

**2016-00979****Malmberg, Maja****Brg1606****Information about applicant****Name:** Maja Malmberg**Doctorial degree:** 2013-01-18**Birthdate:** 19820516**Academic title:** Doktor**Gender:** Female**Employer:** Sveriges lantbruksuniversitet**Administrating organisation:** Sveriges lantbruksuniversitet**Project site:** Biomedicin och veterinär folkhälsovetenskap**Information about application****Call name:** Annual open call 2016**Type of grant:** Future research leaders**Focus:** Future research leaders**Call for proposals subject area:** Formas**Project title (english):** Neurotropic viruses in pigs: the role in congenital disease**Project start:** 2017-01-01**Project end:** 2019-12-31**Review panel applied for:** Brg1606**Classification code:** 40303. Clinical Science incl. Anesthesiology, Diagnostics, Veterinary Nursing, Epidemiology, Surgery, Medicine, Reproduction, 40302. Pathobiology incl. Immunology, Microbiology, Pathology, Toxicology, Pharmacology, Food Safety, 10614. Developmental Biology**Application subject area:** 5103. 22.1 Djurhållning o veterinärmedicin**Keywords:** porcine, viral metagenomics, congenital disease, experimental infection, neurotropic virus**Funds applied for****Year:** 2017 2018 2019**Amount:** 1,024,000 1,065,000 905,000**Participants****Name:** Mikael Berg**Doctorial degree:** 1991-04-12**Birthdate:** 19590324**Academic title:** Professor**Gender:** Male**Employer:** Sveriges lantbruksuniversitet**Country:**Sweden**Name:** Magdalena Jacobson**Doctorial degree:** 2003-09-19**Birthdate:** 19581017**Academic title:** Professor**Gender:** Female**Employer:** Sveriges lantbruksuniversitet**Country:**Sweden**Name:** Juliette Hayer**Doctorial degree:** 2013-02-15**Birthdate:** 19850109**Academic title:** Doktor**Gender:** Female**Employer:** Sveriges lantbruksuniversitet**Country:**Sweden**Name:** Anne-Lie Blomström**Doctorial degree:** 2010-12-03**Birthdate:** 19780503**Academic title:** Doktor**Gender:** Female**Employer:** Sveriges lantbruksuniversitet**Country:**Sweden

Basic information

Number of project years*

3

Calculated project time*

2017-01-01 - 2019-12-31

Project title (Swedish, max 200 characters)*

Neurotrofa virus hos grisar och deras roll i kongenital sjukdom

Project title (English, max 200 characters)*

Neurotropic viruses in pigs: the role in congenital disease

Popular scientific description (Swedish) (max 4500 characters)*

Virus finns precis överallt och i enorma mängder. Det är dock endast ett fåtal av dessa som orsakar sjukdom. Tills väldigt nyligen har det inte funnits metoder för att studera alla virus i en viss miljö för att lära sig mer om hur de påverkar varandra, andra mikroorganismer, värdcellen och deras omgivning. Dock har moderna sekvenseringsmetoder nu gett forskare helt nya möjligheter att undersöka alla virus och det har gjort att vi kan ta oss an många nya frågeställningar.

Virus kan påverka värdjuret på olika sätt. Det vi oftast hör talas om är virus som orsakar allvarliga sjukdomar som t.ex. Ebola, MERS, och SARS eller mindre allvarliga men vanliga sjukdomar som influensa, vinterkräksjukan och förkyllningar. Virus kan även påverka indirekt och ett exempel på det är så kallade fager, det vill säga virus som infekterar bakterier, vilket kan påverka den bakteriella sammansättningen. Det finns cancersjukdomar som orsakas av virus, t.ex. livmoderhalscancer. De oroande rapporterna från Brasilien om zikavirusets troliga påverkan på nyfödda barns hjärnor är ytterligare ett exempel på hur virus kan orsaka stor skada.

I det här projektet kommer vi att titta närmare på virus och deras förmåga att påverka fostret och utvecklingen av hjärnan. Vi har nya forskningsresultat som visar att det finns virus i hjärnan på nyfödda grisar, framför allt hos sjuka grisar som skakar när den föds men även, till vår förvåning, hos till synes friska. Vi vill följa upp dessa resultat för att förstå mer om hur dessa virus påverkar griskultingar och om de orsakar sjukdom.

De två sjukdomar som vi kommer att fokusera på är medfödd skaksjuka och fläksjuka hos griskultingar. Medfödd skaksjuka är en sjukdom som drabbar nyfödda spädkgrisar. Symptomen är skakningar och svårigheter med koordinationen, vilket kan leda till svårigheter att dia och därmed ökad dödlighet. Denna sjukdom anses vara smittsam och det har sedan länge spekulerats i att den orsakas av virus. Fläksjuka är en medfödd förflämning som karakteriseras av begränsad funktion i bakbenen, vilket leder till svårigheter att stå och gå och därmed ökad dödlighet. Det finns en teori om att både skaksjuka och fläksjuka skulle kunna orsakas av samma virus och vi vill titta närmare på detta.

Det övergripande syftet med projektet är att identifiera, karakterisera och utvärdera orsaken till medfödd skaksjuka och fläksjuka. Vi kommer att använda oss av en metod som kallas viral metagenomik för att ta reda på vilka virus som finns i hjärnan hos griskultingar med medfödd skaksjuka, de med fläksjuka samt hos friska spädkgrisar från samma besättning. Viral metagenomik använder storskalig sekvensering och avancerad dataanalys för att förutsättningslöst identifiera vilka virus som finns i ett specifikt prov – t.ex. i fekal, blod eller vävnad.

Till skillnad från metoder som är utvecklade för att identifiera specifika mikroorganismer kan denna metod användas för att förutsättningslöst identifiera helt okända mikrober. De virus vi identifierar kommer vi att isolera och karakterisera för att sedan använda i experimentella infektioner av friska, dräktiga suggor för att utvärdera om dessa virus kan orsaka kongenital skaksjuka och/eller fläksjuka hos spädkgrisar.

Kongenital skaksjuka hos gris beskrevs för första gången 1922 och har sedan 1950-talet antagits bero på ett virus. Trots detta vet vi än idag inte vilket virus det rör sig om. Vår hypotes är att sjukdomen kan orsakas av ett flertal olika virus så länge infektionen sker under den period då fostrets hjärna ännu inte är tillräckligt skyddad mot virus. Med dagens avancerade molekylärbioologiska tekniker, sekvenseringsmöjligheter och databearbetning har vi unika möjligheter att lösa denna gåta.

På kort sikt skulle detta leda till att vi kan utveckla förbättrade metoder för att förhindra utbrott och spridning av kongenital skaksjuka, t.ex. genom diagnostik. Vårt arbete kan i förlängningen leda till förbättrad rådgivning avseende smittskydd och, i nästa steg, till utvecklandet av ett vaccin mot denna sjukdom. Detta skulle minska spädkgrisdödligheten, förbättra djurhälsan och därmed öka lönsamheten i de enskilda besättningarna.

Virus förmåga att infektera foster och eventuellt påverka dess utveckling är något som är relevant inte bara för grisar utan för alla djur och även människan. Genom att öka vår kunskap om transplacentala virusinfektioner kommer vi i förlängningen bidra till förbättrad neonatalhälsa.

Abstract (Swedish) (max 1500 characters)*

Virus finns precis överallt och i enorma mängder. Det är dock endast ett fåtal av dessa som orsakar sjukdom. Ju mer vi lär oss om virus desto tydligare blir det att de utgör en viktig beståndsdel i så gott som varje miljö och vi att vi ännu knappt vet någonting om hur de påverkar denna miljö. I det här projektet kommer vi att undersöka virus förmåga att påverka grisfostrets hjärmutveckling. Vi har identifierat virus i hjärnan på nyfödda grisar, framför allt hos dem med så kallad skaksjuka men även hos till synes friska. Vi vill följa upp dessa resultat med experimentella infektioner för att utreda om de virus vi identifierat kan orsaka medfödd neurologisk sjukdom. Med hjälp av viral metagenomik kommer eventuella nya virus av relevans för kongenital sjukdom identifieras. De virus som identifierats kommer isoleras och karakterisera innan de används i experimentella infektioner. Vår hypotes är att sjukdom hos kulingarna kan orsakas av ett flertal olika virus så länge infektionen sker under den period då fostrets hjärna ännu inte är tillräckligt skyddad mot virus. Genom djupsekvansering för att titta på quasispecies kommer vi även kunna ta reda på vad som skiljer viruspopulationen som finns blodet från den i hjärnan. Genom att öka vår kunskap om transplacentala virusinfektioner kommer vi i förlängningen minska smågris dödligheten samt öka kunskapen om virus påverkan på hjärnan under fostrets utveckling, vilket kan bidra även till förbättrad neonatalhälsa.

Abstract (English) (max 1500 characters)*

Viruses are the most abundant biological entities on earth. Their influence is far beyond pathology and the more we learn about them the more we start understanding that viruses are an integrated part of every environment on earth. The discovery of the roles they play is just in its infant. Our interest is in viruses' role in the very beginning of mammalian life, in the sow uterus more specifically. We have identified viruses in the brain of piglets diagnosed with a disease called congenital tremor. To our surprise, in some of the healthy controls we also identified viruses. With this project we would like to determine the role of newly identified viruses in congenital disease through a controlled proof of concept experiment using experimental infection of sows. Additional viruses of possible relevance for disease or health (?) will be identified using viral metagenomics. Viruses of interest will be isolated and well characterized prior to experimental infections. Our hypothesis is that several different kinds of viruses could cause congenital disease if the sow is infected during a time when the fetus is not well protected. Deep-sequencing will be used to address questions regarding tropism differences between viruses in the blood compared to the brain. By increasing our understanding of transplacental viral infections we will contribute to decreased piglet mortality and increased knowledge about neurotropic viruses role in congenital congenital disease.

Research programme

Specific aims and objectives of the proposed project and a background description containing an overview of the research area, including key references (max 7 000 characters)*

Purpose and aims

This project will elucidate the cause of congenital disease in pigs by identification, isolation and characterization of viruses in combination with experimental infections. The ability of neurotropic viruses to cause devastating congenital disease in newborns has recently been documented in a wide range of animal species. This project will contribute to increased understanding of viruses with this ability.

Specific aims:

- To establish the virome of brain, blood and placenta in diseased and healthy pigs.
- To characterize viruses of likely importance for congenital disease in piglets.
- To discover viruses ability to infect and cause neurological disorders in neonatal piglets.

Overview of the research area

Viruses are the most abundant biological entities on earth. Their influence is far beyond pathology and the more we learn about them the more we start understanding that viruses are an integrated part of every environment on earth. They appear as viral elements in a wide variety of genomes and they are present throughout the body providing a wide range of functions, such as modulation of bacterial communities (phages) and regulating hormone and neurotransmitter production. The relationship between viruses and the host start already in the uterus. It was long believed that the foetus developed within a sterile environment and was only exposed to microbes at delivery. However, recent research has identified bacteria within the amniotic fluids likely exposing the foetus already in the uterus¹. The existence and role of viruses in this early phase of foetus development is largely unknown. Porcine parvovirus is an example of a virus known to be able to cross the placenta and cause reproductive failure in swine. An interesting recent finding of relevance for the role of viral disease in human is the observation that mothers who report fever during pregnancy and the presence of elevated pro-inflammatory cytokines in core blood are associated with an increased risk for autism spectrum disorder in their children².

The focus of this project is on congenital disease in pigs and the possible role of viruses. Congenital tremor is a disease that affects neonatal piglets and was first described 1922. The disease is characterized by severe tremor, which result in difficulties in suckling and increased mortality. The disease has been attributed to an unidentified virus. Recently an atypical pestivirus has been identified as a possible cause of the disease^{3,4}. Interestingly, in the search for viruses in brain tissue from piglets with congenital tremor we have identified porcine astrovirus⁵, porcine circovirus type II⁵, and aichivirus C (previously named kobuvirus)⁶ much more frequently than any pestivirus. This has led us to the hypothesis that congenital tremor could be caused by a variety of viruses with the ability to cross the placenta, probably before the blood brain barrier of the foetus is established. In a recent study on the intestinal virome of diarrheic and healthy neonatal piglets we found viruses present in the intestine less than 1 day post farrowing, suggesting that at least aichivirus C might have a yet not described transplacental transmission route⁷. In brain tissue from healthy control piglets we have identified both porcine astrovirus⁵ and in a few cases aichivirus C and porcine circovirus type II⁵. This raises intriguing questions about the possible role of these viruses in a healthy brain. In addition, not all piglets born to sows experimentally infected with atypical pestivirus developed congenital tremor despite detection of viral RNA³, a finding that warrants further studies into host-virus interactions.

Astrovirus is mainly associated with gastroenteritis but has also has been associated with encephalitis in immunocompromised humans⁸, shaking mink syndrome⁹ and encephalitis in cattle¹⁰. Aichivirus was first detected as the cause of oyster-related gastroenteritis in humans in Japan¹¹, and has thereafter been detected in a wide range of animals globally, both diarrheic and healthy. Aichivirus belongs to the picomaviridae family, which include for example Avian encephalomyelitis virus 1, known to causes neurological disease in young chickens. Astrovirus and aichivirus and are both positive sense single stranded RNA viruses. The high mutation rate of RNA viruses results in a population of genetically different viruses, often referred to as quasispecies. Within the quasispecies cloud minority populations with relevance for example tropism and virulence may hide.

Another congenital disease of relevance for neonatal piglets is splay legs. The syndrome is characterized by temporally limited function in the hind legs resulting in restricted ability to stand and walk. It affects around 0.4% of all piglets and mortality can be as high as 50%. Supposedly, the same virus could cause both congenital tremor and splay legs. In line with this, experimental infection with atypical pestivirus caused both congenital tremor and splayed legs (although splay legs to a lesser extent)³, which encourages further investigations on the possible involvement of the same virus in these two congenital diseases.

With the recent developments in sequencing technologies and bioinformatics it has become possible to study metagenomics, i.e. the method of unbiased sequencing of all genomes within a sample. This culture-independent method does not require prior knowledge about the genomes of the organisms that are being analysed. Thereby enabling detection of known organisms, as well as those previously uncharacterized. Viral metagenomics is focusing on the viral part of the metagenome, also referred to as the virome. In general, knowledge about the role of viruses in brain development in humans and in animals in particular, is lacking and urgently needed.

References

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• Description of the project including a summary of the structure, theory, methods, performance and a plan for scientific deliverables (max 15 000 characters)*

Project description

The proposed project will include identification, isolation and characterization of viruses in combination with experimental infections to elucidate the role of identified viruses in congenital disease. This will increase the general knowledge about transplacental transmission of neotropic viruses with the aim to improve piglet health and survival.

As part of our on-going research on congenital tremor we have identified aichivirus C⁶, porcine astrovirus⁵ and porcine circovirus type II⁵ as possible causes of the disease. In this project we will follow up these findings and conduct a well designed sampling to be able to identify possible additional viruses of relevance. The project is divided into three work packages matching the three specific objectives. All people involved in the project are working at the Swedish University of Agricultural Sciences except for Lena Eliasson-Selling who is working at Gård & Djurhälsan (Farm & Animal Health).

WP1 – To establish the virome of brain, blood and placenta in diseased and healthy pigs.

PI: Maja Malmberg. **Key collaborators:** Lena Eliasson-Selling, Magdalena Jacobson, Mikael Berg, Juliette Hayer, Anne-Lie Blomström.

Objectives: Generate new knowledge about the brain, blood and placenta viromes to discover viruses of relevance for congenital disease in piglets.

Study population: The sampling will be carried out in conventional farms experiencing problems with congenital tremor and/or splay legs. The farms will be identified with the help of Lena Eliasson-Selling. In total 10 piglets with congenital tremor and 10 piglets with splay legs will be included in the study. As we expect the sows to develop immunity before the second farrowing, healthy control piglets from the second litter will be included as well (n=5 per disease).

Sampling: At the time of sampling, clinical examination will be performed and an interview with the farmer will be conducted. Blood samples will be taken from the sow to be able to confirm presence of antibodies at the time of the second litter, i.e. the healthy controls. When proven feasible, placenta will be collected from the sows of the piglets included in the study. All piglets included in the study will be euthanized and brain tissue and blood samples will be taken and used in WP 1 and 2. Faecal samples and lymph nodes will be taken for future follow-up experiments.

Viral metagenomics: A sequencing depth of 1 Gb per sample should be enough to detect even very low abundance of viruses. The Ion S5 platform at SciLifeLab will be used with 400bp chemistry. Both positive and negative controls will be run throughout the processing of samples and all findings will be validated with an independent preparation and Sanger sequencing. For the bioinformatics a viral metagenomics pipeline developed by Juliette Hayer will be used.

Tasks:

- I) Brain tissue and blood from piglets with congenital tremor and splay legs will be analysed using viral metagenomics.
- II) Brain tissue and blood samples from healthy piglets will be analysed using viral metagenomics.
- III) Placenta from sows will be analysed using viral metagenomics.
- IV) Multivariate statistical analysis will be performed to compare viromes between disease and healthy piglets as well as between piglets with congenital tremor vs splay legs to identify viruses associated with disease.

Outcome of relevance for other WPs: Within this WP we will discover viruses associated with congenital tremor and splay legs. These viruses will be used in WP 2 and 3.

Caveats: It will be challenging to get placenta from every sow as by the time the disease has been recognized and sampling can be made the placenta will probably have been eaten by the sow. However, as the disease usually occurs as a small outbreak it could be so that by the time we are at the farm another sow is farrowing and then there could be the possibility to sample placenta from sows with piglets displaying the disease.

WP2 – To characterize viruses of likely importance for congenital disease in piglets.

PI: Maja Malmberg. **Key collaborators:** Lisa Lindström, Anne-Lie Blomström, Mikael Berg, Juliette Hayer.

Objectives: Detailed characterization of viruses identified in WP1 and virus isolation.

Sampling: All work done in this WP will be carried out on the samples collected within WP 1. For the histopathology 20 preparations will be made per piglet (5 from brain/brainstem, 3 from spinal cord (stained with two different staining) and 4 from skeletal muscle). For the immunohistochemistry, four sick (two with congenital tremor and two with splay) and two healthy will be examined using the tissue that displayed the most interesting morphological changes according to histopathology.

Deep-sequencing: For virus with smaller genomes, such as astrovirus and aichivirus (~8kb) long range PCRs will be designed and the amplicons sequenced on a MiSeq (Illumina) and/or a PacBio RS II (Pacific Biosciences) depending on the number of samples. With the MiSeq we can get high coverage rather cheap whereas the advantage with PacBio is that we will be able to get the full genome in one read, although to a higher cost and lower coverage¹.

Isolation: Homogenates from clinical material positive for each respective virus will be used for virus isolation attempts. A variety of different cell lines, such as PK-15A, different porcine primary cells and Vero cells, will be inoculated with the homogenate. The cells will be observed daily for cytopathic effect (CPE), if no CPE is observed 3-5 blind passages will be performed. At each passage nucleic acid will be extracted from the cells and checked for the respective virus using PCR. Isolated viruses will be further propagated in the susceptible cell line/s and purified using gradient ultracentrifugation.

Tasks:

- I) Histopathological analysis to identify changes in brain morphology associated with congenital tremor or splay legs.
- II) Immunohistochemistry to identify the location in brain tissue of the viruses of interest.
- III) Deep sequencing of full genome viruses from different tissue (blood, placenta and brain) in order to study quasispecies differences related to e.g. tropism.
- IV) Isolation of newly identified viruses.

Outcome of relevance for other WPs: The isolated viruses and the full genomes from this WP will be used in WP 3.

Caveats: From our earlier work we have access to brain tissue from both healthy and diseased piglets. These samples could be resourced too in case the sampling takes longer than expected. As we are aware, isolating and cultivating viruses can be challenging wherefore we as a backup plan to use well-characterized serum and/or brain homogenate from infected individuals for the experiential infections. Also, if it is not possible to isolate viruses we will try to do infectious clones.

WP3 – To discover viruses' ability to infect and cause neurological disorders in neonatal piglets.

PI: Magdalena Jacobson **Key collaborators:** Maja Malmberg, Lisa Lindström, Mikael Berg.

Objectives: Establish the role of aichivirus C, porcine astrovirus and possible newly identified viruses in congenital tremor and splay legs.

Study population: Six Specific Pathogen Free (SPF) sows will be experimentally infected (one virus for two sows) and immediately after farrowing four piglets will be euthanized, and thereafter two more every second day in order to investigate the persistence of infection. One SPF sow will be used as a negative control. The sows will be euthanized after the experiment is completed.

Sampling: From the sows and piglets; brain tissue, blood and fecal samples will be sampled and analysed within this WP and lymph nodes will be collected for future work. From the sows, placenta and cerebral spinal fluid (CSF) will be collected and analysed within this WP.

Droplet digital PCRs: Based on conserved genomics regions identified in WP 2 droplet digital PCRs will be designed on in order to be able to make absolute quantification of the specific viruses.

Tasks:

- I) Experimental infections of sows with isolated viruses.
- II) Evaluation of clinical signs in the sow and piglets using physical examination and video recordings.
- III) Histopathological analysis to identify changes in brain morphology associated with clinical signs.
- IV) Detection of viruses in brain, blood, placenta, CSF and fecal samples using droplet digital PCR.

Time plan

WP1: Collection of samples and performance of viral metagenomics will be done during 2017. Publications 2018-2019.

WP2: Characterization of viruses will be carried out during 2017-2018. Publications 2018-2019.

WP3: Experimental infections will be carried out in 2018 with follow-up analysis during 2019. Publications 2019.

Project management

Project leader: **Dr. Maja Malmberg** at the section of Virology at the Department of Biomedicine and Veterinary Public Health (BFV), SLU. Dr. Malmberg is an engineer in medical biotechnology, has a PhD in Medicine and viral metagenomics with expertise in congenital tremor in piglets and viral discovery.

Co-applicants: **Professor Magdalena Jacobson** at the Department of Clinical Sciences, is a veterinarian and PhD with expertise in swine and with long experience of carrying out experimental infections. **Dr. Anne-Lie Blomström** at BVF is an expert in molecular virology and swine health. **Dr. Juliette Hayer** at the Department of Animal Breeding and Genetics (HGEN), is a bioinformatician with expertise in viral metagenomics. **Professor Mikael Berg** at BVF has expertise in veterinary virology and viral metagenomics.

Collaborators: **Lisa Lindström**, a veterinarian and university adjunct at the Section of Pathology (BVF), has extensive experience of histopathology. **Lena Eliasson-Selling**, a PhD and veterinarian working at Gård och Djurhälsan has daily contact with pig farmers and important expertise in farm practices.

Independent line of research – Dr. Maja Malmberg (M.M) developed during her PhD a new method to *in vivo* assessment of drug resistance in *P. falciparum* malaria. Thereafter M.M did postdoctoral research at the Swedish University of Agricultural Sciences focusing on virus discovery and characterization using high-throughput sequencing and bioinformatics. M.M was provided great opportunities to learn new techniques and to independently develop her own line of research in an inter-disciplinary research environment. Her work on congenital tremor in piglets identified for the first time aichivirus in brain tissue. This finding has raised many interesting question that M.M would like to address in her continued research endeavour. By combining viral metagenomics and bioinformatics with virus isolation, characterization and experimental infections, the aim is to address questions related to neurotropic viruses and congenital health in piglets. By merging the field of infectious biology with neurological disease M.M has found a research niche that very well matches her interests. In addition, the design of the project well reflects M.M’s wish to do research within a multidisciplinary environment, something that the facilities at the Centre for Veterinary Medicine and Animal Science (VHC) at SLU are strongly supporting. The design of the proposed project will allow several follow up projects that M.M could use as a foundation in her transition to becoming a research leader. M.M have previous experience of leadership roles, for example as a project leader for the planning and executing of a scout camp with 40 000 participants. M.M supervise bachelor, master and PhD students on a regular basis and her first PhD student (as co-supervisor) will defend his thesis this year. The postdoc has so far generated five manuscripts that will be submitted during the coming months, two as first author and one as last author. During her postdoc M.M has developed adequate communication skills, e.g. five oral presentations at international conferences and being the corresponding author in two published scientific publications. M.M is a suitable project leader of the programme of work described in the proposal and the project as great potential of forming the foundation for her research career.

Existing basic equipment

All basic equipment needed for the proposed project are available. The experimental infections will be carried out in SPF sows bought from the National Livestock Research Centre Lövsta and kept at the research stables at VHC. The facilities at VHC will be used for histopathology, viral metagenomics preparations, virus isolation and culturing. The national genomics infrastructure at SciLifeLab will be used for sequencing of the viromes on the Ion S5 platform. Data will be stored and analysed in collaboration with SLU Global Bioinformatics Center.

National and international collaborations

We have close collaborations with SVA, Public Health Agency of Sweden, National Food Agency, the Swedish Board of Agriculture and Swedish Civil Contingencies Agency. We are part of the Collaborating Centre of the World Organization for Animal Health (OIE) for the Biotechnology-based Diagnosis of Infectious Diseases in Veterinary Medicine.

Confirmation of compliance with international agreements and regulations

We hereby confirm that we within this project will comply with international agreements and regulations.

Gender aspects

The research group consists of six females and one male. This rather well reflects the gender distribution within veterinary medicine where the vast majority of students are women and the majority of PhD students and young researchers are women.

References

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Description of the potential societal value of the research and a plan for communication with stakeholders/end users (max 8 000 characters)*

Societal value of research

This project will produce new insights about viruses in the neonatal pig brain with emphasis on their role in congenital disease. Piglet mortality rates have become a major issue in today's pig production. While production traits such as number of piglets per sow have been improved, the mortality rate has increased dramatically. Piglets are vulnerable already in the womb, with 40% being lost as embryos and fetuses before day 40 of gestation. Thereafter ~8% of piglets fail to survive the birth process, and on average 17.5% die during pre-weaning (PigWin sugg 2014, (gardochdjurhalsan.se)). Increased litter sizes, increased problems with neonatal diarrhea and sows being allowed to move freely (and thereby increasing the risk of stepping or lying on a piglet) are factors contributing to piglet mortality. To what extent viral infection in the sow during pregnancy contributes to piglet disease and mortality is the main focus of this research project.

Infection with neurotropic viruses during pregnancy could result in devastating consequences for the foetus, as exemplified recently with zika virus in humans. With the research proposed in this project we will gain knowledge about porcine astrovirus and aichivirus C, and possibly other viruses ability to infect the foetal brain. These results could benefit future health of piglets and hopefully contribute to decreased pre-weaning mortality. When it comes to anatomy, physiology, immunology and brain growth, the domestic pig (*Sus scrofa*) is considered a clinically relevant model to study factors influencing for example; human gastrointestinal, immune, and brain development. Human astrovirus has been shown to cause encephalitis in immunocompromised humans¹. For aichivirus, our finding in brain is the first case in any animal but we speculate that this is rather because brain viral metagenomics studies still as scarce than the presence so rare. Because of the similarities between pigs and humans it is possible that results generated by this project will in the future benefit also human health. These results could increase the knowledge on viral infections during pregnancy and the consequences for the foetus.

The knowledge generated within this project will serve as a basis for future development of vaccine to combat these diseases. It will also have an impact on the trade with breeding animals since it will enable the screening for relevant viruses while the animals are kept in quarantine before entering the herds. Further, in the future it may be of interest to screen for relevant viruses also in the boar sperm.

For the research community, this project will result in highly valuable baseline viromes of placenta, blood and brain in diseased and healthy piglets, which can be used in future studies investigating viromes. In addition, the samples that will be kept could in the future be used to investigate the role of the immune response and the bacterial part of the microbiome. This project will generate knowledge about viruses' ability to cause disease in piglets and thereby contribute to increased understanding of factors of importance in the field of neurotropic virus infection in the neonatal piglet.

Communication with stakeholders and end users and scientific deliverables

Throughout the project there will be communication with stakeholders and end users. In the beginning focus will be on identification of farms with problems with congenital diseases among their piglets. As results are generated from the project dissemination of these results will take place to different parties in various ways described in more detail below. The main purpose with the communication related to this project is to make the research results available to the people that would benefit from it. It is the responsibility of the researchers involved in the project to communicate the findings so that it will:

- I) lead to improved knowledge based practices at the farm level.
- II) form the basis for further research within the research community.
- III) increase the knowledge in the general public about the findings.

The main target groups for the communication:

Farmers: It is important for the farmers to get access to the results of this project in order for them to be able to improve pig management for better pig welfare and improved economy. Hopefully it would provide them with new ideas how to make the production system more sustainable.

People within the pig industry and pig advisory companies (e.g. Gård & Djurhälsan): People working in the pig sector will be able to use the results for improved advice to farms affected with problems with congenital diseases.

Veterinarians: It is important for veterinarians to know the results so that they are updated on the causes of congenital diseases in piglets and know how to manage these in the future. Hopefully they would feel that they now have evidence-based research for the causes of congenital tremor and splay legs and that there would also be molecular based assays available for diagnostic purposes.

Students: It is important for veterinary and animal health students to get education based on the latest developments within the field of neurotropic disease in piglets and the causes for them.

Companies of interest in development of diagnosis and vaccine: Depending on the findings it could become relevant to communicate the findings with a company that would be interested in proceeding with the development of a diagnostic test and/or a vaccine.

Researchers: For the research community it is key with prompt communication through conferences and scientific publications in peer-reviewed open access journals in order to continue answering important questions within the field. The baseline virome from the healthy subjects blood, placenta and brain would be of relevance for future virome and microbiome work.

Experience of communication

Within the project group there is extensive knowledge in communication of research findings. Magadalena Jacobson has 45 popular science articles in the field of porcine health and management and has actively participated in communication with stakeholders and end users for many years. She has noted that people are usually very interested to hear about the on-going research and her reflection is that this is an important part of any research project. Mikael Berg has 5 popular science publications within the field of virology. Maja Malmberg, Anne-Lie Blomström and Juliette Hayer have one popular science publication. Lena Eliasson-Selling, working at Gård & Djurhälsan, which covers 85% of the Swedish pig farms, is a key person for the communication of the research findings from this project.

These are examples of forum where we plan to communicate our finding:

- Conferences such as Gård & Djurhälsan spring conference, Veterinärkongressen, International Pig Veterinary Society Congress, European Symposium of Porcine Health Management, Epizone, European Society of Veterinary Virology International Congress.
- Popular science articles in Veterinärtidningen
- Information on relevant web sites like www.slu.se, www.gardochdjurehalsan.se, www.facebook.com/forskningVH/
- Articles in journals of relevance for people working in the pig sector: E.g. Grisföretagaren, Djurhälsövärdens tidskrift, Jordbruksaktuellt.
- Yearly animal owners and consultants meetings arranged by Gård & Djurhälsan
- All sequence data will be available to the research community through the ENA database (ebi.ac.uk)
- Article in the News letter from *Future Animal Health and Welfare (SLU)*
- Open house at SLU Campus Ultuna
- Scientific publications in peer-reviewed open access international journals

References

1. Quan, P. L. *et al. Emerging infectious diseases* **16**, 918-925, (2010).
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Budget

Salaries including social fees

Role in the project	Name	Percent of salary
1 Participating researcher	Juliette Hayer	5
2 Participating researcher	Magdalena Jacobson	5
3 Applicant	Maja Malmberg	55
4 Participating researcher	Anne-Lie Blomström	3
5 Other personnel without doctoral degree	Lisa Lindström	8
6 Other personnel without doctoral degree	Labassistent	5
Total		

	2017	2018	2019	Total
1	33,000	33,000	33,000	99,000
2	58,000	58,000	58,000	174,000
3	360,000	360,000	360,000	1,080,000
4	20,000	20,000	20,000	60,000
5	42,000	42,000	42,000	126,000
6	25,000	13,000	13,000	51,000
Total	538,000	526,000	526,000	1,590,000

Dedicated time for this project

Role in the project	Name	Percent of full time
1 Applicant	Maja Malmberg	55
2 Participating researcher	Mikael Berg	5
3 Participating researcher	Magdalena Jacobson	5
4 Participating researcher	Juliette Hayer	5
5 Participating researcher	Anne-Lie Blomström	3
6 Other personnel without doctoral degree	Lisa Lindström	8
7 Other personnel without doctoral degree	Labassistent	3

Running Costs

Running Cost	Description	2017	2018	2019	Total
1 Sampling	Piglets and material related to sampling	50,000			50,000
2 Histopathology and immunohistochemistry	Preparation of histopathology and immunohistochemistry samples etc.	15,000			15,000
3 Viral Metagenomics and bioinformatics	Enzymes, primers, kits, sequencing etc.	80,000	80,000	20,000	180,000
4 Isolate and characterize viruses	Cell medium, primers, sequencing etc.	25,000	50,000	40,000	115,000
5 Experimental infections	Sows, costs for keeping the sow in stables, sampling equipment		90,000		90,000
6 Consultant fee	Fee to consultants at Gård och Djurhälsan	5,000	5,000	5,000	15,000
7 Travel	Sampling and conference	10,000	10,000	10,000	30,000
8 Publication	Open-access fees		10,000	10,000	20,000
Total		185,000	245,000	85,000	515,000

(1) - Materiel etc. refers to equipment and other research materiel not classified as fixed assets, e.g. chemicals, literature, and software.

Equipment depreciation costs

Depreciation cost	Description	2017	2018	2019
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Premises

Type of premises	2017	2018	2019	Total
1 Kontor och lab	91,000	89,000	89,000	269,000
Total	91,000	89,000	89,000	269,000

Total Budget

Specified costs	2017	2018	2019	Total, applied	Other costs	Total cost
1 Salaries including social fees	538,000	526,000	526,000	1,590,000		1,590,000
2 Running costs	185,000	245,000	85,000	515,000		515,000
3 Depreciation costs				0		0
4 Premises	91,000	89,000	89,000	269,000		269,000
5 Subtotal	814,000	860,000	700,000	2,374,000	0	2,374,000
6 Indirect costs	210,000	205,000	205,000	620,000		620,000
7 Total project cost	1,024,000	1,065,000	905,000	2,994,000	0	2,994,000

Budget specification (max 7000 characters)*

The project is based on collaborations between several groups at different departments of SLU. Each member of the team has unique and complementary competences and the project cannot be completed successfully without the participation of all. This is a trans-disciplinary research project merging a variety of different disciplines such as molecular virology, bioinformatics, neurology, pathology and clinical sciences. The consortium will work in collaboration with existing VR and Formas projects. Other funds are also available for some of the participants in the consortium, but not directly related to the present project.

Salaries

1080 kSEK for Maja Malmberg (M.M) - total sum over three years. M.M is a PhD and engineer in biotechnology with expertise in infectious diseases, viral metagenomics, molecular biology and drug resistance. M.M is the principal investigator with main responsibility for the project coordination, experimental design, molecular biology and large-scale sequencing as well as overall data analysis and interpretation. M.M has experience of being a project leader and her part will be of vital importance for the running of this project. M.M will work 55% of her time in this project.

Given that the proposal is granted the Department of biomedical sciences and veterinary public health (BVF) will write a professional development plan that would support M.M's academic career. This would include teaching and other relevant departmental tasks that would be of importance for her career. The support from the department will correspond to 20% salary.

174 kSEK for Magdalena Jacobson (M.J) - total sum over three years. M.J is a professor at the Department of Clinical Sciences (SLU), specialised on swine health. M.J is a veterinarian with long experience of carrying out experimental infections, working in close contact with the herd owners and investigating causes of diseases. M.J will be the main responsible for WP3 and she plays a crucial role for the completion of this project. She will work 5% of her time in this project.

61 kSEK for Anne-Lie Blomström (A-L.B) - total sum over three years, a researcher at BVF, with a PhD in viral metagenomics and extensive experience in molecular virology and swine diseases. Her contribution to the project will be mainly in WP 1 and 2. She will work 3% of her time in this project and her expertise is very important.

99 kSEK for Juliette Hayer (J.Ha) - total sum over three years. J.Ha is a PhD in bioinformatics with expertise in viral metagenomics, databases building and protein modeling. J.Ha will be responsible for the bioinformatics part, as well as overall data analysis and interpretation. J.Ha will work 5% of her time in this project.

Mikael Berg (M.B) is professor in veterinary virology with many years of experience with viral metagenomics and molecular biology. M.B will provide general guidance in relation to molecular work and viral genetics in WP 1 and 2. He will work 5% of his time in this project (but no salary is applied for here).

127 kSEK Lisa Lindström (L.L) - total sum over three years. L.L is a veterinarian and university adjunct at the Section of Pathology, BVF, with expertise in histopathology. She will work 8% in this project. She will work together with a lab assistant whom will work 3.3% in this project, corresponding to 51 kSEK over the three years.

Veterinary students will master students from the infection biology program will be involved throughout the project, when suitable sub-projects are identified.

Other costs

WP 1 – Field work 50 kSEK: will covering 1000 SEK per piglet times 30 animals, plus other costs related to sampling.

WP 1 – Metagenomics 180 kSEK: it is presently costly to run a large scale sequencing effort, even if the prizes are getting lower. Various enzymes and other reagents will be needed for treatment of the samples prior to sequencing and validation follow-up molecular tests. These include nucleases, polymerases, nucleotides, primers, purification kits and so forth. The costs will cover viral metagenomics for blood and brain samples, from a total of 30 animals (10 with congenital tremor, 10 with splay legs, 10 healthy).

WP 2 – Histopathology and immunohistochemistry 15 kSEK: costs for preparation of samples for histopathology and immunohistochemistry

WP 2 – Isolate, culture, characterize 115 kSEK: Reagents for virus isolation and cell culture and molecular reagents and costs for deep-sequencing of amplicons for the identification of quasispecies.

WP 3 – Experimental infections 90 kSEK: buying seven SPF sows and keeping them at the facilities at VHC prior to farrowing, plus costs for video recording and sampling.

Fee for consultant at Gård & Djurhälsan - 15 kSEK

Travel 30 kSEK: travels needed for collection of samples. Also, the plan is to when needed, travel to present data in animal health conferences or in workshops together with the stakeholders.

Publication costs 20 kSEK: all scientific data will be published in open access journals, for which there is a cost for publication.

Ethics

Animal testing



Type of animal (max 4 000 characters)

Ethical questions that this project raises relate to the sampling and experimental infections.

The rationale for using the pig for experimental infection is foremost because we are studying diseases that affect pigs and therefore the best model is the pig. Before we do experimental infections we will do in vitro work on cell cultures in the lab, in order to isolate and characterize the virus of interest for experimental infections. The justification of performing experimental infections in this study is because there is no other way to study trans-placental transmission and infection of the brain of fetuses and the knowledge that we aim to generate has the possibility to greatly improve pig health and management in the future. Experimental infections are needed as a proof of concept and to fulfill the Koch's postulate.

The viruses that we are planning to infect the sow with will be viruses that have been identified in piglets from similar environments so we do not expect the viruses to constitute a serious risk for the sows. The experimental infection will take place at the research stables at the Centre for Veterinary Medicine and Animal Science (VHC) where the sows will be kept until farrowing. The facilities are designed for experimental infections and the personnel are well trained. The physical and health condition of the animals will be assessed through daily clinical examination by a trained veterinarian and if the sow does not recover properly after the infection or if any other serious event happens she will be euthanized to avoid suffering. Five days after farrowing, i.e. when all piglets have been euthanized the sow will also be euthanized. The person responsible for performing the experimental infections and euthanizing animals is a veterinarian well qualified to handle the animals.

In the project we keep the number of animals as low as possible to not cause unnecessary suffering but still be able to find relevant differences. From the animals we euthanize we will do rigorous sampling not to waste any material. The samples will be stored in a way so that they can be used to address a wide range of future research questions.

Animal caretakers at the farms will be economically compensated with 1000 SEK per piglet. Informed consent from every individual animal owner participating in the study will be obtained prior to the start of the sampling. The necessary ethical permissions will be sought from the Swedish Board of Agriculture, the regional ethics committee for animal experimentation.

Human testing



Classifications

Subject area (min/max 1 subject area)* 51. PROGRAMOMRÅDE JORDBRUK MM > 5103. 22.1 Djurhållning o veterinärmedicin

SCB-codes (min 1, max 3 SCB-codes)* 40303. Clinical Science incl. Anesthesiology, Diagnostics, Veterinary Nursing, Epidemiology, Surgery, Medicine, Reproduction
40302. Pathobiology incl. Immunology, Microbiology, Pathology, Toxicology, Pharmacology, Food Safety
10614. Developmental Biology

Keyword 1*

porcine

Keyword 2

viral metagenomics

Keyword 3

congenital disease

Keyword 4

experimental infection

Keyword 5

neurotropic virus

Appendices

Appendix J. Illustrations. If figures, tables or images are needed to describe the project, an appendix may be uploaded here. The total size of the attachments can be maximum 4 MB in the formats jpg, png or gif

Appendix J

Appendix K. Climate and environmental data (The [form for the publication of data](#) that is available from the ECDS (Environment Climate Data Sweden) must be used.)

Appendix K

No file has been attached

CV

CV - Maja Malmberg

Name: Maja Malmberg
Birthdate: 19820516
Gender: Female
Country: Sweden

Doctorial degree: 2013-01-18
Academic title: Doktor
Employer: Sveriges lantbruksuniversitet

Educational history

Research education

Examination	Organisation	Dissertation title (en)
Doctors degree, 30401. Medical Biotechnology (focus on Cell Biology (incl. Stem Cell Biology) Molecular Biology, Microbiology, Biochemistry or Biopharmacy), 2013-01-18	Karolinska Institutet, MedS (Institutionen för medicin, Solna)	The role of molecular markers in emerging artemether-lumefantrine resistant Plasmodium falciparum

Basic education

Year	Examination
2009	10602. Biochemistry and Molecular Biology incl. Biochemical Research Methods, Degree of Master of Science in Engineering, Umeå University

Professional history

Employments

Period	Position	Part of research in employment	Employer
augusti 2015 - Present	Researcher	100	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap
februari 2010 - januari 2013	PhD student	100	Karolinska Institutet, MedS (Institutionen för medicin, Solna)
februari 2009 - december 2010	Research assistant	100	Karolinska Institutet, MedS (Institutionen för medicin, Solna)

Post doctoral assignments

Period	Organisation	Subject
augusti 2013 - augusti 2015	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap	40301. Medical Bioscience incl. Anatomy, Physiology, Biochemistry
maj 2013 - maj 2013	Karolinska Institutet, MedS (Institutionen för medicin, Solna)	30109. Microbiology in the medical area
mars 2013 - april 2013	University of Nagasaki, NEKKEN	30109. Microbiology in the medical area
januari 2013 - februari 2013	Karolinska Institutet, MedS (Institutionen för medicin, Solna)	30209. Infectious Medicine

Research exchange assignments

Period	Type	Organisation	Subject
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Period	Type	Organisation	Subject
november 2015 - november 2015	Guest researcher	Chilenian Antarctic Institute	10606. Microbiology (medical to be 30109 and agricultural to be 40302) incl. Virology, Mycology
november 2014 - november 2014	Guest researcher	University of Sao Paulo, School of Veterinary Medicine	40301. Medical Bioscience incl. Anatomy, Physiology, Biochemistry
februari 2014 - februari 2014	Guest researcher	University of South Florida, Global Health	30401. Medical Biotechnology (focus on Cell Biology (incl. Stem Cell Biology) Molecular Biology, Microbiology, Biochemistry or Biopharmacy)
maj 2010 - maj 2010	Utbyte under doktorandperioden	London School of Hygiene and Tropical Medicine, Department of Immunology	30209. Infectious Medicine

Merits and awards

Supervised persons		
Year	Supervised persons	Role
2016	PhD student, Oskar Karlsson, Sveriges lantbruksuniversitet	Secondary supervisor
2015	Student, Simon Larsson, Sveriges lantbruksuniversitet	Main supervisor

Research grants awarded in competition				
Period	Funder	Project leader	Your role	Total amount (SEK)
2013 - 2014	Erik and Edith Fernströms foundation	Maja Malmberg		70000
2012 - 2013	Stiftelsen Sigurd och Elsa Goljes Minne	Maja Malmberg		50000
2011 - 2012	Stiftelsen Sigurd och Elsa Goljes Minne	Maja Malmberg		50000
2009 - 2010	Stiftelsen Sigurd och Elsa Goljes Minne	Maja Malmberg		100000

Awards and distinctions		
Year	Name of award/distinction	Issuer
2015	EPIZONE young scientist travel grant	EPIZONE

Other merits		
Period	Type of merit	Description
2011 - 2016	Bibliometric summary	i) My nine peer-reviewed publications have generated a total number of 217 citations and my h-index is 7, according to Google Scholar. My publication range is 2011-2015. ii) I have 9 peer-reviewed publications, 5 oral and 2 poster presentations at international conferences and I have one popular science article in Svensk Veterinärtidning. iii) My postdoctoral research has resulted in 5 manuscripts soon to be submitted, out of which one is as last author and two as first author.
2011 - 2016	External reviewer	External reviewer for the scientific journals "Antimicrobial Agents and Chemotherapy", "International Journal for Parasitology: Drugs and Drug Resistance", "Journal of Infection Genetics and Evolution" and "Healthcare in Low-resource Settings"
2016 - 2016	Member of examination board	Member of examination board, PhD dissertation; Jenny Larsson 4/4 2016

Period	Type of merit	Description
2015 - 2015	Field work with penguins	I initiated a study with the aim to investigate the fecal microbiome of Magellanic penguins on an island close to Punta Arenas in Chile. I was responsible for the logistics, the field work, the lab work, transport of samples etc.
2014 - 2014	Cloning and transfection of P. falciparum	I got experience of working with cloning and transfection of P. falciparum in Prof. Adams lab at University of South Florida, US.
2009 - 2011	Project leader at the world scout jamboree	I was project leader at the world scout jamboree in Sweden 2011. It was an event with 40 000 people from 160 different countries. My role included planning and preparing for two years prior to the event, as well as an executive function involving education, leadership and quality assurance.

CV - Mikael Berg

Name: Mikael Berg	Doctorial degree: 1991-04-12
Birthdate: 19590324	Academic title: Professor
Gender: Male	Employer: Sveriges lantbruksuniversitet
Country: Sweden	

Educational history

Research education		
Examination	Organisation	Dissertation title (en)
Doctors degree, 40304. Other Veterinary Science incl. Animal Ethics, 1991-04-12	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap	Studies of genetic relationships and variation of negative-strand RNA viruses causing infection in animals

Basic education	
Year	Examination
1984	10602. Biochemistry and Molecular Biology incl. Biochemical Research Methods, Degree of Bachelor, Uppsala universitet

Professional history

Employments			
Period	Position	Part of research in employment	Employer
januari 2010 - Present	Professor	75	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap

Post doctoral assignments		
Period	Organisation	Subject
september 1993 - mars 1996	Cold Spring Harbor Laboratory	30599. Other Medical and Health Sciences not elsewhere specified

Merits and awards

Docentur		
Year	Subject	Organisation

Year	Subject	Organisation
1997	40304. Other Veterinary Science incl. Animal Ethics	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap

Supervised persons

Year	Supervised persons	Role
2016	Postdoc, Maja Malmberg, Sveriges lantbruksuniversitet	Main supervisor
2016	Postdoc, Juliette Hayer, Sveriges lantbruksuniversitet	Main supervisor
2015	PhD student, Sandra Cuevas, Sveriges lantbruksuniversitet	Main supervisor
2014	Postdoc, Eduardo Samo Gudo, Sveriges lantbruksuniversitet	Main supervisor
2014	PhD student, Giorgi Metreveli, Sveriges lantbruksuniversitet	Main supervisor
2012	PhD student, Caroline Bröjer, Sveriges lantbruksuniversitet	Main supervisor
2012	PhD student, Josefine Elving, Sveriges lantbruksuniversitet	Main supervisor
2011	PhD student, Jonas Wensman, Sveriges lantbruksuniversitet	Main supervisor
2011	PhD student, Muhammad Munir, Sveriges lantbruksuniversitet	Main supervisor
2010	PhD student, Anne-Lie Blomström, Sveriges lantbruksuniversitet	Main supervisor
2009	PhD student, Siamak Zohari, Sveriges lantbruksuniversitet	Main supervisor
2006	Postdoc, Sophie Escutenaire, Sveriges lantbruksuniversitet	Main supervisor
2004	Postdoc, Sirje Timmusk, Sveriges lantbruksuniversitet	Main supervisor

Research grants awarded in competition

Period	Funder	Project leader	Your role	Sub amount (SEK)	Total amount (SEK)
2015 - 2016	Formas	Anne-Lie Blomström	Co-applicant	0	2641000
2014 - 2016	VR - Vetenskapsrådet	Mikael Berg	Applicant	0	681000
2013 - 2016	Formas	Mikael Berg	Applicant	0	8700000

Other merits

Period	Type of merit	Description
2011 - 2016	Bibliometrisk sammanfattning	Citat: 1522 h-index: 22 i10-index: 52 Peer review: 43 Chapters in books: 3 Books: 1 Popular science: 5

CV - Magdalena Jacobson

Name: Magdalena Jacobson	Doctorial degree: 2003-09-19
Birthdate: 19581017	Academic title: Professor
Gender: Female	Employer: Sveriges lantbruksuniversitet
Country: Sweden	

Educational history

Research education

Examination	Organisation	Dissertation title (en)
Doctors degree, 30599. Other Medical and Health Sciences not elsewhere specified, 2003-09-19	Swedish University of Agricultural Sciences	Enteric diseases in pigs from weaning to slaughter.

Basic education

Year	Examination	Specialist training
1987	30599. Other Medical and Health Sciences not elsewhere specified, Degree of Master of Science in Veterinary Medicine, Swedish University of Agricultural Sciences	Other specialist qualification

Professional history

Employments				
Period	Position	Part of research in employment	Employer	Other information
oktober 2014 - Present	Professor, Permanent employment	80	Swedish University of Agricultural Sciences	
juni 2011 - september 2014	Senior lecturer, Permanent employment	50	Swedish University of Agricultural Sciences	
september 2007 - juni 2011	Assistant professor, Permanent employment	75	Swedish University of Agricultural Sciences	
mars 2005 - september 2007	Adjunkt 50%, Permanent employment	0	Swedish University of Agricultural Sciences	
mars 2005 - september 2007	Researcher, Temporary employment	50	Swedish University of Agricultural Sciences	
juni 2004 - mars 2005	Postdoctoral fellow, Temporary employment	100	Swedish University of Agricultural Sciences	
september 2003 - juni 2004	Postdoctoral fellow, Temporary employment	100	National Veterinary Institute, SVA	Postdoc, laboratorieveterinär
september 1998 - september 2003	PhD student, Temporary employment	80	Swedish University of Agricultural Sciences	
september 1998 - september 2003	Assistant professor, Temporary employment	20	National Veterinary Institute, SVA	
september 1992 - september 1998	Adjunkt, Temporary employment	20	Swedish University of Agricultural Sciences	teacher in swine medicine
december 1987 - oktober 1991	Swine health veterinarian 50%, Temporary employment	20	Swedish board of agricultural science	
december 1987 - oktober 1991	Large animal practitioner /distriktsveterinär 50%, Temporary employment	0	Swedish board of agricultural science	

Post doctoral assignments		
Period	Organisation	Subject
september 2003 - mars 2005	National Veterinary Institute, SVA	30401. Medical Biotechnology (focus on Cell Biology (incl. Stem Cell Biology) Molecular Biology, Microbiology, Biochemistry or Biopharmacy)

Interruptions in research

Interruptions in research

Period	Description
1994-10-13 - 1995-10-31	barnledig
1991-11-01 - 1992-09-10	Barnledig
1988-09-01 - 1989-06-01	Barnledig

Merits and awards**Docentur**

Year	Subject	Organisation
2008	305. Other Medical and Health Sciences	Swedish University of Agricultural Sciences, Kliniska vetenskaper

Supervised persons

Year	Supervised persons	Role
2016	PhD student, Jenny Larsson	Main supervisor
2016	Student, Lina Göransson	Main supervisor
2015	PhD student, Kokas Ikwap, Makerere University	Secondary supervisor
2013	PhD student, Helena Chalkias	Secondary supervisor
2012	Student, Hanna Johansson	Main supervisor
2011	PhD student, Annette Backhans	Secondary supervisor
2011	Student, Thorsten Muley	Main supervisor
2010	Student, Jennifer Andersson	Main supervisor
2009	Student, Helena Frohm	Main supervisor
2007	Student, Frida Arnlund	Main supervisor
2006	Student, Linda Billström	Main supervisor
2005	Student, Ted Johansson	Main supervisor
2004	Student, Susanne Wennerbo	Main supervisor
1998	Student, Carolina Södereng	Main supervisor
1998	Student, Merete Lysaker	Main supervisor
1996	Student, Helen Andersson	Main supervisor
1995	Student, Ann Karlsson	Main supervisor
1995	Student, Christina Hagberg	Main supervisor

Research grants awarded in competition

Period	Funder	Project leader	Your role	Sub amount (SEK)	Total amount (SEK)
2015 - 2016	KSLA	Magdalena Jacobson	Applicant	0	120000
2013 - 2016	Sweden - Defence agencies (eg Armed Forces, FMV or FOI)	Magdalena Jacobson	Applicant	0	1650000
2013 - 2017	Not Sweden - Governmental agencies	Videncenter for svineproduktion, Denmark	Co-applicant	0	1056000
2011 - 2015	Sweden - Research and technology organisations	Magdalena Jacobson	Applicant	0	2220000
2008 - 2010	Sweden - Research and technology organisations	Magdalena Jacobson	Applicant	0	195000
2007 - 2010	FORMAS	Magdalena Jacobson	Applicant	0	3647050
2006 - 2007	Sweden - Research and technology organisations	Magdalena Jacobson	Applicant	0	390000

Period	Funder	Project leader	Your role	Sub amount (SEK)	Total amount (SEK)
2005 - 2007	Sweden - Research and technology organisations	Magdalena Jacobson	Applicant	0	340000
2004 - 2006	Sweden - Research and technology organisations	Magdalena Jacobson	Applicant	0	824000
2004 - 2006	Sweden - Research and technology organisations	Magdalena Jacobson	Applicant	0	130000

Other merits

Period	Type of merit	Description
2012 - 2016	Popular scientific publications, examples	Jacobson, M. 2012. "Månadens sjukdom – actinobacillos", Svenska Pig's hemsida, oktober, http://svenskapiig.se/fakta-3/djuromsorg-och-halsa/ Jacobson, M. 2013. "Månadens sjukdom -trikinos", Svenska Pig's hemsida, april, http://svenskapiig.se/fakta-3/djuromsorg-och-halsa/ Jacobson, M. 2014. "Månadens sjukdom – afrikansk svinpest", Svenska Pig's hemsida, januari, http://svenskapiig.se/fakta-3/djuromsorg-och-halsa/ Jacobson, M. 2014. "Månadens sjukdom – spiroketal diarré", Svenska Pig's hemsida, maj, http://svenskapiig.se/fakta-3/djuromsorg-och-halsa/ Jacobson, M. 2015. "Månadens sjukdom – parakeratos, automatskorv", Svenska Pig's hemsida, april, http://svenskapiig.se/fakta-3/djuromsorg-och-halsa/ Jacobson, M. 2015. "Månadens sjukdom – selen-vitamin E-brist relaterade sjukdomar", Svenska Pig's hemsida, maj, http://svenskapiig.se/fakta-3/djuromsorg-och-halsa/ Jacobson, M. 2016. "Månadens sjukdom – gränsningsfeber, PPDS", Svenska Pig's hemsida, jan, http://svenskapiig.se/fakta-3/djuromsorg-och-halsa/
1994 - 2016	Other publications	H-index 15. Number of citations: 482. Abstract, popular scientific publications: 45 abstracts in conference proceedings, 55 popular scientific articles, and one book chapter.
2005 - 2016	expert reviewer of grant applications	Ivar och Elsa Sandbergs stipendiefond 2005 - 2011 Skogsbergs stipendiefond 2010 SLF (Swedish Farmers Foundation) 2008-2014 Member of the international review panel for the H.C. Ørsted Postdoc Programme, co-funded by Marie Curie Actions 2016
2011 - 2016	member of scientific boards	Member of the board (treasurer) for the Swedish society for Veterinary Research 2005-2011; Member of the credential committee in the European College for Porcine Health Management 2014 -to date; Member of the election committee for the Swedish society for Veterinary Research 2011-to date; Substitute in the election committee, FORMAS board 2012
2014 - 2016	Extension duties	Programme director for the Swedish/Norwegian training institution within ECPHM (European College of Porcine Health Management) 2014 -to date
2008 - 2016	opponentship /member of examination board	Opponent PhD dissertation Ken Pedersen, Faculty of Life Sciences, University of Copenhagen, Denmark 2/3 2012. Opponent PhD dissertation Hanne Kongsted, Faculty of Life Sciences, University of Copenhagen, Denmark 29/8 2014. Opponent PhD dissertation Marie Louise Hermann-Bank, Faculty of Life Sciences, University of Copenhagen, Denmark 27/2 2015. Member of examination board, PhD dissertation; Annica Thomsson 11/4 2008. Chair of examination board, PhD dissertation; Desiree Jansson 13/3 2009. Member of examination board, PhD dissertation; Erik Eriksson 5/2 2010. Chair of examination board, PhD dissertation; Marie Sjölund 3/12 2010. Chair of examination board, PhD dissertation; Anna Granlund 1/6 2011 Chair of examination board, PhD dissertation; Johanna Lindahl 26/10 2012.
2004 - 2016	External reviewer	External reviewer for the scientific journals "Acta Veterinaria Scandinavica", "American Journal of Veterinary Research", "Animal", "Annals of Animal Science", "APMIS", "Berliner und Münchener Tierärztliche Wochenschrift", "BMC Veterinary Research", "Epidemiology and Infection", "Equine Veterinary Journal", "Journal of Medical Microbiology", "Laboratory Animals", "Livestock Science", "Reproduction – Nutrition – Development", "the Veterinary Journal", "Veterinary Microbiology", and "Svensk Veterinärtidning", in total 42 assignments. External reviewer for the positions as teacher in swine diseases and prophylactic health management" and "herd management within veterinary public health" at the Norwegian Veterinary University, 2010 External reviewer for the position as associate professor in Veterinary Medicine, University of Helsinki, 2015.

Period	Type of merit	Description
2015 - 2015	Research evaluation committee work	Member of the international expert committee for the evaluation of the scientific research at the Danish Technical University, section for veterinary medicine (DTUvet), 2015
2012 - 2014	Senior lecturer with extension duties (samverkanslektor)	Position obtained in open competition, including 40-50% collaboration duties. Within the position an information series, "månadens sjukdom" (see below) has been created and published on the Svenska Pigs/Farm & Animal Health web page, several popular scientific lectures has been given, an active collaboration with the stakeholders has been established in applied research, and a practitioner exchange programme has been established with the Farm and Animal Health Service. The position also included active participation in several working groups at the Swedish board of Agriculture, the National Veterinary Institute and the Farm & Animal Health Service.
2000 - 2013	Member of organizing committee for international scientific conferences	Co-organizer for the "Colonic Spirochetal Infections in Animals and Humans –The Ekenäs meeting" 2–4/4-2000. Member of the scientific board at the 15th International Conference on Production Diseases in Farm Animals 24-28/6 2013. Co-organizer for the "Livestock Extension and Research Network", LEARN conference, 27/11 -2013.

CV - Juliette Hayer

Name: Juliette Hayer
Birthdate: 19850109
Gender: Female
Country:Sweden

Doctorial degree: 2013-02-15
Academic title: Doktor
Employer: Sveriges lantbruksuniversitet

Educational history

Research education

Examination	Organisation	Dissertation title (en)
Doctors degree, 10610. Bioinformatics and Systems Biology (methods development to be 10203), 2013-02-15	Lyon University - National Scientific Research Center, Bioinformatics Structures and Interactions	Development of a database for Hepatitis B Virus. Integration of analysis tools and application to polymerase molecular modeling

Basic education

Year	Examination
2008	10610. Bioinformatics and Systems Biology (methods development to be 10203), Degree of Master, University of Méditerranée, Marseille
2006	10602. Biochemistry and Molecular Biology incl. Biochemical Research Methods, Degree of Bachelor, University of Méditerranée, Marseille

Professional history

Employments

Period	Position	Part of research in employment	Employer
september 2013 - augusti 2016 (Present)	Postdoctoral fellow, Temporary employment	100	Swedish University of Agricultural Sciences, Husdjursgenetik
oktober 2009 - februari 2013	PhD student, Temporary employment	100	Lyon University - National Scientific Research Center
oktober 2008 - september 2009	Other	100	National Medical Research Center, Inserm U827

Post doctoral assignments

Period	Organisation	Subject
september 2015 - augusti 2016	Swedish University of Agricultural Sciences	10610. Bioinformatics and Systems Biology (methods development to be 10203)
september 2013 - september 2015	Swedish University of Agricultural Sciences, Husdjursgenetik	10610. Bioinformatics and Systems Biology (methods development to be 10203)

Merits and awards

Supervised persons		
Year	Supervised person	Role
2017	PhD student, Harindranath Cholleti	Secondary supervisor

Other merits		
Period	Type of merit	Description
2012 - 2016	Bibliometrics summary	i) My 4 peer-reviewed publications have generated a total number of 63 citations and my h-index is 3, according to Google Scholar. My publication range is 2012-2016. ii) I have 4 peer-reviewed publications, 3 conference contributions published online, 3 oral and 4 poster presentations at international conferences and my PhD thesis is published online (mostly in French). iii) My postdoctoral research has resulted in 1 article published, 1 article accepted in mBio journal, 1 manuscript submitted as last author, and at least 2 more soon to be submitted.

Intellectual property

Intellectual property	
Type	Product classification
free access database	72. Tjänster avseende vetenskaplig forskning och utveckling

CV - Anne-Lie Blomström

Name: Anne-Lie Blomström	Doctorial degree: 2010-12-03
Birthdate: 19780503	Academic title: Doktor
Gender: Female	Employer: Sveriges lantbruksuniversitet
Country: Sweden	

Educational history

Research education		
Examination	Organisation	Dissertation title (en)
Doctors degree, 40302. Pathobiology incl. Immunology, Microbiology, Pathology, Toxicology, Pharmacology, Food Safety, 2010-12-03	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap	Applications of viral metagenomics in the veterinary field - looking for the unknown

Basic education	
Year	Examination
2004	10602. Biochemistry and Molecular Biology incl. Biochemical Research Methods, Degree of Master, Swedish University of Agricultural Sciences

Professional history

Employments

Period	Position	Part of research in employment	Employer
januari 2015 - Present	Researcher, Permanent employment	50	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap
oktober 2012 - januari 2013	Researcher, Temporary employment	100	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap
januari 2012 - september 2012	Universitetsadjunkt, Temporary employment	60	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap
december 2010 - december 2011	Researcher, Temporary employment	90	Swedish University of Agricultural Sciences, Biomedicin och veterinär folkhälsovetenskap
oktober 2005 - februari 2006	Forskningsingenjör, Temporary employment	100	National Veterinary Institute, SVA

Post doctoral assignments

Period	Organisation	Subject
februari 2013 - januari 2015	University of Glasgow, Center for virus research (CVR)	30599. Other Medical and Health Sciences not elsewhere specified

Merits and awards

Supervised persons

Supervised persons	Role	Number
PhD student	Secondary supervisor	4
Student	Main supervisor	1
Student	Main supervisor	2
Student	Main supervisor	6

Research grants awarded in competition

Period	Funder	Project leader	Your role	Sub amount (SEK)	Total amount (SEK)
2015 - 2017	Formas	Anne-Lie Blomström	Applicant	0	2641000
2013 - 2015	VR - Vetenskapsrådet	Anne-Lie Blomström	Applicant	0	3150000
2013 - 2015	VR - Vetenskapsrådet	Anne-Lie Blomström	Applicant	0	2700000
2013 - 2015	Formas	Mikael Berg	Co-applicant	0	8700000

Awards and distinctions

Year	Name of award/distinction	Issuer
2015	Award from "Stiftelsen Konung Carl XVI Gustafs 50-årsfond för vetenskap, teknik och miljö" for the topic "Smittbärare orsakar nya hot mot svensk djurhållning".	Stiftelsen Konung Carl XVI Gustafs 50-årsfond för vetenskap, teknik och miljö
2011	Best scientific publication 2008-2010	Sällskapet för veterinärmedicinsk forskning

Other merits

Period	Type of merit	Description
2015 - 2018	ICTV Anelloviridae Study Group	Member of the ICTV Anelloviridae Study Group
2011 - 2016	bibliometric summary	bibliometric summary from last five years: i) Citations 470; h-index 10; i10-index 10 ii) Peer-reviewed original papers 14; Peer reviewed review articles 3; Popular science articles 1

Publications

Publications - Maja Malmberg

Name: Maja Malmberg	Doctorial degree: 2013-01-18
Birthdate: 19820516	Academic title: Doktor
Gender: Female	Employer: Sveriges lantbruksuniversitet
Country: Sweden	

Scientific publication - peer-reviewed

Original journal article

Title: Alternatively spliced transcripts and novel pseudogenes of the Plasmodium falciparum resistance-associated locus pfcrt detected in East African malaria patients

Authors: Nahla B. Gadalla, Maja Malmberg, Ishag Adam, Mary C. Oguike, Khalid Beshir, Salah-Eldin Elzaki, Izdihar Mukhtar, Amal A. Gadalla, David C. Warhurst, Billy Ngasala, Andreas Martensson, Badria B. El-Sayed, J. Pedro Gil, Colin J. Sutherland

Date of publication: 2015 **Volume:** 70 **Issue number:** 1

Name of journal: JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY

Academic publication - peer-reviewed: Original journal article

Title: Polymorphisms in Plasmodium falciparum Chloroquine Resistance Transporter and Multidrug Resistance 1 Genes: Parasite Risk Factors that Affect Treatment Outcomes for P-falciparum Malaria after Artemether-Lumefantrine and Artesunate-Amodiaquine

Authors: Meera Venkatesan, Nahla B. Gadalla, Kasia Stepniewska, Prabin Dahal, Christian Nsanzabana, Clarissa Moriera, Ric N. Price, Andreas Martensson, Philip J. Rosenthal, Grant Dorsey, Colin J. Sutherland, Philippe Guerin, Timothy M. E. Davis, Didier Menard, Ishag Adam, George Ademowo, Cesar Arze, Frederick N. Baliraine, Nicole Berens-Riha, Anders Bjorkman, Steffen Borrmann, Francesco Checchi, Meghna Desai, Mehul Dhorda, Abdoulaye A. Djimde, Badria B. El-Sayed, Teferi Eshetu, Frederick Eyase, Catherine Falade, Jean-Francois Faucher, Gabrielle Froberg, Anastasia Grivoyannis, Sally Hamour, Sandrine Houze, Jacob Johnson, Erasmus Kamugisha, Simon Kariuki, Jean-Rene Kiechel, Fred Kironde, Poul-Erik Kofoed, Jacques LeBras, Maja Malmberg, Leah Mwai, Billy Ngasala, Francois Nosten, Samuel L. Nsohya, Alexis Nzila, Mary Oguike, Sabina Dahlstrom Otienoburu, Bernhards Ogotu, Jean-Bosco Ouedraogo, Patrice Piola, Lars Rombo, Birgit Schramm, A. Fabrice Some, Julie Thwing, Johan Ursing, Rina P. M. Wong, Ahmed Zeynudin, Issaka Zongo, Christopher V. Plowe, Carol Hopkins Sibley

Date of publication: 2014 **Volume:** 91 **Issue number:** 4

Name of journal: AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE

Academic publication - peer-reviewed: Original journal article

Title: Single nucleotide polymorphisms in Plasmodium falciparum V type H⁺ pyrophosphatase gene (pfvp2) and their associations with pfcrt and pfmdr1 polymorphisms

Authors: Irina Tatiana Jovel, Pedro Eduardo Ferreira, Maria Isabel Veiga, Maja Malmberg, Andreas Martensson, Akira Kaneko, Sedigheh Zakeri, Claribel Murillo, Francois Nosten, Anders Bjorkman, Johan Ursing

Date of publication: 2014 **Volume:** 24 **Issue number:**

Name of journal: INFECTION GENETICS AND EVOLUTION

Academic publication - peer-reviewed: Original journal article

Title: Plasmodium falciparum Drug Resistance Phenotype as Assessed by Patient Antimalarial Drug Levels and Its Association With pfmdr1 Polymorphisms

Authors: Maja Malmberg, Pedro E. Ferreira, Joel Tarning, Johan Ursing, Billy Ngasala, Anders Bjorkman, Andreas Martensson, Jose P. Gil

Date of publication: 2013 **Volume:** 207 **Issue number:** 5

Name of journal: JOURNAL OF INFECTIOUS DISEASES

Academic publication - peer-reviewed: Original journal article

Title: Temporal trends of molecular markers associated with artemether-lumefantrine tolerance/resistance in Bagamoyo district, Tanzania

Authors: Maja Malmberg, Billy Ngasala, Pedro E. Ferreira, Erik Larsson, Irina Jovel, Angelica Hjalmarsson, Max Petzold, Zul Premji, Jose P. Gil, Anders Bjorkman, Andreas Martensson

Date of publication: 2013 **Volume:** 12 **Issue number:**

Name of journal: MALARIA JOURNAL

Academic publication - peer-reviewed: Original journal article

Title: pfmdr1 Amplification Is Related to Increased Plasmodium falciparum In Vitro Sensitivity to the Bisquinoline Piperaquine

Authors: M. I. Veiga, P. E. Ferreira, M. Malmberg, L. Jornhagen, A. Bjorkman, F. Nosten, J. P. Gil

Date of publication: 2012 **Volume:** 56 **Issue number:** 7

Name of journal: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY

Academic publication - peer-reviewed: Original journal article

Title: Effectiveness of artemether-lumefantrine provided by community health workers in under-five children with uncomplicated malaria in rural Tanzania

Authors: Billy E. Ngasala, Maja Malmberg, Anja M. Carlsson, Pedro E. Ferreira, Max G. Petzold, Daniel Blessborn, Yngve Bergqvist, Jose P. Gil, Zul Premji, Andreas Martensson, Andreas Mårtensson

Date of publication: 2011 **Volume:** 10 **Issue number:**

Name of journal: Malaria Journal

Academic publication - peer-reviewed: Original journal article

Title: Efficacy and Effectiveness of Artemether-Lumefantrine after Initial and Repeated Treatment in Children < 5 Years of Age with Acute Uncomplicated Plasmodium falciparum Malaria in Rural Tanzania: A Randomized Trial

Authors: Billy E. Ngasala, Maja Malmberg, Anja M. Carlsson, Pedro E. Ferreira, Max G. Petzold, Daniel Blessborn, Yngve Bergqvist, Jose P. Gil, Zul Premji, Anders Bjoerkman, Andreas Martensson

Date of publication: 2011 **Volume:** 52 **Issue number:** 7

Name of journal: CLINICAL INFECTIOUS DISEASES

Academic publication - peer-reviewed: Original journal article

Title: Molecular genotypes and clearance of different P. falciparum sub populations in children treated with ACT

Authors: M. Malmberg, A. Carlsson, P. E. Ferreira, M. I. Veiga, M. Petzold, B. Ngasala, A. Bjorkman, J. P. Gil, A. Martensson

Date of publication: 2011 **Volume:** 16 **Issue number:**

Name of journal: TROPICAL MEDICINE & INTERNATIONAL HEALTH

Academic publication - peer-reviewed: Original journal article

Title: Novel Polymorphisms in Plasmodium falciparum ABC Transporter Genes Are Associated with Major ACT Antimalarial Drug Resistance

Authors: Maria Isabel Veiga, Pedro Eduardo Ferreira, Louise Jornhagen, Maja Malmberg, Aminatou Kone, Berit Aydin Schmidt, Max Petzold, Anders Bjorkman, Francois Nosten, Jose Pedro Gil

Date of publication: 2011 **Volume:** 6 **Issue number:** 5

Name of journal: PLOS ONE

Academic publication - peer-reviewed: Original journal article

Name: Mikael Berg
Birthdate: 19590324
Gender: Male
Country: Sweden

Doctorial degree: 1991-04-12
Academic title: Professor
Employer: Sveriges lantbruksuniversitet

Scientific publication - peer-reviewed

Original journal article

Title: The Intestinal Eukaryotic Virome in Healthy and Diarrhoeic Neonatal Piglets
Authors: Oskar Karlsson, Jenny Larsson, Juliette Hayer, Mikael Berg, Magdalena Jacobson
Date of publication: 2016-03-22 **Volume:** **Issue number:**
Name of journal: PLOS One
Academic publication - peer-reviewed: Original journal article

Title: Long-term RNA persistence of Porcine rubulavirus (PorPV-LPMV) after an outbreak of a natural infection: The detection of viral mRNA in sentinel pigs suggests viral transmission
Authors: Julieta Sandra Cuevas-Romero, Mikael Berg, Jorge Moreno-lopez
Date of publication: 2014 **Volume:** 188 **Issue number:**
Name of journal: Virus Research
Academic publication - peer-reviewed: Original journal article

Title: The X proteins of bornaviruses interfere with type I interferon signalling
Authors: Jonas Johansson Wensman, Muhammad Munir, Srinivas Thaduri, Katarina Hornaeus, Muhammad Rizwan, Anne-Lie Blomstrom, Thomas Brieese, W. Ian Lipkin, Mikael Berg
Date of publication: 2013 **Volume:** 94 **Issue number:**
Name of journal: JOURNAL OF GENERAL VIROLOGY
Academic publication - peer-reviewed: Original journal article

Title: METAGENOMIC DETECTION METHODS IN BIOPREPAREDNESS OUTBREAK SCENARIOS
Authors: Oskar Erik Karlsson, Trine Hansen, Rickard Knutsson, Charlotta Lofstrom, Fredrik Granberg, Mikael Berg
Date of publication: 2013 **Volume:** 11 **Issue number:**
Name of journal: BIOSECURITY AND BIOTERRORISM-BIODEFENSE STRATEGY PRACTICE AND SCIENCE
Academic publication - peer-reviewed: Original journal article

Title: First time molecular detection and phylogenetic relationships of torque teno sus virus 1 and 2 in domestic pigs in Uganda: further evidence for a global distribution
Authors: Mikael Berg, Anne-Lie Blomström, Matilda Brink, Charles Masembe, A R Okurut, Karl Ståhl
Date of publication: 2012 **Volume:** 9 **Issue number:**
Name of journal: Virology Journal
Academic publication - peer-reviewed: Original journal article

Title: Complete Genome Sequence of a Velogenic Neurotropic Avian Paramyxovirus 1 Isolated from Peacocks (Pavo cristatus) in a Wildlife Park in Pakistan
Authors: Muhammad Munir, Muhammad Z. Shabbir, Tahir Yaqub, Muhammad A. B. Shabbir, Nadia Mukhtar, Muhammad R. Khan, Mikael Berg
Date of publication: 2012 **Volume:** 86 **Issue number:** 23
Name of journal: JOURNAL OF VIROLOGY
Academic publication - peer-reviewed: Original journal article

Title: Genomic and biological characterization of a velogenic Newcastle disease virus isolated from a healthy backyard poultry flock in 2010
Authors: Muhammad Munir, Muhammad Abbas, Muhammad Tanveer Khan, Siamak Zohari, Mikael Berg
Date of publication: 2012 **Volume:** 9 **Issue number:**
Name of journal: VIROLOGY JOURNAL
Academic publication - peer-reviewed: Original journal article

Title: Viral metagenomic analysis of bushpigs (*Potamochoerus larvatus*) in Uganda identifies novel variants of Porcine parvovirus 4 and Torque teno sus virus 1 and 2

Authors: Sandor Belak, Mikael Berg, Karl Ståhl, Anne-Lie Blomström

Date of publication: 2012 **Volume:** 9 **Issue number:**

Name of journal: Virology Journal

Academic publication - peer-reviewed: Original journal article

Title: Detection of a Novel Astrovirus in Brain Tissue of Mink Suffering from Shaking Mink Syndrome by Use of Viral Metagenomics

Authors: Anne-Lie Blomstrom, Frederik Widen, Anne-Sofie Hammer, Sandor Belak, Mikael Berg

Date of publication: 2010 **Volume:** 48 **Issue number:** 12

Name of journal: JOURNAL OF CLINICAL MICROBIOLOGY

Academic publication - peer-reviewed: Original journal article

Title: Studies of porcine circovirus type 2, porcine bocavirus-like virus and torque teno virus indicate the presence of multiple viral infections in postweaning multisystemic wasting syndrome pigs

Authors: Lisbeth Fuxler, Caroline Fossum, Sandor Belak, Mikael Berg, Anne-Lie Blomström, P Wallgren

Date of publication: 2010 **Volume:** 152 **Issue number:** 1-2

Name of journal: Virus Research

Academic publication - peer-reviewed: Original journal article

Publications - Magdalena Jacobson

Name: Magdalena Jacobson

Doctorial degree: 2003-09-19

Birthdate: 19581017

Academic title: Professor

Gender: Female

Employer: Sveriges lantbruksuniversitet

Country:Sweden

Scientific publication - peer-reviewed

Original journal article

Title: The intestinal eukaryotic virome in healthy and diarrhoeic neonatal piglets.

Authors: Oskar Karlsson, Jenny Larsson, Juliette Hayer, Mikael Berg, Magdalena Jacobson

Date of publication: 2016-03-16 **Volume:** 11 **Issue number:** 3

Name of journal: PLoS ONE

Academic publication - peer-reviewed: Original journal article

Title: Pathological and bacteriological characterisation of neonatal porcine diarrhoea with uncertain aetiology.

Authors: Jenny Larsson, Anna Aspan, Ronny Lindberg, Rodrigo Grandon, Viveca Båverud, Nils Fall, Magdalena jacobson

Date of publication: 2015-08-31 **Volume:** 64 **Issue number:** 8

Name of journal: Journal of Medical Microbiology

Academic publication - peer-reviewed: Original journal article

Title: Astrovirus as a possible cause of congenital tremor type All in piglets?

Authors: Blomström Anne-Lie, Ley Cecilia, Jacobson Magdalena

Date of publication: 2014-11-24 **Volume:** 56 **Issue number:** 82

Name of journal: Acta Veterinaria Scandinavica

Academic publication - peer-reviewed: Original journal article

Title: Neonatal piglet diarrhoea associated with enteroadherent *Enterococcus hirae*

Authors: Jenny Larsson, Aspan Anna, Grandon Rodrigo, Lindberg Ronny, Westergren Eva, Jacobson Magdalena

Date of publication: 2014-04-07 **Volume:** 151 **Issue number:**

Name of journal: Journal of Comparative Pathology

Academic publication - peer-reviewed: Original journal article

Title: Inverted teats (Mammillae invertitae) in gilts – effects on piglet survival and growth rate
Authors: Chalkias Helena, Ekman Elisabeth, Lundeheim Nils, Rydmer Lotta, Jacobson Magdalena
Date of publication: 2014-03-05 **Volume:** 92 **Issue number:** 6
Name of journal: Journal of Animal Science
Academic publication - peer-reviewed: Original journal article

Title: Microarray and cytokine analyses of field cases of pigs with diarrhoea
Authors: Magdalena Jacobson, Märit Andersson, Ronny Lindberg, Caroline Fossum, Marianne Jensen Waern
Date of publication: 2011 **Volume:** 153 **Issue number:** 3-4
Name of journal: Veterinary Microbiology
Academic publication - peer-reviewed: Original journal article

Title: Porcine proliferative enteropathy: An important disease with questions remaining to be solved
Authors: Magdalena Jacobson, Claes Fellström, Marianne Jensen Waern
Date of publication: 2010 **Volume:** 184 **Issue number:** 3
Name of journal: Veterinary Journal
Academic publication - peer-reviewed: Original journal article

Title: Consecutive pathological and immunological alterations during experimentally induced swine dysentery - A study performed by repeated endoscopy and biopsy samplings through an intestinal cannula
Authors: M. Jacobson, R. Lindberg, R. Jonasson, C. Fellstrom, M. Jensen Waern
Date of publication: 2007 **Volume:** 82 **Issue number:** 3
Name of journal: RESEARCH IN VETERINARY SCIENCE
Academic publication - peer-reviewed: Original journal article

Title: A simulation-based study comparing a traditional and an alternative design for studies of experimentally induced intestinal diseases in pigs
Authors: Ulf Emanuelson, Marianne Jensen Waern, Magdalena Jacobson
Date of publication: 2007 **Volume:** 54 **Issue number:** 9
Name of journal: Journal Of Veterinary Medicine Series A-Physiology Pathology Clinical Medic
Academic publication - peer-reviewed: Original journal article

Title: Experimental swine dysentery: comparison between infection models
Authors: Magdalena Jacobson, Claes Fellström, Ronny Lindberg, Marianne Jensen Waern, Per Wallgren
Date of publication: 2004 **Volume:** 53 **Issue number:** 4
Name of journal: Journal Of Medical Microbiology
Academic publication - peer-reviewed: Original journal article

Publications - Juliette Hayer

Name: Juliette Hayer	Doctorial degree: 2013-02-15
Birthdate: 19850109	Academic title: Doktor
Gender: Female	Employer: Sveriges lantbruksuniversitet
Country: Sweden	

Scientific publication - peer-reviewed

Original journal article

Title: The Intestinal Eukaryotic Virome in Healthy and Diarrhoeic Neonatal Piglets
Authors: Oskar E Karlsson, Jenny Larsson, Juliette Hayer, Mikael Berg, Magdalena Jacobson
Date of publication: 2016-03-16 **Volume:** **Issue number:** **Name of journal:** plos one
Academic publication - peer-reviewed: Original journal article

Title: Ultradeep Pyrosequencing and Molecular Modeling Identify Key Structural Features of Hepatitis B Virus RNase H, a Putative Target for Antiviral Intervention
Authors: Juliette Hayer, Christophe Rodriguez, Georgios Germanidis, Gilbert Deleage, Fabien Zoulim, Jean-Michel Pawlotsky, Christophe Combet
Date of publication: 2014 **Volume:** 88 **Issue number:** 1
Name of journal: JOURNAL OF VIROLOGY
Academic publication - peer-reviewed: Original journal article

Title: HBVdb: a knowledge database for Hepatitis B Virus
Authors: Juliette Hayer, Fanny Jadeau, Gilbert Deleage, Alan Kay, Fabien Zoulim, Christophe Combet
Date of publication: 2013 **Volume:** 41 **Issue number:** D1
Name of journal: NUCLEIC ACIDS RESEARCH
Academic publication - peer-reviewed: Original journal article

Title: Mutations That Alter Use of Hepatitis C Virus Cell Entry Factors Mediate Escape From Neutralizing Antibodies
Authors: Isabel Fofana, Samira Fafi-Kremer, Patric Carolla, Catherine Fauvelle, Muhammad Nauman Zahid, Marine Turek, Laura Heydmann, Karine Cury, Juliette Hayer, Christophe Combet, Francois-Loic Cosset, Thomas Pietschmann, Marie-Sophie Hiet, Ralf Bartenschlager, Francois Habersetzer, Michel Doffoel, Zhen-Yong Keck, Steven K. H. Fong, Mirjam B. Zeisel, Francoise Stoll-Keller, Thomas F. Baumert
Date of publication: 2012 **Volume:** 143 **Issue number:** 1
Name of journal: GASTROENTEROLOGY
Academic publication - peer-reviewed: Original journal article

Research review article

Title: The Bee Microbiome: Impact on Bee Health and Model for Evolution and Ecology of Host-Microbe Interactions
Authors: Philipp Engel, Waldan K. Kwong, Quinn McFrederick, Kirk E. Anderson, Seth Michael Barribeau, James Angus Chandler, R. Scott Cornman, Jacques Dainat, Joachim R. de Miranda, Vincent Doublet, Olivier Emery, Jay D. Evans, Laurent Farinelli, Michelle L. Flenniken, Fredrik Granberg, Juris A. Grasis, Laurent Gauthier, Juliette Hayer, Hauke Koch, Sarah Kocher, Vince Martinson, Nancy Moran, Monica Munoz-Torres, Irene Newton, Robert J. Paxton, Eli Powell, Ben M. Sadd, Paul Schmid-Hempel, Regula Schmid-Hempel, Se Jin Song, Ryan S. Schwarz, Dennis vanEngelsdorp, Benjamin Dainat
Date of publication: **Volume:** **Issue number:**
Name of journal: mBio
Academic publication - peer-reviewed: Research review article

Editorial proceedings

Title: STRUCTURE OF THE HEPATITIS B VIRUS RNase H, A TARGET FOR NEW ANTIVIRAL DRUG DEVELOPMENT, UNRAVELED BY ULTRA-DEEP PYROSEQUENCING AND MOLECULAR MODELING
Authors: J. Hayer, C. Rodriguez, G. Germanidis, G. Deleage, F. Zoulim, J. -M. Pawlotsky, C. Combet
Date of publication: 2013 **Volume:** 58 **Issue number:**
Name of journal: JOURNAL OF HEPATOLOGY
Academic publication - peer-reviewed: Editorial proceedings

Title: CELL ENTRY FACTOR USAGE AND VIRAL EVASION IN HEPATITIS C VIRUS INFECTION IN VIVO
Authors: P. Carolla, I. Fofana, S. Fafi-Kremer, M. N. Zahid, K. Cury, M. Turek, M. Bastien-Valle, F. -L. Cosset, T. Pietschmann, J. Hayer, C. Combet, F. Habersetzer, M. Doffoel, Z. -Y. Keck, S. K. H. Fong, M. B. Zeisel, F. Stoll-Keller, T. F. Baumert
Date of publication: 2011 **Volume:** 54 **Issue number:**
Name of journal: JOURNAL OF HEPATOLOGY
Academic publication - peer-reviewed: Editorial proceedings

Publications - Anne-Lie Blomström

Name: Anne-Lie Blomström
Birthdate: 19780503
Gender: Female
Country: Sweden

Doctorial degree: 2010-12-03
Academic title: Doktor
Employer: Sveriges lantbruksuniversitet

Scientific publication - peer-reviewed

Original journal article

Title: Transcriptome analysis reveals the host response to Schmallenberg virus in bovine cells and antagonistic effects of the NSs protein

Authors: Anne-Lie Blomström, Quan Gu, Gerald Barry, Gavin Wilkie, Jessica K Skelton, Margaret Baird, Melanie McFarlane, Esther Schnettler, Richard M Elliott, Massimo Palmarini, Alain Kohl

Date of publication: 2015 **Volume:** 16 **Issue number:**

Name of journal: BMC Genomics

Academic publication - peer-reviewed: Original journal article

Title: Astrovirus as a possible cause of congenital tremor type All in piglets?

Authors: Anne-Lie Blomström, Cecilia Ley, Magdalena Jacobson

Date of publication: 2014 **Volume:** 56 **Issue number:**

Name of journal: Acta Veterinaria Scandinavica

Academic publication - peer-reviewed: Original journal article

Title: Serological Screening Suggests Presence of Schmallenberg Virus in Cattle, Sheep and Goat in the Zambezia Province, Mozambique

Authors: Anne-Lie Blomström, Mikael Berg

Date of publication: 2014 **Volume:** 61 **Issue number:** 4

Name of journal: Transboundary And Emerging Diseases

Academic publication - peer-reviewed: Original journal article

Title: Genetic characterisation of a porcine bocavirus detected in domestic pigs in Uganda

Authors: Anne-Lie Blomström, Karl Ståhl, A R Okurut, Charles Masembe, Mikael Berg

Date of publication: 2013 **Volume:** 47 **Issue number:** 2

Name of journal: Virus Genes

Academic publication - peer-reviewed: Original journal article

Title: Development of a real-time RT-PCR method for detection of porcine rubulavirus (PoRV-LPMV)

Authors: Sandra J. Cuevas, Anne-Lie Blomström, Arcelia Alvarado, pablo hernandez-Jauregui, Francisco Rivera-Benitez, Humberto Ramirez-Mendoza, Mikael Berg

Date of publication: 2013 **Volume:** 189 **Issue number:** 1

Name of journal: Journal Of Virological Methods

Academic publication - peer-reviewed: Original journal article

Title: Viral metagenomic analysis of bushpigs (Potamochoerus larvatus) in Uganda identifies novel variants of Porcine parvovirus 4 and Torque teno sus virus 1 and 2

Authors: Anne-Lie Blomström, Karl Ståhl, Sándor Belák, Mikael Berg

Date of publication: 2012 **Volume:** 9 **Issue number:**

Name of journal: Virology Journal

Academic publication - peer-reviewed: Original journal article

Title: Development of an in situ assay for simultaneous detection of the genomic and replicative form of PCV2 using padlock probes and rolling circle amplification

Authors: Sara Henriksson, Anne-Lie Blomström, Lisbeth Fuxler, Caroline Fossum, Mikael Berg, Mats Nilsson

Date of publication: 2011 **Volume:** 8 **Issue number:**

Name of journal: Virology Journal

Academic publication - peer-reviewed: Original journal article

Title: Viral metagenomics as an emerging and powerful tool in veterinary medicine

Authors: Anne-Lie Blomström

Date of publication: 2011 **Volume:** 31 **Issue number:** 3

Name of journal: Veterinary Quarterly

Academic publication - peer-reviewed: Original journal article

Title: Detection of a Novel Astrovirus in Brain Tissue of Mink Suffering from Shaking Mink Syndrome by Use of Viral Metagenomics

Authors: Anne-Lie Blomström, Frederik Widén, Anne-Sofie Hammer, Sándor Belák, Mikael Berg, F Widén

Date of publication: 2010 **Volume:** 48 **Issue number:** 12

Name of journal: Journal Of Clinical Microbiology

Academic publication - peer-reviewed: Original journal article

Title: Detection of a novel porcine bocavirus-like virus in the background of porcine circovirus type 2 induced postweaning multisystemic wasting syndrome

Authors: Anne-Lie Blomström, Sándor Belák, Caroline Fossum, John McKillen, Gordon Allan, Per Wallgren, Mikael Berg

Date of publication: 2009 **Volume:** 146 **Issue number:** 1-2

Name of journal: Virus Research

Academic publication - peer-reviewed: Original journal article

Register

Terms and conditions

Ansökan ska förutom av den sökande även signeras av behörig företrädare för medelsförvaltaren. Företrädaren är vanligtvis prefekten vid den institution där forskningen ska bedrivas, men ska i vissa fall utgöras av exempelvis rektor. Detta framgår i sådana fall av den aktuella utlysningstexten för bidraget.

Signering av *den sökande* innebär en bekräftelse av att:

- uppgifterna i ansökan är korrekta och följer Formas instruktioner
- bisysslor och kommersiella bindningar har redovisats för medelsförvaltaren och att det där inte framkommit något som strider mot god forskningssed
- nödvändiga tillstånd och godkännanden ska finnas senast vid projektstart, exempelvis avseende etikprövning.

Signering av *medelsförvaltaren* innebär en bekräftelse av att:

- den beskrivna forskningen, anställningen och utrustningen kan beredas plats inom institutionen under den tid och i den omfattning som anges i ansökan
- institutionen godkänner kostnadsberäkningen i ansökan
- projektet bedrivs i enlighet med svensk lagstiftning.

Ovanstående punkter ska ha diskuterats mellan parterna innan företrädaren för medelsförvaltaren godkänner och signerar ansökan.

Ansökningar där en organisation är sökande signeras automatiskt vid registrering av ansökan.

