor in the field validation of the novel analyses of the diagnostic PCR-analyses for resistance monitoring developed by PatoGen. First-hand information on needs and demands from the industry gives Lerøy an important role in the SLRC.

**PatoGen AS** is a biotechnology company that develops and sells gene technology analyses that are used to reduce disease related loss in the aquaculture industry. PatoGen has the most modern laboratories for Real-Time PCR analyses for detecting fish pathogens in Norway, and work in close collaboration with research partners and industrial partners in the SLRC. PatoGen is mainly involved in WP1 and WP4, and collaborate with the partners UiB, NMBU, Marine Harvest ASA, Lerøy Seafood Group ASA and Elanco Animal Health.

**Elanco Animal Health** is the former partner Novartis Animal Health AG. The Animal Health part of Novartis was sold to Eli Lilly& Company from January 2015 and the partner in the SLRC is Elanco Animal Health – fully owned by Eli Lilly& Company. Elanco develops and commercializes leading animal treatments that meet the needs of pet owners, farmers and veterinarians. Both the Aqua Health part at Prince Edward Island, Canada, and the Animal parasite unit in Switzerland take part in the SLRC work.

**Marine Harvest ASA** is a world leading Seafood Company and is present in all major salmon farming regions. The knowledge and international network which Marine Harvest brings is clearly an added value for the centre. Marine Harvest has been an important contributor in the field validation of the novel diagnostic PCR-analyses for resistance monitoring, developed by PatoGen Analyse. In addition, Marine Harvest is a supplier of raw materials and facilities for field trials in the SLRC.
MANAGEMENT

UiB is, as host for the SLRC, responsible for the coordination of all activities in the centre. The Centre Director Frank Nilsen and the administrative coordinator Ingunn Wergeland carry out the day-to-day management at UiB.

The overall decision-making body is the SLRC board, where all the partners have one representative each.

The Board takes decisions on strategy, annual work plans, activities, budget and the organisation. Benedicte Fossum is the chairman of the SLRC board; she is an independent chairman elected by the partners of the centre. There has been several changes in the board during the year; four out of eight board members representing the partners are new members. The board has established a task force planning the Exit strategy for the centre.

SLRC Board Members in 2017:
- Bjarne Reinert, Lerøy Seafood Group ASA
- Trude Hagland/Ragna Heggebo, EWOS Innovation AS
- Jose Fernando Rodrigues, Elanco Animal Health
- Gordon Ritchie, Marine Harvest ASA
- Vidar Aspehaug, ParoGen Analyse AS
- Karin Kroon Boaspen, Institute of Marine Research
- Amund Måge/Lise Øvreås, University of Bergen
- Ole Taugbol, Norwegian University of Life Sciences
- Benedicte Fossum, Chairman of the board
The SLRC Board has appointed a working group planning various models for the future of the SLRC. The models have been presented for the board, who have made a selection of them for further development. Structure of a new organisation without the SFI frame will be different from today’s SLRC, and it is important for the partners to evaluate their role and potential contribution.

**Scientific Advisory Board (SAB) for 2016**

There are selected three members in the SAB for the last period of the centre. The main task is guidance to future work based on the SLRC project description, and to give the centre recommendations regarding experiments and new projects. The new project on RNAi interference in WP4 is a result of discussions and feedback from SAB members. The SAB is also an important source of information on what is going on in related areas of research and to seek for new possibilities. In 2017, the SAB members participated at the SLRC Workshop in May and in meeting a WP-leader meeting in September where plans for research in SLRC were presented. The SAB is also involved in the future of the centre. Various models for organizing a new centre have been presented for the SAB together with ideas for targeted themes and projects. The feedback given has been of great value for the progress of the task force working with the Exit strategy.

The members of the SAB are:

- Dr Ian Denholm, Rothamsted Research/University of Hertfordshire
- Professor Chris Secombes, University of Aberdeen
- Professor Kurt Buchmann, University of Copenhagen
SLRC Arrangements in 2017

The centre arranged two open seminars in 2017 where research and new findings in the SLRC were the main themes. 80–110 persons participated at the two seminars.

The first seminar was arranged in August in connection to AquaNor 2017 where various industries and academic institutions were represented.

In October, the SLRC arranged a one day seminar divided into two parts. The first part presented a selection of research and results from the centre while the second part presented some of the research behind Traffic Light system.

Two workshops for the SLRC personnel have been arranged during the year:

10–11 May at Marstein, outside Bergen with participation from all the partners. The main purpose of the workshop was to update all participants on the research going on in the various parts of the centre, and to further develop and identify areas for collaboration between WPs and partners. PhD students and postdocs gave detailed scientific presentations. To share knowledge is an important tool to enable a dynamic work in the SLRC and this meeting is an important facilitator to update partners on scientific progress.

16–17 November in Oslo, where the main focus was on related research outside the SLRC. The Norwegian Food Authority (Mattilsynet) and the Institute of Marine Research were invited to give presentations on the political and administrative framework on Sea Lice Control and future perspective on new regulations.
Cooperation between the centre’s partners

One of the focus points in the revised project plan was vaccine related work. To facilitate this, collaboration between four WPs (WP3, WP4, WP5 and WP6) has been strengthened. The increased effort applies to all part of the work and includes bioinformatics approach to identify vaccine candidates, initial studies and validation on these candidates (including RNAi) to clinical trials and measurements on immune response. Development and assessment of clinical trial models is also an important part of the work.

Vaccine trials at the SLRC

Two large vaccine trials have been conducted at the SLRC. Both were carried out as common garden experiments, which means that all fish from all groups are infected with copepodids in one big tank. Fish are individually marked with tags. This is done to ensure, that all fish are exposed to the same infection pressure and that tank effects caused by keeping fish in different tanks are excluded.

In the first trial nine different vaccine groups as well as one non-vaccinated control group were included. Different types of vaccines were used: protein/peptide, DNA and replicon types. In the second trial twelve vaccine groups and the unvaccinated control group were tested, all belonging to protein/peptide type of vaccines. Vaccine candidates were chosen by different criteria: The proteins should be expressed on contact areas from fish/fish blood to lice (mainly intestine) and they had to be essential for lice survival, development or reproduction. These criteria were verified in advance by expression studies as well as functional studies with gene knock-down. Only genes, which knock-down giving a louse phenotype with impaired survival, development or reproduction, were included.

Salmon were vaccinated and boost vaccinated in the fresh water period, smoltified and transferred to full seawater where infection with copepodids took place. Fish were sampled about two weeks after infection when lice were at the chalimus 2 and preadult 1 stage. This time point was chosen to ensure limited jumping of lice between different fish, which takes place from the preadult stages. Fish weight was on average 250 or 200 gram respectively for trial 1 and trial 2. On average there were 20 (trial 1) or 30 (trial 2) lice on fish in the two trials. Lice numbers were quite variable within each group. No group showed significant different lice numbers compared to the control group (Fig. Vaccine trials).

For the second trial, additional fish vaccinated with five of the vaccines were transferred to single fish tanks where they were infected with 60 copepodids each. These will be kept until lice are egg-producing adults to assess the effect of these vaccines on the older lice stages, which are characterized by a higher blood consumption and are able to move freely on the fish. This experiment will be completed in March 2018.

Vaccine trials: Lice numbers of the 9 and 13 vaccine groups as well as for the unvaccinated control group (ctr) for trial 1 and trial 2 respectively
SCIENTIFIC ACTIVITIES AND RESULTS

WP1: Chemotherapy and resistance
Principal Investigator: Tor Einar Horsberg, NMBU

General introduction
Work package 1 deals with exploration of possible new treatments against salmon lice and resistance development towards chemotherapeutants and other control methods. These two activities overlap, as failures of traditional treatments induces activity towards finding new treatments, and resistance development can lead to a better understanding of the mechanism of action for the compound in question.

Chemotherapy
A study of efficacy of all compounds within the neonicotinide class, which are agonists on the nicotinergic acetyl choline receptor (a ligand-gated sodium channel), was conducted in 2016. The study revealed that some of these agents are highly effective against salmon lice, both in bioassays and when administered to the fish through the feed. In 2017, a study to explore the relative efficacy of these in an ex vivo experimental system was initiated. The study was conducted together with the Swiss company INVENesis Sàrl. To identify genes coding for subunits of this receptor in salmon lice, the salmon louse genome (licebase.org), the ENSMBL predicted salmon louse transcriptome (ftp.ensemblgenomes.org/pub/metazoa/release-36/fasta/lepeophtheirus_salmonis) and an in-house de-novo transcriptome have been screened. Eight putative nAChR subunit genes were identified and cDNA from seven of these have been fully sequenced (including RACE-pcr). In 2018, they will be cloned into Xenopus oocytes to see if a working ex vivo model can be established. If so, a screening of compounds acting on this receptor will be conducted.

Figure 1.1: Cloning of cDNA or mRNA into Xenopus eggs
Nilsen and Espedal discovered earlier that resistance towards pyrethroids was maternally inherited in salmon lice. The most likely mechanism is that resistance is transferred through mitochondrial genes. This discovery also points to mitochondria as a possible target for pyrethroids, which has not been described earlier in any arthropods. Biochemical, physiological and molecular studies were initiated in 2017 to try to identify a potential mitochondrial target for pyrethroids. These studies will be continued in 2018 through an SLRC-associated post-doc project.

Functional studies on the mode of action for hydrogen peroxide have also been carried out, mainly through the associated project “Resistance to hydrogen peroxide in salmon lice”. The results showed that the compound had an almost immediate immobilizing effect on sensitive parasites, later followed by development of gas bubbles that subsequently disrupted the tissue structures inside the parasite. Parasites not developing these interior gas bubbles recovered within 1 to 3 hours after exposure, while parasites with visible gas bubbles did not.

A set of bioassays have previously been developed to screen new active ingredients for their efficacy towards salmon lice. These are based on bioassays on different developmental stages: a) nauplii to explore effects on molting, b) copepodides for a rapid screening of immobilizing effect, and c) preadults to explore direct effects on larger parasites. In 2017, a new screening of commercial available compounds and experimental compounds was initiated, in cooperation with Elanco.

**Resistance**

In 2017, the activities around resistance development have been focused on mechanisms behind pyrethroid and hydrogen peroxide resistance, tolerance towards non-chemical treatment options with fresh- and warm water, and modelling of resistance development.

A maternal inheritance of pyrethroid resistance in salmon lice has previously been demonstrated by Nilsen and Espedal and a patent application filed by UiB and PatoGen. Several studies have been conducted to pinpoint the underlying mechanism. A sequencing study revealed 20 non-synonymous changes in the mitochondrial genome of a resistant versus a sensitive strain. It is unlikely that all changes are of relevance for resistance, thus a screening of additional strains was started to narrow down the candidates. Furthermore, apoptosis was detected in several tissues of the parasite after exposure to deltamethrin. Most notably, the degree of apoptosis in skeletal muscle was high, whereas it was low or absent in the central ganglion. These results are in press. In addition, mechanistic studies on the electron transport chain in the mitochondrion have been initiated. For initiation of this work, Professor Thomas Van Leeuwen, University of Gent, visited the lab in 2017. In 2018, the researcher working on this project will visit his lab in Belgium to learn some specific techniques.
The mechanism behind resistance towards hydrogen peroxide, overexpression of the enzyme catalase, was revealed in 2014 and a patent application was later submitted by PatoGen. In 2017, the focus has been on identification of additional markers that also are differentially regulated between resistant and sensitive parasites. Several genes displaying a significant differential expression were identified, and the validation of their strength and importance is still ongoing.

The trend in salmon lice control has in 2016 and 2017 moved from chemical to non-chemical control methods. Non-chemical methods include prolonged baths in fresh water and short dips in warm water. None of these methods are 100% effective, and there is therefore a risk that the surviving parasites may cause a shift in the sensitivity towards these methods. In 2017, a paper was published by some researchers from the SLRC, demonstrating genetic variation among full-sibling families of lice in tolerance of both fresh- and warm-water (Ljungfeldt et al., 2017). This demonstrates that the louse has genetic variation in tolerance of these treatments and may therefore develop reduced sensitivity to such treatments. Also in 2017, test methods (bioassays) for temperature and salinity tolerance were established and a small study on different laboratory – and field strains was carried out. For both procedures, a variation in sensitivity between copepodides and preadults of different strains were detected, confirming results from the parallel study using full-sibling families. The results from the fresh water study, describing baseline variations in sensitivity and a bioassay protocol, have been submitted for publication. Further experiments are necessary before the results from the warm water study can be submitted.

For emamectin, the focus has been on several ion channels. The researcher working on this task has been on maternity leave for most of 2017, thus the progress has been limited.

From the Integrated Pest Management project, one publication on resistance selection by azamethiphos and deltamethrin was published in 2017. The PhD student visited Dr. Crawford Revie and Dr. Gregor McEvan at the University of Prince Edward Island, Canada, to learn more about mathematical modelling in 2017. A collaborative study using data from BarentsWatch and several other sources has been initiated. A publication regarding correlations between sensitivity, doses and efficacy of hydrogen peroxide against salmon lice in the years 2013–2017 is in preparation.

**Dispersal of resistance**

In collaboration with IMR, NTNU (Ålesund group) and Patogen AS, two new studies on the dispersal of resistant lice have been published by the SLRC in 2017. The first of these studies demonstrated that lice collected from wild salmon and sea trout in Norway had a high frequency of the Phe362Tyr mutation which causes resistance to organophosphates (Fjørtoft et al., 2017). For lice captured on sea trout, the frequency was “identical” to the frequency observed on lice collected from salmon in neighboring net pens. As development of resistance is driven by the use of chemicals to treat fish in net pens, this work therefore unequivocally demonstrates, for the first time, that the primary source of infection from sea lice, over time, comes from farmed salmonids in farming regions of Norway. It also
shows that lice on wild salmonids cannot be regarded as a reservoir of chemical-sensitive lice. In the second study, a set of spatial and temporal lice samples throughout the Atlantic were genotyped for the Phe362Tyr mutation in order to investigate development and dispersal of this mutation in time and space (Kaur et al., 2017). Analyses revealed that this mutation existed in lice in very low frequency prior to use of organophosphates in aquaculture, and that it was selected for in multiple regions simultaneously as and where the chemical was used.
WP2: Anti-attachment

Principal Investigator: Stanko Skugor, EWOS

The work on the development of phytogenic-based functional feeds that target two species of lice (*L. salmonis* and *C. rogercresseyi*) continued during 2017; *In Vivo* feeding and challenge trials were performed at two Cargill/EWOS Innovation research locations (Colaco, Chile and Dirdal, Norway) while most of the *In Vitro* trials were done in Chile.

During 2017, a number of novel phytogenic ingredients were acquired and tested. Selection of candidate phytogenics for *In Vivo* trials was based on their putative mode of action and *In Vitro* findings. Masking the smell and/or taste of the Atlantic salmon host by feed has previously been shown to interfere with the host recognition and settlement, hence it remained an important line of research within the work package. Lice infections have also been associated with immunomodulatory mechanisms that ensure their persistence on the host. Building further on this knowledge, we proposed and tested the hypothesis that masking host’s olfactory properties by feed reduces the propensity of lice to immunomodulate.

Several candidate ingredients were tested for their ability to modulate other protective responses. The most well studied endogenous mechanism of protection involves host’s immunity. However, a lot remains to be learned. It has previously been shown that immune responses of Atlantic salmon can be appropriately stimulated by feed, away from Th2 immune responses and towards the more protective Th1 (or Type 1) immunity, which results in the active rejection of parasites. Going forward, it will be important to further delineate factors that control the competition between these two pathways in salmon, and how they can be modulated by feed.

Phytogenic ingredients with novel modes of action were also explored during 2017. It is expected that by combining phytogenics with different modes of action a synergistic effect will be achieved, thereby resulting in further reduction of the number of attached lice.

**In Vitro / Ex Vivo methods and assay techniques**

*In Vitro* In Vitro methods are higher throughput and are less expensive than *In Vivo* lice challenge trials. We have established different *In Vitro* and *Ex Vivo* methods, and results obtained from these tests have been helpful in indicating the potential mode of action of a novel phytogenic. A combination of established *In Vitro* tests has also been used to prioritize phytogenics for further studies.

In 2017, LD50 and the *C. rogercresseyi* frontal filament assay were used to evaluate several single ingredients and mixtures of ingredients. Briefly, frontal filament assay is based on the ability of copepodids of *C. rogercresseyi* to extrude their frontal filament (used for attachment to the host) when Atlantic salmon mucus is added to the solidified substrate of agar that is covered by a thin layer of seawater. In the absence of Atlantic salmon mucus, or in the presence of mucus combined with the phytogenic ingredient that has anti-lice properties, lice do not extrude their frontal filament.
An in Vitro frontal filament assay was used to evaluate the mixture of essential oils that was planned to be tested in the In Vivo challenge trial. The mixture containing specific proportion of different essential oils with the highest inhibitory ability was outlined as most promising for the In Vivo trial. Promising In Vivo results has been achieved in 2017 in Dirdal, Norway, which will be further explored. The Ex Vivo fin tissue assay will be used to explore the mode of action of the phytogenic ingredient. This will require that a number of fish is fed by the phytogenic-enriched feed and control feed for two weeks prior to removing pectoral fins and incubating them with copepodids of L. salmonis. Reduced numbers of lice settled on the test fins suggests that the phytogenic feed acts in the early phases of lice attachment.

are higher throughput and are less expensive than In Vivo lice challenge trials. We have established different In Vitro and Ex Vivo methods, and results obtained from these tests have been helpful in indicating the potential mode of action of a novel phytogenic. A combination of established In Vitro tests has also been used to prioritize phytogenics for further studies.

In 2017, LD50 and the C. rogercreseyi frontal filament assay were used to evaluate several single ingredients and mixtures of ingredients. Briefly, frontal filament assay is based on the ability of copepodids of C. rogercreseyi to extrude their frontal filament (used for attachment to the host) when Atlantic salmon mucus is added to the solidified substrate of agar that is covered by a thin layer of seawater. In the absence of Atlantic salmon mucus, or in the presence of mucus combined with the phytogenic ingredient that has anti-lice properties, lice do not extrude their frontal filament.

An In Vitro frontal filament assay was used to evaluate the mixture of essential oils that was planned to be tested in the In Vivo challenge trial. The mixture containing specific proportion of different essential oils with the highest inhibitory ability was outlined as most promising for the In Vivo trial. Promising In Vivo results has been achieved in 2017 in Dirdal, Norway, which will be further explored. The Ex Vivo fin tissue assay will be used to explore the mode of action of the phytogenic ingredient. This will require that a number of fish is fed by the phytogenic-enriched feed and control feed for two weeks prior to removing pectoral fins and incubating them with copepodids of L. salmonis. Reduced numbers of lice settled on the test fins suggests that the phytogenic feed acts in the early phases of lice attachment.

**In vivo methods**

Two In Vivo trials during 2017 have shown moderate efficacy of tested products.

Product tested against C. rogercreseyi showed statistically significant reduction of 17% in comparison to control feed, while the one tested against L. salmonis showed 20% reduction of total lice 5 weeks post infection (Figure 2.1).
Figure 2.1: Fish were fed three levels of the functional anti-attachment ingredient (low, medium and high). Number of salmon lice (*L. salmonis*) on Atlantic salmon 5 weeks post challenge was significantly reduced in the group fed medium dose compared to the control diet.

The product tested in Chile will not be pursued further due to difficulties around the regulatory aspects for this product. The phytogenic product that showed efficacy in Norway is on the list of approved feed additives, and so it has been further explored. Here, we aimed to address potentially novel modes of action of the phytogenic ingredient and endogenous mechanisms of protection. In addition to skin, we outlined gills as a tissue relevant for further investigation of protective mechanisms. RNA from gills of infected fish exposed to phytogenic test feeds and control feed has been screened for changes in gene expression by qPCR and GeXP, while RNA from skin of the same fish has been prepared for RNA sequencing.

In Vivo trial with the same phytogenic alone and in combination with other promising phytogenics will be completed by the end of April 2018 in Dirdal, Norway.

Previous comparative work between resistant Pacific and susceptible salmonids (Atlantic salmon) shed more light on the type of immune responses effective against lice. We maintained our interest in this area and contributed to it during 2017. Skin immunohistochemistry of coho and Atlantic salmon infected with *C. rogercresseyi* is ongoing and is expected to further increase understanding of endogenous protection mechanisms and how they can be stimulated by nutrition (Figure 2.2).
Positive color reaction in immune cells in skin below the louse

**Figure 2.2:** Histological images reveal a much smaller number of immunoreactive cells (coloured red) in Atlantic salmon (a) in comparison to coho salmon (b) in skin below the louse attachment site 14 days after infestation.

**Molecular methods**

Gene expression profiling remains as the main tool for evaluating fish and lice responses to functional feeds. Medium throughput GeXP profiling now relies on four multiplex sets (general, viral, bacterial and liver specific panel) of around 25 Atlantic salmon genes each. These panels cover genes involved in immune responses, lipid metabolism, iron regulation and other biological processes potentially implicated in endogenous protection mechanisms.

RNA sequencing of fish tissues from a promising *In Vivo* trial performed in 2017 in Norway is planned at the Norwegian Sequencing Center in Oslo.

Optimization of immunohistochemistry methods for two proteins previously not explored in coho and Atlantic salmon was successfully completed.

**WP3: Immunomodulation of the host**

**Principal Investigator: Øystein Evensen, NMBU**

WP3 addresses Immunomodulation of the host. The concept is that sea lice releases a series of secretory/excretory products (SEP) into the host tissue, via salivary glands to prevent strong inflammatory responses to infection. To better understand and design therapeutic intervention that can alleviate or counteract the effects of the secretory products, the underlying mechanisms of inflammation and anti-inflammatory processes must be understood. Further to this, immunoprophylactic measures have been studied over the last year with a focus on vaccines or vaccine formulations that reduce infection load after experimental challenge.
In vivo fish (Atlantic salmon) challenge with copepodid. Assessment and characterization of local responses to infection

Through collaboration between WP3 and WP4 (NMBU/UiB) the responses at early time post infection have been studied in fin versus skin compartments. Expression of immune genes at early time post infection were contrasted in the dorsal fin tissue and in skin samples, collected behind the dorsal fin. The purpose of these studies was to understand the early, contrasting responses in fin and skin tissue.

At 5 days post infection, Atlantic salmon smolts (n=5) were sacrificed and skin, fin, head kidney and spleen were collected from each fish. Real-time PCR was performed to investigate the local (fin and skin) and corresponding systemic (spleen and head kidney) inflammatory responses by assaying the expression of different inflammatory, cell and macrophage activation markers. In addition, immunohistochemical examination was performed to assess the presence of MPO (myeloperoxidase) and MIF (macrophage migration inhibition factor) positive cells in fin tissues.

Inflammatory markers were found upregulated in infected fin tissues when compared to controls.

![Figure 3.1: Inflammatory markers in fin, head kidney, skin and spleen in controls (non-infected) and lice-infected fish.](image)

Markers of macrophages were skewed towards a profile that includes iNOS production and high expression of IFNγ and TNFα.

By immunohistochemistry, significantly increased infiltration of MPO positive cells in the fins of infected fish while MIF remained unchanged. At early time post infection elicits there is a heightened inflammatory response in the fin while the skin shows down-regulation.
of the immune response. These findings contrast previous studies that showed immune dampening post lice infection in salmon. To what extent fin responses represent cues that guide the copepodids towards skin attachment remains to be shown.

Figure 3.2: Fin from Atlantic salmon, 5 days post infection, red cells MPO positive. Square in a) represents the magnified area in b).
**Vaccination and challenge experiment**

A vaccination and challenge experiment was carried out where parr of salmon were vaccinated with two injections of protein of defined antigens from sea lice, including whole sea lice preparations (minced sea lice). Proteins were formulated in water-in-oil emulsions and injected at 0.1ml per fish, intraperitoneal. Boost was done approximately 450–500 degree days post prime injection. Challenge was done 6 weeks after boost, approx. 60 copepodids/fish. The experiment was run as a common-garden setup with all groups kept in the same tank (no replicates).

At 4 weeks post challenge (pre-adult stage), the fish were sacrificed, and different stages of lice were counted.

The number of lice for the different categories is shown in figure 3.3.

**Fig. 3.3:** A) Number of sea lice (± standard error of the mean) for the different development stages in the different vaccine groups and controls (A, L, N) are shown. Average number of lice / group is shown in B). There are no differences between the different vaccine groups. The lowest number was seen in the adjuvant control (group N).
**WP4: Molecular parasitology – the basis for novel treatment methods**

**Principal Investigator: Rune Male, UiB**

The activity in WP4 covers three biological areas, Copepodid biology, reproduction & endo and exocrine systems. The research has been thematically wide, including mechanisms of perception and signal transfer, glands and excretory products, stress responses, energy metabolism, and molting gene expression and endocrine regulation. Some of these topics will receive continued or even increased attention in the last period of the SFI, while others will end. Vaccine development has received special attention. This work includes identification of candidate antigens, antigen production and vaccination trials and will continue as an important commitment for the last period of the center. This work has been done with close collaboration with WP3, WP5 and WP6.

**Molting: biology and endocrine regulation**

Molting is a finely tuned process that is necessary for the louse to grow. It must be highly regulated as building of the new exoskeleton take place at the same time as the old one is shed. A better understanding of the molting process and its regulation may open for new treatment methods.

A gene co-expression network has been constructed in WP5 to identify important regulators of molting. Experiments to validate both input from biological data as well as experimental validation have been performed. 17 RNAinterference targets predicted to have high impact on molting were tested in larvae. In a first trial, nauplia larvae were incubated with dsRNA to validate the degree of down-regulation with the dsRNA fragments produced. As nauplia undergo a molt to become copepodids, down-regulation of the target genes could also influence this molt. However, no unusual phenotype was observed. After completed efficiency, testing another trial will be conducted in the same way as the first experiment but in addition, with infection of salmon with the RNAi treated copepodids to study the chalimus molts.

We have established that the regulation of molting in salmon lice depends on several hormone receptors and gene regulatory mechanisms such as the Ecdyson receptor. This year the enzymes in the pathway of hormone synthesis have been studied (Sandlund et al 2018) and show that the intestine and reproductive tissues are most important in the production with some differences depending on sex and developmental stage. LC/MS methods are established to monitor levels of the relevant steroid hormones, and show that ponasteron A, expected to be of major importance from other studies, was only present in low amounts in adult animals and relatively more but still at low levels in larva (Sandlund 2018).

The ecdyson receptor is a main regulator of molting and is predicted to have a leading role in a network of regulators. The members of this network have been predicted and analyzed for their expression profiles through the molt cycle and functionally tested by
RNAi knock-down studies (Figure 4.1). One example, the gene regulator named FTZ-F1, appears as two isoforms in salmon lice. One isoform result in a molting arrest after RNAi knock-down in larva and a no egg strings phenotype after knock-down in adults (Figure 2, Figure 3). Larval development and adult female lice seemed unaffected when treating for the other isoform, which may have a function in male reproduction as judged from its cell specific expression. Similar experiments with gene regulators indicate a regulatory cascade that drives and determines the timing of the molting process.

Figure 4.1: a) Pre-adult salmon lice show substantial instar growth, which is for the most part limited to the genital segment. By taking measurements of the louse, individuals can be separated based on a ratio between the length of the cephalothorax (CT) and length of the entire animal (TL). This ratio represents the instar age of the individual louse. b) Measuring the expression of candidate genes and plotting it against the CT/TL-ratio, reveals how the expression is regulated within a developmental stage. This graph shows the expression profile of a nuclear receptor believed to be involved in reproduction and molting within a molt cycle.

Figure 4.2: RNA interference of a nuclear receptor results in molting arrest. Larvae at the nauplius 1 stage were treated with a dsRNA-probe specific for a nuclear receptor. a) The resulting nauplius 2 were unable to molt to the copepodid stage and appeared to be trapped alive inside their old exoskeleton. b) Control larvae developed normally into copepodids after being subjected to a non-salmon louse specific dsRNA-probe.
Figure 4.3: RNA interference of a nuclear receptor involved in the ecdysone regulatory cascade regulating reproduction. Female pre-adult two were injected with dsRNA targeting a nuclear receptor believed to be involved in regulating reproduction in the salmon louse. The resulting adult females (left image) were unable to produce egg strings, while control lice injected with dsRNA unspecific for salmon louse transcripts were unaffected (right image).

Chitin is a major component of the louse exoskeleton. To molt, the salmon louse both produces new chitin in addition to recycling of chitin from the old exoskeleton. Molecular characterization of six enzymes involved chitin synthesis was performed. All the enzymes were conserved and show large similarities to enzymes in other species. Functional studies of chitin synthase 1 and 2 were initiated by dsRNA knock-down and development of a molecular assay for enzyme and inhibitor activity. This assay may also be used to detect enzyme inhibitors that could be used in chemical treatments against the parasite.

RNAi project
Based on advice from the SAB and discussion in the board, an extended activity receiving additional funding from some of the SLRC partners on exploring RNAi as a possible treatment was initiated in 2017. RNAi has been used as a research tool for several years but the idea for the present project is to explore ways of delivering the RNAi through the host to induce gene silencing in the salmon louse. The project is made as a PhD project and a PhD student has been working on the project from August.
Reproduction; germ cell differentiation and maturation

Salmon lice have a high reproductive capacity, meaning that one individual can produce a high number of offspring. In the case of salmon lice, every egg string can produce more than 200 new lice and a female produce new egg strings continuously as new egg strings are released short time after the old pair has hatched. The large production of larvae is a major challenge in the management of salmon lice in aquaculture. Further understanding of reproduction and potential tools to limit it, is therefore crucial to manage the parasite in a sustainable manner.

Most studies of reproduction in salmon lice have focused on females. Males produce spermatoophores, which are transport vessels for male sperm cells and are attached to the females by the males during mating. We have identified several key genes that are important in male reproduction. Some of these genes belong to a new gene family that has not been described in any other species before. The family was named Mucin-like spermatoophore wall proteins (MLSWPs). The MLSWP-genes are active in sperm ducts of males and produce proteins that are present in a very high concentration in the inner spermatoophore wall. When the genes were silenced by RAN interference, the affected males produced spermatoophores that were missing their inner wall. Females that were kept together with these males did not obtain any spermatoophores by the males, thus the gene knock-down of the MLSWPs made the males infertile (Figure 4.4). Further work is necessary to translate these results into an applicable salmon lice treatment.

Figure 4.4: Genital segment of a female that has been kept with males with deactivated MLSWP-genes: Yellow cement is present, indicating a mating attempt, but spermatoophores are missing.
Immunomodulation and exocrine systems in sea lice; characterization and function at host infection.

A detailed morphological and functional study of exocrine glands has been published previously. Further morphological and molecular studies of labial glands, the gland type secreting into the oral cavity of the louse, have continue with an important goal to identify new vaccine targets. Thereby, RNA sequencing has been conducted to identify genes expressed by the labial glands. Interesting candidate genes have been sequenced and confirmed to be localized to the salivary glands. Furthermore, knock-down studies with subsequent infestation trials and tissue sampling was done to analyze the potential effect the gene products have on the salmon immune and clotting response.

Among the exocrine gland transcripts, a heme peroxidase was identified that catalyzes $\text{H}_2\text{O}_2$-dependent oxidation of a wide variety of substrates. Heme peroxidases are involved in different processes including the innate immune response, hormone and prostaglandin synthesis. However, the isolated heme peroxidase showed similarity to chorion peroxidases and proteins involved in cuticle hardening or adhesion. Knock-down in nauplius larvae decreased the swimming activity of emerging copepodids. Histological analysis of knock-down animals showed changes in muscles, subepithelial and exocrine gland tissue. We speculate that the studied heme peroxidase may have a role in crosslinking molecules of salmon louse ECMs (Øvergård et al 2017).

Prostaglandins excreted by parasites are known to modulate the immune system of the host in the host-parasite interaction. Prostaglandins have also been detected in salmon lice excretions and are one of the few known candidates for host modulation by the salmon louse. Earlier studies by the SLRC of the salmon louse prostaglandin synthesis was therefore extended and included analysis of two additional potential prostaglandin E2 synthases (PGES) identified by bioinformatics analysis (WP5). These synthases have been sequenced and knock-down studies have been conducted with subsequent infestation studies and...
sampling of salmon skin to study their potential immune modulatory effect (Figure 4.6). However, the studies indicated that prostaglandins are not involved in immune modulation, as previously indicated (Eichner et al. 2015).

Gland secretions from parasites are not only important for the host-parasite interaction, but also for lubrication and antifouling of the exoskeleton. In *L. salmonis*, two gland types have been suggested to secrete anti-fouling substances, namely tegumental (teg) type 1 and 2 glands where teg 1 glands are the most abundant. Knowledge about these exocrine gland types is however limited. To obtain more information about the role of the glands, three genes (LsFNII1, 2 and 3) containing multiple fibronectin type II (FNII) domains highly expressed in teg 1 glands were examined (Harasimczuk et al. 2018). LsFNII domains are unusual in this type of animal and the functional role of the domains is not certain but is possibly involved in collagen binding.

Localization studies in salmon lice of the three gene transcripts showed expression in teg 1 glands only, with highest expression in pre-adult and adult lice, correlating with the developmental increase in the number of teg one glands. LsFNII1, 2 and 3 were successfully knocked-down by RNAi, however; this did not lead to changes in the morphology of the glands, the surface of the exoskeleton or infestation success. Investigation of further fibronectin type II (FNII) domain-containing proteins will continue in 2018.
Novel treatment targets
A study of gene expression by transcript sequencing has revealed distinct patterns of expression in larval stages, not only detecting differences between stages but also depending on age within each stage. These results give an important understanding of the natural variation in transcription between and within stages. This variation is important to consider when sampling of sea lice (Eichner et al. 2017). Heme and iron metabolism are recognized as very important, and as the salmon louse is unable to synthesize heme by itself, it is completely dependent upon its host for supplies. A potential heme receptor has been found in the intestine of the salmon louse. The transcript and protein were detected using in situ hybridization and immunohistochemistry. A functional study was performed by RNA interference where the transcript was knocked-down. This knock-down resulted in shorter egg strings and a lower hatching success of the offspring from the knock-down group (Figure 4.7). Additionally, the knock-down group has significantly less heme than the control. A starvation experiment has also been conducted to investigate the effect on the mRNA levels of the heme receptor. Increased starvation caused a decrease in the mRNA levels. All of these results are used in a manuscript, which will be published in 2018. The putative heme receptor is included as antigen in vaccine trials.

Vaccine development has continued in 2017. The work has included identification of antigen candidates and subsequent evaluation by RNAi. A new clinical trial started at LiceLab (WP6) in September 2017 and will be terminated early 2018.

Figure 4.7: Adult louse phenotype after knocking-down the heme receptor by RNAi. Louse 1 is a control louse, and lice 2–5 are representative knock-down animals.
New medicines and strategies for parasite control

Induced stress has been introduced as a method in treatment to control salmon lice where manipulation by temperature and osmolality that have been applied. However, there is little knowledge on the mechanisms and effects of induced stress in salmon lice. Therefore, thermotolerance and stress response of salmon lice was tested. Nauplii larva acclimated to 10 °C were shown to survive heat treatment up to 30 °C. The salmon louse genome was examined for transcripts coding for heat shock proteins (HSP) and tested if they are induced after heat shock, change in salinity or treatment with hydrogen peroxide, employing microfluidic qPCRs. A total of 38 candidate genes were tested, representing small HSP, HSP40, HSP70 and HSP90 families. Of these, nine genes were induced after a non-lethal heat shock, while three genes were induced by low salinity and two genes responded to incubation in hydrogen peroxide (Borchel et al, 2017). These results provide the basis for further work on the stress response in salmon lice.

Na+/K+-ATPase has a key function in a variety of physiological processes including membrane excitability, osmoregulation, regulation of cell volume, and transport of nutrients. The Na+/K+-ATPase is a large protein with high sequence identity to other invertebrate and vertebrate species and it is expressed in a wide variety of tissues. Transcript knock-down by RNAi resulted in muscle degeneration in larval stages, severe changes in the oocyte formation and maturation in females and abnormalities in tegumental glands. In conclusion, the Na+/K+-ATPase activity may be further investigation for its role in development and regulation for development of new treatment strategies (Komisarczuk et al 2018).
WP5: LiceBase

Principal Investigators: Michael Dondrup and Inge Jonassen, UiB

Within work-package 5, we are developing LiceBase, a database of genomic resources relevant for sea lice research and research on related species, with a special focus on supporting functional genomics experiments, such as RNA-interference.

Access to LiceBase is instrumental to understanding the biology of the salmon louse

The aim is to develop LiceBase into the primary online-resource for sea lice research, by constantly upgrading it and integrating new data and functionality. It is also an aim that the resource is of interest outside the sea lice louse research area. The primary focus is to achieve excellence in data coverage and presentation, combined with ease of use to create relevance for the user community.

In addition, WP5 provides state-of-the-art bioinformatics support to all projects within the SLRC including analysis of high-throughput sequencing data and general bioinformatics resources. In the long term, we are aiming at achieving an impact on the sea lice research community and beyond, comparable to that of other larger model organism databases such as FlyBase or WormBase have on their respective communities. Since 2014, LiceBase has also been an international deliverable of the Norwegian Node within ELIXIR, the European infrastructure for bioinformatics.

LiceBase web portal

The LiceBase portal is a web-application operating on our servers making heavy use of virtualization infrastructure at the Computational Biology Unit (CBU). It provides a convenient interface to the underlying genome sequences and annotation data through an easy to use portal including support for browsing and searching for specific genes and their functions. The portal infrastructure is based on free open-source software. The core components are the community portal, which is based on the open source content management system Drupal and its genomics extensions, Tripal, the genome browser GBrowse and a Blast interface. The community portal contains a laboratory information management system (LIMS) for the annotation and retrieval of functional genomics experiments using RNA-interference (RNAi) which is highly used by members of the centre. The server has been in service since 2014 and is within the ELIXIR service delivery plan. The server is freely available at https://licebase.org.

By the end of 2017, there were 251 annotated RNAi experiments in LiceBase, out of which 51 were available to the public. It is the intention to increase the utility and visibility of LiceBase for users internationally, also outside the sea louse domain, by granting access to more experimental data. In a first attempt, we have made available data on all RNAi experiments performed prior to 2014, making 25 additional experiments public. More data will be made public subsequently in the course of 2018.
In the course of 2017, we have enabled a tracking system to collect data about key performance indicators and to establish a quality assurance system for the service.

Key performance indicators are for example the number of users, the geographical distribution of users, number of page visits, session duration, and the amount of curated data available. Our current implementation relies on Google Analytics, but this system will be replaced with a local installation in the course of 2018 (Fig. 5.2). According to the tracking data, there have been nearly 9000 page views since April 2017, when the engine was activated, and approximately 800 unique users. Most views originate from Norway and USA. Returning visitors account for over 60% of user sessions and spend on average 8m:29s interacting with the site. To collect such data and to establish such process is also a requirement of the ELIXIR service delivery plan for node-funded services. We are very positive about the utility of establishing a formal quality assurance process and an expected positive impact on the long-term success and availability of the SLRCs core data resource, also after the end of center’s funding period.

**Modeling and Data Analysis**

An important task has been facilitating the analysis of a large transcriptional time-series experiment performed using RNA-sequencing, taking into account that the developmental rate of salmon lice on the host is not uniform requiring proper sampling techniques. In this study, a total of 66 RNA-seq samples were analyzed. The study was submitted in 2017 and is expected to appear early in 2018 the corresponding data have been uploaded to LiceBase and been made available in SRA (Bioproject PRJNA413461). A second and even larger set of RNA-sequencing samples has been analyzed in 2017 and is likely to be published within 2018.

Members of WP5 have been further involved in the discovery of new potential targets of drugs and vaccines. We have maintained close collaborations with our industrial partner Elanco on the adaptation of a pipeline for discovery of new vaccine targets for vaccine trials conducted at the SLRC. Identification of possible vaccine targets has included filtering by various parameters such as their expression in intestine or glands, sub-cellular localization, and specifically their association to membrane. A tracking system for vaccine candidates has been implemented in the LiceBase portal. The system allows for expert review of selected candidates. Computational identification of promising vaccine targets is far from trivial. Factors representing a large challenge include the lack of measurements of MHC complex binding affinities for non-model organisms, and the lack of knowledge about the immunogenic potential and the viability of immunoglobulin in the intestinal environment that is essentially controlled by the parasite. Our aim is to engage in the design of experiments to elucidate the molecular mechanisms of host-parasite interactions. Based on the investigation of existing tools such as IEDB MHC-1 and MHC-2 and reverse vaccinology pipelines, for example Vacceed, we advise for caution when attempting to transfer results from e.g. MHC affinity prediction tools calibrated on few mammalian model organisms to the salmon.
With respect to target prediction, WP5 has been instrumental in the discovery of a cryptic pathway mediating intestinal heme uptake together with WP4. Heme is an essential co-factor of many important proteins and involved in many important pathways such as gas transport, stress response and cellular respiration. How intestinal heme uptake is mediated, is very poorly understood even in vertebrates. The salmon louse is an obligatory heme auxotroph, which we could show by pathway reconstruction. Therefore, it needs a pathway to take up heme from the blood-filled intestine. By analyzing gene clusters and gene-expression data, we have predicted hypothetical candidates for this function, which we further characterized in-silico by reconstruction of the protein 3D structure and by docking with the molecule protoporphyrin IX (the heme precursor to without the iron atom) as ligand (Fig. 5.2). Docking studies showed a viable binding pocket for heme with similar affinity as native heme-binding proteins. By successful candidate selection by bioinformatics methods, we significantly reduced the number of candidates to test and thereby the workload of experimental validation. We expect the results to be published in 2018. Members of WP5 have also been involved in the reconstruction and analysis of the chitin synthesis pathway, which is another joint effort with outcome to be published in 2018.

The automatic selection of knock-out targets is another core topic in WP5. To achieve this we are building the Atlas of gene-expression, which essentially is based on gene networks resulting from the analysis of various data. Our primary interest has been on the improvement of target selection for RNA-interference. If automated predictions of target genes could be made that improve the chances of seeing a phenotype in an RNAi experiment, even slightly, this would have a large impact on the experimental effort required for target discovery. Therefore, we have constructed a variety of gene co-expression networks and analyzed their topology to identify potential hub genes involved in regulatory control of the molting cycle. From the analysis, RNAi has selected a list of 17 high-scoring candidates for further characterization of their phenotype. If successful, the network analysis will be made available in LiceBase and have a high impact on future gene prioritization of the parasite.

Figure 5.1: In-silico analysis of the putative heme receptor. The optimal 3D model (by i-TASSER) is depicted in ribbon representation with predicted secondary-structure (loop, helix, and sheet) and transparent surface. Amino acids forming a hydrophobic heme-binding pocket are colored in red. A heme molecule is shown in dark-red at its predicted binding-site inside the pocket (AutoDock Vina).
**Figure 5.2:** Google analytics report of LiceBase showing an overview of interaction statistics. The number of page-views per week is depicted for the period April 1 (activation of analytics module in LiceBase) to December 31, 2017.
WP6: LiceLab

Principal investigators Sussie Dalvin, IMR, and Lars Are Hamre, UiB

LiceLab provides state of the art infrastructure and expertise for the SLRC to study sea lice and host parasite interaction. The Lice lab facilities are located at the University of Bergen, at the Institute of Marine Research, and at EWOS Innovation in Dirdal. These facilities have a unique capacity to study sea louse biology, to perform large-scale efficacy assays and RNAi experiments as well as capacity to cultivate material for research and to maintain lice strains with specific properties. This is of vital importance to:

- obtain detailed knowledge of sea lice biology to identify points of attack
- efficiently evaluate new candidate medicines
- effectively screen vaccine candidate targets and evaluate test vaccines
- identify drug resistance mechanisms and establish tools to determine optimal use of medicines
- evaluate effects of non-medicinal methods

The activities in WP6 are divided in four main areas:

Sea lice lab facilities
Production of sea lice strains and experiments
RNAi screening
Production of lice and experiments at EWOS facilities
Sea lice lab facilities
The wet lab area at UIB was rebuilt in 2017 providing a new room serving as a combined hatchery/dry lab. The old hatchery will be fitted with 24 single fish tanks.

Production of sea lice strains and experiments
A total of nine sea lice strains were maintained in 2017, hereunder two Caligus elongatus strains, three chemical-sensitive salmon lice strains, one inbred strain and strains resistant to various medicines and/or multiresistant strains. Material for in vitro experiments and RNA and DNA purification was produced and sampled for academic partners in Bergen and Oslo. In total, LiceLab has served about 35 researchers, PhDs and master students with material for ongoing research.

Salmon lice viruses are present at a prevalence close to 100% in lice sampled along the Norwegian coast, and thus also in our laboratory strains. Considering their omnipresence, these viruses must be considered an integral part of the total biology of the salmon louse. As other collaborating research groups identify new viruses, we screen our strains so that we have an overview of the status of the strains of lice we work with. The interactions between sea lice, their viruses and the fish host are assessed in collaboration with the ParaFishControl project. This allows us to assess whether the viruses may affect the outcome of other studies taking place in the Centre and improve our experimental control.

A new feature of salmon louse anatomy was discovered and work to describe this has been initiated in collaboration with partners at NMBU.

A trial testing 13 candidate vaccines was started in 2017, and is scheduled for termination early 2018. All candidates were identified at the SLRC and validated as potential vaccine targets by RNAi screening. The experiment assesses the potential effect of the vaccines on infection and development success of salmon lice until the preadult 1 stage in a common garden design. Vaccine effects, potentially acting on life processes among preadults and
adults is assessed in single fish tanks. This provides a complete overview of the loss from each individual fish in the second half of the salmon louse growth phase and the first part of its egg production phase. Finally, hatching and development success of eggs will be evaluated for each female in individual continuous flow incubators.

**RNAi screening**

Silencing or knock-down of a gene through a molecular technique named RNA interference (RNAi) can provide crucial information about biological role of a protein. RNAi is accomplished by introduction of double-stranded RNA into salmon lice either by soaking or direct injection. After incubation in which the level of the targeted gene product is lowered (2 to 40 days) the effects of the silencing are assessed by inspection of the treated lice: whole animals and in some cases sections of these are inspected. Effects can range from changes in development, lack of reproduction, decreased digestion to behavioural changes and mortality. At the SLRC, this technique is used as a medium-throughput tool to evaluate targets for vaccines or alternative treatments. Two types of RNAi screens were carried out in the wet lab; I) RNAi in nauplius and II) RNAi in preadult and adults. Evaluation of RNAi screens from 2017 is ongoing, and results for specific genes is reported in WP4. An overview of all experiment and results obtained is summarized in the table below.

<table>
<thead>
<tr>
<th>Year</th>
<th>Method</th>
<th>Total RNAi screen</th>
<th>Total gene targets</th>
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_Table 6.1:_ RNAi screens performed at the SLRC. Total RNAi screens reflect the total number of fragments injected or incubated. Total gene targets: this number shows how many different genes have been tested, i.e. total numbers minus controls and replicated experiments.

**Production of lice and experiments at CARGILL facilities**

The salmon louse hatchery has been moved away from the part of the Sea Lice Lab where the experimental fish tanks are kept to provide more space for additional fish tanks. All hatchery related work now takes place outside of the Sea Lice Lab, which reduces time spent around fish tanks and fish stress during challenge trials. The hatchery has been made bigger and with the ability to use two different water temperatures. This allows us to synchronize hatching of mature and immature egg strings.
ASSOCIATED PROJECTS

Most of the new projects applied for are linked to the SLRC as associated projects. New projects are not a formal part of the defined work within the consortium, and of the projects have partners from the centre, others have both the SLRC and other external partners.

The table shows a broad variety in sources of funding and two of the associated projects are presented.

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<tr>
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<td>2 642 429</td>
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<td>9 363 610</td>
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**ParaFishControl**

ParaFishControl is an EU Horizon 2020 funded research and innovation project, aiming to develop advanced tools and research strategies for parasite control in European farmed fish (www.parafishcontrol.eu). Participating in the project are public research and education organizations, private research institutions and small to large enterprises from 13 European countries. In total, 29 partners are working with 17 different parasitic species and seven different fish species. The University of Bergen takes part in research involving the salmon louse, and are looking at the host-parasite interaction by means of salivary gland proteins and viruses replicating in salmon lice glands.

Five salivary gland proteins with unknown function have been studied in the salmon louse. They are short proteins, mostly with signal peptides that are expressed in the salivary gland during its parasitic stages. Three are highly expressed at the time of attachment, while four are only/also highly expressed in pre-adult and adult stages. They have been fully sequenced and RNAi studies have been conducted (Fig 1 A–C). Three of these proteins have been knocked-down in copepodids and infestation studies have indicated an immune modulatory role for these three proteins (Fig 1 D). Further studies are planned to repeat and for the unknowns highly expressed in adults.

Rhabdovirus infections in salmon lice have been studied. We have developed a method to cure a cohort of lice for two *L. salmonis* rhabdoviruses (LsRVs) by the introduction of dsRNA. Three strains of lice have been established from a common origin, one with both
viruses, one with only one of the two viruses and one that are virus free. Further, we have infested fish with these strains to see if it affects survival, development and reproduction capacity of the lice and if they modulate the immune response of the host. No effect on survival and reproduction was seen, but some increase in inflammatory genes were seen in fish infested with rhabdovirus free lice (Fig 2). The inflammatory response is important for louse clearance, and the present results suggest that LsRV infections can be beneficial for lice by dampening inflammation.

**Figure knock-down:** A–C) Knock-down of three genes of unknown function expressed by the salivary gland in early lice stages. D) Knock-down copepodids were allowed to infest fish, and samples were taken 36 day degrees post infection (copepodid stage) of salmon skin. Interleukin (IL) 8 mRNA level were measured.
**Figure L. salmonis rhabdoviruses:** A–B) Localization of two *L. salmonis* rhabdoviruses (LsRVs) in the salivary gland of the salmon louse. C–D) Infestation studies with LsRV free (LsVF) and LsRV infected (LsV) lice strains. Skin samples were taken from attachment site of lice, and IL1β and IL8 mRNA levels were measured.
Resistance to hydrogen peroxide in salmon lice

This project is a collaboration between a biotechnology company (PatoGen AS), a university (NMBU, Faculty of Veterinary Medicine), a fish health service (Aqua Kompetanse AS) and two aquaculture companies (Marine Harvest AS and Sinkaberg-Hansen AS). It aims at refining hydrogen peroxide (H$_2$O$_2$) bioassays, further developing high-capacity molecular biology resistance diagnostic methods, estimating selection pressures for different treatment scenarios, and implementing knowledge in the companies’ action plans against salmon lice.

In 2012, reports of individual cases with reduced H$_2$O$_2$ treatment effect from central Norway began to emerge (Helgesen et al., 2015). The problem is growing and in 2017, almost full sensitivity has been reported from northern Norway. To monitor and control resistance development, effective and sensitive monitoring methods for resistance development must be established. Shortly before the start of the project, the university partner found that resistance to hydrogen peroxide was associated with increased expression of the enzyme catalase in resistant populations (Helgesen et al., 2017). This finding was patented by PatoGen AS and a molecular assay was developed.

In 2017, the focus has been on identification of additional markers that are also differentially regulated between resistant and sensitive parasites (RNAseq survey). Several genes displaying a significant differential expression were identified, and validation of their strength and importance is still ongoing. A H$_2$O$_2$ selection experiment has been initiated. Preliminary results show that lice could develop further resistance after several H$_2$O$_2$ exposures.

Figure adult lice: Adult female salmon lice exposed to H$_2$O$_2$. Left panel, immobilized louse. Right panel, immobilized louse with inner gas bubbles
Functional studies on the mode of action for hydrogen peroxide have also been carried out. The results showed that the compound had an almost immediate immobilizing effect on sensitive parasites, later followed by development of gas bubbles that subsequently disrupted the tissue structures inside the parasite. When immobilized parasites are transferred to seawater not containing $\text{H}_2\text{O}_2$, they can recover within 1–3 hours post-exposure. Lice with extensive inner damage due to gas bubbles cannot recover however. Differences in the response to $\text{H}_2\text{O}_2$ were found between genders, stages and lice strains. The effect of temperature in the lice response to $\text{H}_2\text{O}_2$ was also studied. It showed that salmon lice withstand significantly higher concentrations of hydrogen peroxide at low temperatures (2–4 degrees) than at higher (10–12 degrees), both in vitro and in vivo. Collectively, these results will help to improve treatments in the field as well as the use of bioassays and molecular markers.

INTERNATIONAL COOPERATION

The SLRC and the individual partners are leading scientists within their field and are attractive for international collaboration. Well-established networks and collaborations have been further developed in 2017 through exchange of personnel and joint research projects. Mobility between Norwegian and Canadian scientists has been facilitated through the INPART project Cross Atlantic Sea Lice (CASL), where focus has been on students in addition to scientists. Activities at the SLRC have included exchange of laboratory procedures and performance of experiments in both the molecular and the wet-labs.

The young researchers in the SLRC have and continue to be encouraged to establish their own international network through participation in research projects and representation at international seminars and conferences.

In 2017, Canada and Chile have been the major countries for mobility and joint research projects, but there is also an increasing cooperation with other European research institutions.

Mobility in 2017

• Visit from Professor Thomas Van Leeuwen, University of Gent, to NMBU in November 2017 to initiate work on the mitochondrial electron transport chain in salmon lice.
• Elena Myhre Jensen, NMBU, visited University of Prince Edward Island (Dr. Crawford Revie and Dr. Gregor McEvan) for one week in October 2017. Collaboration on epidemiology and modelling initiated.
• Dylan Michaud, Visit from University of Prince Edward Island to UiB
• Sarah Purchell, visit from University of Prince Edward Island to UiB
• Kimberly Bouckaert, Erasmus student from Howest University, Belgium visiting UiB in the spring semester
• Monique Sarah Straub, IAESTE exchange student from ETH Zurich, Switzerland, visiting UiB September and October.
• Elisabeth Midtbø, visit from UiB to the University of Prince Edward Island
• Sussie Dalvin, visit from UiB to the University of Valparaiso and Universidad de Concepcion

In 2017, the SLRC has established a collaboration with University of Copenhagen, Denmark. Shared experiments have been performed in Bergen and analyzed in Copenhagen. The collaboration includes a one-year stay for a senior researcher in Copenhagen, starting in August 2017. Researchers at NMBU has a dialogue with Dr. Lucien Rufener at the Swiss company INVENesis Sàrl on electrophysiology. In addition, the established collaboration between NMBU and the Austral University in Puerto Montt, Chile on resistance development in *Caligus rogercresseyi* has been developed further.

A number of scientific and industry workshops in Norway, Canada, Chile and UK were held over the past 12 months where the information on functional feeds has been presented. In addition, the knowledge has been transferred through technical and marketing teams directly to the main salmon farming operations globally. The applied use of the anti-attachment functional feeds (ROBST) have contributed to improving sustainability of other control methods against sea lice. The Canadian GAPP project between Cargill, Atlantic Veterinary College and Memorial University on lice and microbial co-infections is ongoing.
Exchange to Canada
Elisabeth Midtbø, Masterstudent in Aquamedicine.

In the summer of 2017, I spent four weeks at Atlantic Veterinary College (AVC), University of Prince Edward Island (UPEI) in Canada. The exchange was a part of my master thesis, which I am taking in collaboration with the Sea Lice Research Centre. I also participated in the summer school 2017 “Advanced Techniques in Fish Health”, which is a part of the CASL project that encourages collaboration between researchers and students in Norway and Canada. The course consisted of a mixture of lectures, laboratory exercises and student presentations.

The stay was a unique experience for me, where I got to learn a lot from the researchers and students at AVC. The main focus of my stay was to practice different lab methods that I have later used for my thesis. I also had to practice some methods of my choosing, like sectioning and mounting of tissue. During my stay, I also got to see some differences between the institutions, and how the research is conducted. I also liked the experience I got from the sturgeons; previously I have not known much about them. Therefore, it was interesting to see the scientific focus around the sturgeon at the AVC.

I could see how devoted many people are to the research they are doing, and I am glad that I had the possibility to meet so many wonderful people. I have kept in touch with some of them, and they have been very helpful whenever I have encountered questions. My stay in Canada was a great possibility to see a broader perspective of aquaculture and the science behind it.
COMMUNICATION AND DISSEMINATION ACTIVITIES

Dissemination of research activities is a crucial part for the activities in the SLRC. Throughout the year, researchers and industrial partners have presented the SLRC activities at a broad range at international meetings and conferences. The Director of SLRC, Frank Nilsen, has been featured in various news channels both nationally and internationally.

The SLRC will be an important part of the Norwegian documentary “Den fantastiske villaksen” which will be shown at NRK in February/March 2018. During 2017 the center has also been an important contributor to the documentary on farmed salmon produced by the French Canal Plus www.canalplus.fr/infos-documentaires.

At national level, industry, authorities, private and public organizations and society in general, are interested in sea lice research and news from the SLRC. LicLab and the facilities for experiments on sea lice are interesting to visit for existing and potential collaborative partners for SLRC. A major task for the center is to explain about sea lice and the importance of its management and control. As examples, a delegation from the Portuguese Ministry of Research and Education visited the SLRC and UiB, where the purpose was to find new possibilities for collaboration in the area of marine research.

General information and results from SLRC are posted on the center’s website www.slrc.no

The highlights for dissemination of SLRC results in 2017

Seven Scientists from the SLRC participated at the 18th International Conference on Diseases of Fish and Shellfish arranged by the European Association of Fish Pathologists (EAFP) in Belfast, UK 4–8 September. The Director of the SLRC, Frank Nilsen, was invited to the conference as a keynote speaker in addition to chair the session on Sea Lice.

The conference was quite large, with 213 oral presentations in 3 parallel sessions, and with 238 posters. The topics were diverse, with sessions ranging from sea lice to fish immunity to viral diseases etc. Several representatives from the SLRC presented their work at the conference as talks and poster presentations. In addition to acquiring a lot of new knowledge about diseases of fish and shellfish, this is an important arena for making new networks and possibilities for future collaborative projects.
Andreas Borchel

I had the chance to visit the ICIRD-2017, the “Fourteenth International Congress on Invertebrate Reproduction and Development” which was taking place in Italy from August 28 to September 02, 2017. Luckily, the organization “International Society for Invertebrate Reproduction and Development” covered parts of the travel costs as part of a travel grant, which I was awarded based on the submitted abstract. Overall, the congress featured fourteen sessions on all aspects of invertebrate reproduction and development. Although this was not a conference specifically on sea lice or fish health, the topics of the conference were very relevant and important for my own sea lice research. Overall around 100 researchers gathered first in Naples for two days, then taking the train together to Florence for the second half of the conference. I presented my results in a symposium on crustacean biology and reproduction, which took place in the “Hall of the Five-hundred”, which was built already 1494 and contains a lot of artwork. Being a tourist attraction, the presentation took place in a very special, probably unique atmosphere, with science-interested researchers in the audience in the foreground and art-interested tourists in the background. The presentation was well received and the concluding discussion yielded several new ideas for future work. An additional highlight of the conference was the presence of the two Nobel laureates Martin Chalfie and Tim Hunt who shared their stories of how they won their Nobel prizes, which were quite inspiring. In an event especially for PhD students and postdocs, all kind of questions could be asked and were answered by the Nobel laureates. Overall, participating in this conference was a very interesting and rewarding experience.

During 2017, parts of the UiB building facilitating SLRC has been renovated. SLRC has contributed with several photos of sea lice to a collage decorating the entrance. The collage symbolizes the marine activity at UiB where SLRC is an important part.
Summary of dissemination activities in 2017

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RECRUITMENT

Two new PhD students have been recruited to the center in 2017, both through additional funding from the SLRC partners. One PhD is working with the RNAi project presented under WP4 and the second PhD student is developing results from trials on controlling reproduction of sea lice. This work is also a part of WP4.

Mats Solberg Solberg is an anthropologist who has observed the SLRC as a part of his doctoral research. The main topic of his work was to observe and describe the relationship between social organization and knowledge-production. Mads defended his thesis “Experiment, Cognition, and the Science of Salmon Lice” in October. Even if Mads is not an SLRC scientist, he was a part of the research environment during his PhD. Rich in knowledge, and with an impressive understanding of biology, he was a very welcome and inspiring part of social life and of scientific discussions in the Centre.
# Personnel Sea Lice Research Centre 2017

## KEY RESEARCHERS

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<thead>
<tr>
<th>Name</th>
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<th>Main Research Area</th>
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<tr>
<td>Frank Nilsen</td>
<td>UiB</td>
<td>WP1/WP4</td>
</tr>
<tr>
<td>Sussie Dalvin</td>
<td>IMR</td>
<td>WP4/WP6</td>
</tr>
<tr>
<td>Rune Male</td>
<td>UiB</td>
<td>WP4</td>
</tr>
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<td>Tor Einar Horsberg</td>
<td>NMBU</td>
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<td>Øystein Evensen</td>
<td>NMBU</td>
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<td>Simon Wadsworth</td>
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<td>Inge Jonassen</td>
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<td>Christiane Eichner</td>
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<td>Michael Dondrup</td>
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<td>Kevin Glover (Professor II)</td>
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<td>W4/WP6</td>
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<td>Peder Jansen (Professor II)</td>
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<td>Stanko Skugor</td>
<td>EWOS</td>
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## POSTDOCTORAL RESEARCHERS WITH FINANCIAL SUPPORT FROM THE CENTRE BUDGET

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<td>Kiranpreet Kaur*</td>
<td>01.01.17–01.08.19</td>
<td>Norwegian</td>
<td>F</td>
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<tr>
<td>Amr Gamil*</td>
<td>01.04.12–08.09.17</td>
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<td>Marit Bakke*</td>
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<td>Melanie Andrews</td>
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<td>South African</td>
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<td>Andreas Borchel</td>
<td>15.01.16–14.01.20</td>
<td>German</td>
<td>M</td>
<td>WP4</td>
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<td>Liv Sandlund</td>
<td>28.04.16–31.05.19</td>
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<td>F</td>
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<td>Helle Holm</td>
<td>01.04.17–31.03.19</td>
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* Researchers working at Post doc. level

## POSTDOCTORAL RESEARCHERS WORKING ON PROJECTS IN SLRC WITH FINANCIAL SUPPORT FROM OTHER SOURCES

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<td>Celia Agusti-Ridaura*</td>
<td>Spanish</td>
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<td>Anna Komisarczuk*</td>
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<td>01.01.17–28.02.18</td>
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<td>Aina-Cathrine Øvergård</td>
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* Researchers working at Post doc. level
### PhD Students with Financial Support from the Centre Budget

| Name                  | Nationality | Period          | Sex | Topic |
|-----------------------|-------------|-----------------|     |       |
| Mohammad T. Kahn      | Pakistani   | 28.08.12–25.03.17 | M   | WP4   |
| Ewa Harasimczuk       | Polish      | 01.05.13–05.06.17 | F   | WP4   |
| Zhaoran Zhou          | Chinese     | 01.02.15–31.01.19 | F   | WP5   |
| Erna Irene Heggland   | Norwegian   | 26.10.15–25.10.19 | F   | WP4   |
| Hulda Hardardottir    | Icelandic   | 26.10.15–25.10.19 | F   | WP4   |
| Elisabeth Gislefoss   | Norwegian   | 01.01.16–31.12.19 | F   | WP3   |
| Elena Myhre Jensen    | Norwegian   | 01.02.16–31.01.20 | F   | WP1   |
| Joao Barbosa          | Portuguese  | 07.08.17–20.10.20 | M   | WP4   |

### PhD Students Working on Projects in SLRC with Financial Support from Other Sources

| Name                  | Nationality | Period          | Sex | Topic |
|-----------------------|-------------|-----------------|     |       |
| Helene B. Fjørtoft    | Norwegian   | 01.05.14–30.04.18 | F   | WP4   |
| Joakim Brunet         | Norwegian   | 01.02.17–31.01.21 | M   | WP4   |

### Master Degrees

| Name                  | Nationality | Period          | Sex | Topic |
|-----------------------|-------------|-----------------|     |       |
| Elisabeth Midtbø      | Norwegian   | 2017/2018       | F   | WP4   |
| Yue Gao               | Chinese     | 2016/2017       | M   | WP5   |

### Technicians with Financial Support from the Centre Budget

| Name                  | Nationality | Period          | Sex | Topic |
|-----------------------|-------------|-----------------|     |       |
| Lars Are Hamre        | Norwegian   | 01.09.2011–      | M   | WP6   |
| Bjørnar Skjold        | Norwegian   | 01.07.2015–      | M   | WP6   |
| Per Gunnar Espedal    | Norwegian   | 01.09.2016–      | M   | WP6   |
| Heidi Kongshaug       | Norwegian   | 15.06.2012–      | F   | WP4   |
| Lourdes Tan (10%)     | Norwegian   | 01.01.2012–      | F   | WP2/ WP3 |
| Wei Zhang (50%)       | Chinese     | 01.09.2015–      | M   | WP5   |
| Daniela Dulgheriu (25%) | Romanesque  | 01.18.2015–      | F   | WP1   |
| Elisabeth Midtbø      | Norwegian   | 15.08.16–23.12.17 | F   | WP6   |
| Joao Barbosa          | Portuguese  | 12.09.16–11.4.17 | M   | WP6/ WP6 |
| Joakim Brunet         | Norwegian   | 01.12.16–31.01.17 | M   | WP4   |
### ADMINISTRATIVE PERSONNEL WITH FINANCIAL SUPPORT FROM THE CENTRE BUDGET

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<td>Ingunn Wergeland</td>
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### Accounts

**ALL FIGURES IN 1000 NOK**

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* Give names for each group of partners.
## SLRC Publications

### 2017

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<td>AC Øvergård, C Eichner, F Nilsen, S Dalvin</td>
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<td>KO Helgesen, MJ Bakke, K Kaur, TE Horsberg</td>
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<td>AZ Komisarczuk, S Grotmol, F Nilsen</td>
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<td>A screening of multiple classes of pharmaceutical compounds for effect on preadult salmon lice Lepeophtheirus salmonis Journal of Fish Diseases, 2016 Apr 1. doi: 10.1111/jfd.12463</td>
<td>PLOS ONE – accepted 22.05.2017</td>
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<td>E Myhre Jensen, Sevatdal, M Jørgensen Bakke, K Kaur, TE Horsberg</td>
<td>NMBU</td>
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<td>A selection study on a laboratory-designed population of salmon lice (Lepeophtheirus salmonis) using organophosphate and pyrethroid pesticides. PLoS ONE 12(5): e0178068. journals.plos.org/plosone/article?id=10.1371/journal.pone.0178068</td>
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<td>A Borchel, AZ Komisarczuk, A Rebl, T Goldammer, F Nilsen</td>
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<td>LE Robin Ljungfelt, MQ Quintela, FBesnier, F Nilsen, KA Glover</td>
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<td>A pedigree-based experiment reveals variation in salinity and thermal tolerance in the salmon louse, Lepeophtheirus salmonis Wiley Evolutionary Applications onlinelibrary.wiley.com/doi/10.1111/eva.12505/epdf</td>
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<td>K Kaur, F Besnier, K Glover, F Nilsen, VT Aspehaug, H Barretzen Fjørtoft, TE Horsberg</td>
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<td>The Phe362Tyr mutation conveying resistance to organophosphates occurs in high frequencies in salmon lice collected from wild salmon and trout. Scientific Reports 2017; Volum 7:14258. s. 1-10, October 2017 <a href="http://www.nature.com/articles/s41598-017-14681-6">www.nature.com/articles/s41598-017-14681-6</a></td>
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<td>K Glover, TJ Hansen, F Besnier, MF Solberg, PG Fjølidal, AG Eide Sørvik, S Dalvin, F Nilsen</td>
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| 10 | MT Khan, S Dalvin, F Nilsen, R Male  
Microsomal triglyceride transfer protein in the ectoparasitic crustacean salmon louse (*Lepeophtheirus salmonis*).  
Journal of Lipid Research 2017; Volum 58(8) s. 1613-1623, August 2017  
www.ncbi.nlm.nih.gov/pubmed/2860181 | IMR, UiB |
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RNAi-mediated treatment of two vertically transmitted rhabdovirus infecting the salmon louse (*Lepeophtheirus salmonis*).  
Scientific Reports 2017 Oct 25;7(1):14030. doi: 10.1038/s41598-017-14282-3  
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| 12 | F Nilsen, IH Ellingsen, B Finstad, PA Jansen, Ø Karlsen, AB Kristoffersen, AD Sandvik, H Sægrov, O Ugedal, K Wiik Vollset  
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www.regjeringen.no/ekspertgruppe_hovedrapporten_2017.pdf | UiB, IMR |
| 2016 | No | Publications |
| 1 | Celia Agusti, Sandra Bravo, Gustavo Contreras, Marit J. Bakke, Kari O. Helgesen, Cristina Winkler, Ma. Teresa Silva, Julio Mendoza and Tor E. Horsberg  
Sensitivity assessment of *Caligus rogercresseyi* to anti-louse chemicals in relation to treatment efficacy in Chilean salmonid farms  
Aquaculture, Volume 458, 1 May 2016, Pages 195–205  
sciencedirect.com/science/article/pii/S004484861630117X | NMBU |
| 2 | Aaen SM, Hamre LA and Horsberg TE  
A screening of medicinal compounds for their effect on egg strings and nauplii of the salmon louse *Lepeophtheirus salmonis* (Krøyer)  
Journal of Fish Diseases, 2016 Apr 1. doi: 10.1111/jfd.12462  
www.ncbi.nlm.nih.gov/pubmed/27038351 | NMBU, UiB |
| 3 | Aaen SM and Horsberg TE  
A screening of multiple classes of pharmaceutical compounds for effect on preadult salmon lice *Lepeophtheirus salmonis*  
Journal of Fish Diseases, 2016 Apr 1. doi: 10.1111/jfd.12463  
www.ncbi.nlm.nih.gov/pubmed/27037538 | NMBU |
| 4 | Kaur K, Jansen PA, Aspehaug VT and Horsberg TE  
Phe362Tyr in AChE: A Major Factor Responsible for Azamethiphos Resistance in *Lepeophtheirus salmonis* in Norway  
journals.plos.org/plosone/article?id=10.1371/journal.pone.0149264 | NMBU, UiB, PatoGen |
| 5 | Jansen PA, Grantrød NT, Tarpai A, Helgesen KO, Horsberg TE  
Surveillance of the Sensitivity towards Antiparasitic Bath-Treatments in the Salmon Louse (*Lepeophtheirus salmonis*).  
journals.plos.org/plosone/article?id=10.1371/journal.pone.0149006 | UiB, NMBU |
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<td>7</td>
<td>Liv Sandlund, Frank Nilsen, Rune Male, Sussie Dalvin</td>
<td>The ecdysone receptor (EcR) is a major regulator of tissue development and growth in the marine salmonid ectoparasite, <em>Lepeophtheirus salmonis</em> (Copepoda, Caligidae).</td>
<td>Molecular and Biochemical Parasitology, Volume 208, Issue 2, August 2016, Pages 65–73</td>
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2015

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www.sciencedirect.com/science/article/pii/S0014489414000484 | UiB, IMR

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Pacific and Atlantic Lepeophtheirus salmonis (Krøyer, 1838) are allopatric subspecies: *Lepeophtheirus salmonis salmonis* and *L. salmonis oncorhynchi subspecies novo* 
www.biomedcentral.com/1471-2156/15/32

7 Lina Eva Robin Ljungfeldt, Per Gunnar Espedal, Frank Nilsen, Mette Skern-Mauritzen, Kevin Alan Glover
A common-garden experiment to quantify evolutionary processes in copepods: the case of emamectin benzoate resistance in the parasitic sea louse *Lepeophtheirus salmonis*
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8 Christiane Eichner, Lars Are Hamre, Frank Nilsen
Instar growth and molt increments in *Lepeophtheirus salmonis* (Copepoda: Caligidae) chalimus larvae.
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12 Helle Holm, Nina Santi, Sissel Kjøglum, Nebojsa Perisic, Stanko Skugor, Øystein Evensen
Difference in skin immune responses to infection with salmon louse (*Lepeophtheirus salmonis*) in Atlantic salmon (*Salmo salar L*) of families selected for resistance and susceptibility Fish & Shellfish Immunology 
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Molecular characterisation of the salmon louse, *Lepeophtheirus salmonis salmonis* (Krøyer, 1837), ecdysone receptor with emphasis on functional studies of female reproduction 
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4 Dalvin, S., Nilsen, F., Skern-Mauritzen, R.
Localization and transcription patterns of LsVasa, a molecular marker of germ cells in
Lepeophtheirus salmonis (Krøyer). (2012).
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Dalvin, S., Mæhle, S., Kongshaug, H., Glover, K.
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Journal of Natural History, online Nov 2012

6 Nilsen, F.
Sea Lice Police

7 Horsberg, T.E.
Avermectin use in aquaculture.

2011

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Office Location: University of Bergen, Department of Biology, Thormøhlens gt. 55, Bergen
Postal Address: P. O. Box 7803, NO-5020 Bergen, NORWAY
Contact: Phone +47 55 58 44 00 / E-mail: post.slr@uib.no / slrc.no