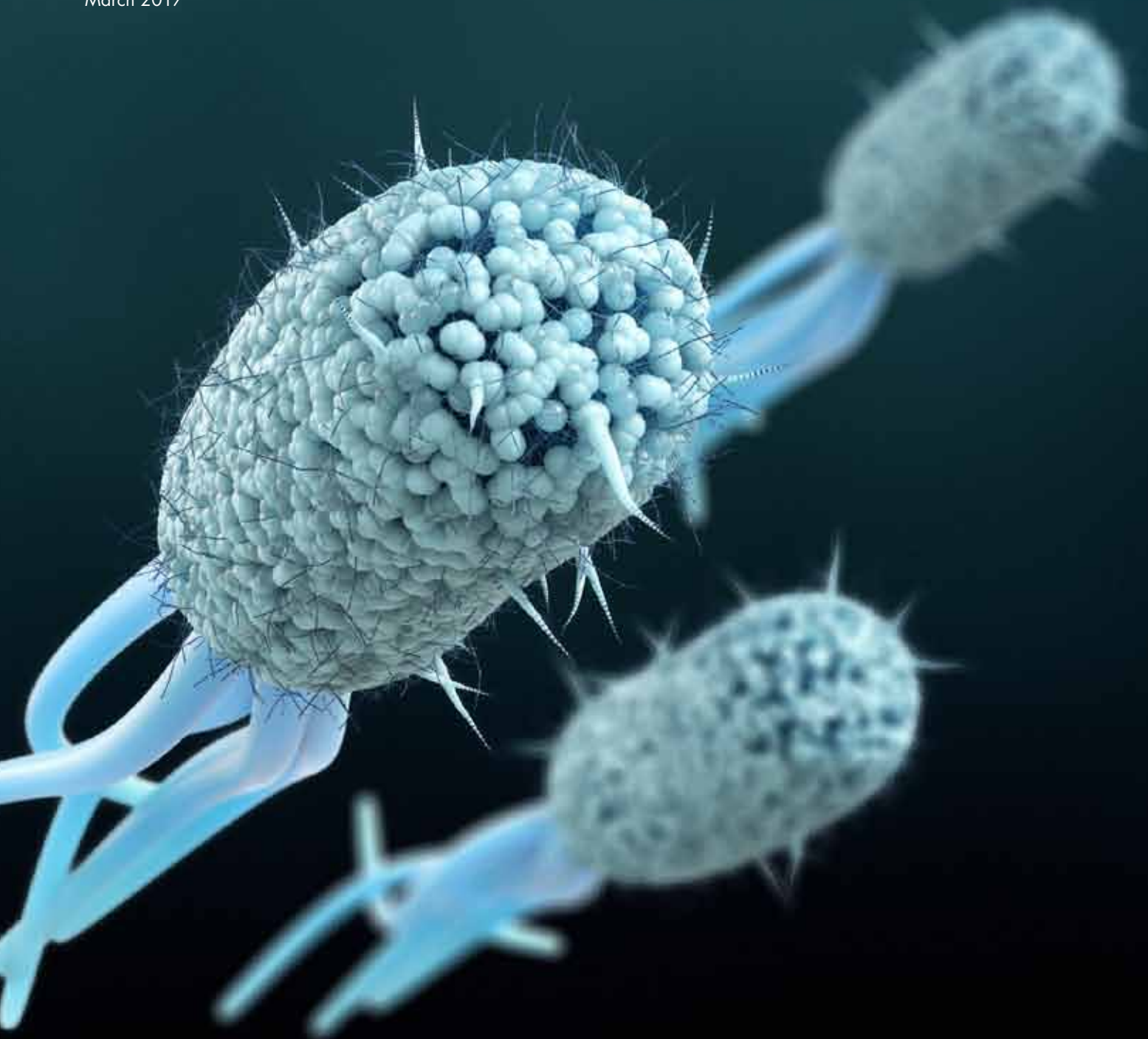


Infectious Diseases

World-Leading Research and
Business Opportunities in
the Stockholm-Uppsala Region

March 2017



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1. World-leading hub for infectious disease research

Infectious illnesses account for a significant part of global disease. New pathogens are discovered on a regular basis while familiar microbes continue to cause problems through changes in their pathogenesis and transmission. Add the looming problem of resistance to antimicrobial drugs and the relative lack of global funding for research into infectious diseases becomes even more puzzling.

The Stockholm-Uppsala region differs in this regard. It has several awarding bodies that support pre-clinical science, observational studies, clinical trials, and translational research – not least within the field of infectious diseases. This goes some way to explain why there are so many research groups focusing on infectious disease in the region, and of course: the many commercial opportunities that follow.

There is a longstanding history of collaboration in the Life Sciences sector between universities, industry and hospitals, which has nurtured the development of multinational pharmaceutical businesses in the region, including Astra, today a part of AstraZeneca, and Pharmacia, now a part of GE Healthcare. This unique approach will soon be amplified further with one of Sweden's largest urban development projects ever undertaken, Hagastaden – a world class science city.

The region outperforms in relation to its size with regard to innovation and infrastructure. In 2015, Stockholm was the most popular Nordic city for international companies to set up regional Northern European headquarters and was ranked second in Europe in scale up according to the European Digital City Index 2016. Sweden as a whole was ranked second in the world in innovation according to the Global Innovation Index 2016 and is also the world's third most IT-mature country, according to the 2016 Global Information Technology Report. In 2017, Forbes ranks Sweden the best country for business.

The legacy of Nobel and free university studies has created an advanced and pioneering workforce, which thanks to the so-called "Professors' privilege" enjoys the full ownership of their university-derived innovations. Let's have a look at some of the exciting things that are happening in infectious diseases in the most creative life science hub in Europe.

2. The region's Nobel laureates

The legacy of chemist, entrepreneur and Stockholmer Alfred Nobel strongly permeates the region. Tomas Lindahl, who was awarded the Nobel Prize in Chemistry in 2015 is the 31st Swede to receive a Nobel Prize since 1903 and the 24th from the Stockholm-Uppsala region.

Chemistry

1. Svante Arrhenius, Stockholm University (1903)
2. Theodor Svedberg, Uppsala University (1926)
3. Hans von Euler, Stockholms University (1929)
4. Arne Tiselius, Uppsala University (1948)
5. Tomas Lindahl, Karolinska Institutet (2015)

Physiology or Medicine

1. Allvar Gullstrand, Uppsala University (1911)
2. Hugo Theorell, Karolinska Institutet (1955)
3. Ragnar Granit, Karolinska Institutet (1967)
4. Ulf von Euler, Karolinska Institutet (1970)
5. Torsten Wiesel, Karolinska Institutet (1981)
6. Sune Bergström, Karolinska Institutet (1982)
7. Bengt Samuelsson, Karolinska Institutet (1982)

Physics

1. Gustaf Dalén, worked in Stockholm (AGA) (1912)
2. Manne Siegbahn, first worked at Lund University and Uppsala University, then at the Royal Swedish Academy of Sciences (1924)
3. Hannes Alfvén, Royal Institute of Technology (1970)
4. Kai Siegbahn, worked at Stockholm University, Uppsala University, Royal Institute of Technology (1981)

Economic Sciences

1. Gunnar Myrdal, worked at the Stockholm School of Economics and Stockholm University (1974)
2. Bertil Olin, worked at the Stockholm School of Economics (1977)

Literature

1. Tomas Tranströmer (2011)

Peace

1. Klas Pontus Arnoldson (1908)
2. Hjalmar Branting (1921)
3. Nathan Söderblom (1939)
4. Dag Hammarskjöld (1961)
5. Alva Myrdal, worked on different public service tasks in Stockholm (1982)

3. Universities and Centers of excellence

Stockholm-Uppsala is the most prominent academic center in Northern Europe, attracting many foreign students and researchers. For over 500 years, Uppsala University has conducted world-leading research and provided a first class education. Karolinska Institutet in Stockholm is the tenth best medical university in the world according to the QS world university rankings for 2016. The Nobel Assembly at Karolinska Institutet is responsible for selecting the Nobel Laureates in Physiology or Medicine.

Karolinska Institutet and Karolinska University Hospital

Karolinska Institutet was established in 1810 in Stockholm and today it accounts for over 40 percent of the medical academic research conducted in Sweden. Karolinska Institutet is in close proximity to Karolinska University Hospital and other hospitals, where clinical trials are conducted. The Karolinska University Hospital is currently being expanded and the New Karolinska Solna is scheduled to be completed in 2018. To ward off risks of infection, and give greater patient comfort and privacy, single rooms are at the heart of the care at the new hospital. At Karolinska Institutet two new research centers are currently being built: Neo and Biomedicum.

Centre for Infectious Disease Research (CID)

The CID covers biologically relevant infectious disease research with a focus on antimicrobial resistance & drug development, diagnostics, epidemiology & transmission and pathogenesis. One of its goals is to make CID a meeting ground to promote commercialization of new ideas and concepts that can form the basis for new biotechnology company start-ups that will help to transform successful academic Research & Development programs into products.

Center for Infectious Medicine (CIM)

The research at the Center for Infectious Medicine is focused around studies of the human immune system and infection-immunity in humans. The center operates within the Department of Medicine, Huddinge at Karolinska Institutet. Since its inauguration in 2002, CIM has grown rapidly and gained national and international recognition. The vision is to become one of the leading translational research centers relating to immunity and infectious diseases in Europe.

Development platform for E-health

In March 2015, KI Holding presented HIP.se, a health innovation platform that provides developers and entrepreneurs with a tool for developing E-health services. It also gives researchers the possibility of carrying out medical studies in an entirely different way. For example, compared to Apple's Research Kit, HIP is also equipped with the security services demanded by the Swedish system.

Uppsala University and Uppsala Akademiska University Hospital

Uppsala University was established in 1477 and has produced several Nobel Prize Laureates. The University is affiliated with Uppsala University Hospital, which was established in 1708 and is where the clinical trials are conducted.

Uppsala Antibiotic Center (UAC)

A new center for research, education and innovation, which aims to tackle and find solutions to the global challenge around antibiotic resistance. At UAC interdisciplinary research and education is conducted by involving all the three scientific disciplines at Uppsala University. Activities at the center started in autumn 2016 through an open call for applications of 14 interdisciplinary doctorate projects at Uppsala University.

Centre For Diagnostics of Zoonoses (CDZ)

Uppsala offers comprehensive expertise in the area of zoonosis through the Zoonotic Science Center at IMBIM BMC, the CVI reception at the clinic for Infectious Diseases at the University Hospital along with the diagnostics of KMB and BMC in both daily operations and research.

Centre of Excellence, inflammation

Uppsala Akademiska University Hospital's Centre of Excellence for Inflammatory processes deals with the causes of nearly three-quarters of all the illnesses that humans are susceptible to. This area is enormous and includes infectious diseases. The researchers at the center are constantly developing new diagnostic methods and treatments that in many respects lead the world. The close cooperation amongst doctors from many different areas of the hospital gives unique opportunities to offer help to patients with very difficult-to-diagnose and difficult-to-treat inflammatory diseases.

Royal Institute of Technology

The Royal Institute of Technology was founded in 1827 and is Sweden's largest technical university. It accounts for one third of the country's technical research. Life science technology is one of five multidisciplinary focus areas at KTH that is formed by the convergence of engineering, natural and mathematical sciences with life sciences. Several research groups at KTH are world leading in their areas of expertise within life science technology. The Institute also has extensive international research and educational exchanges.

ProNova VINN Excellence Centre for Protein Technology

ProNova Centre for Protein Technology performs multi-disciplinary research in protein technology, including technology-driven research in protein engineering, bioimaging, micro-fluidics, affinity technology, biomarker discovery and analysis. The center is collaborating with the Human Protein Atlas program that provides the world's largest set of antibodies and recombinant human protein fragments and eight companies in the life science sector.

Wallenberg Centre for Protein Research

As a continuation of the Human Protein Atlas, a new protein research center, the Wallenberg Center for Protein Research (WCPR) was opened in 2016. The center director is Mathias Uhlén, Professor of Microbiology, who led the Human Protein Atlas project. Research will be carried out at the Science for Life Laboratory, Uppsala University and Chalmers University of Technology. Furthermore, the Center will characterize human protein, but also develop protein pharmaceuticals and new techniques for manufacturing such pharmaceuticals. AstraZeneca is financing a part of the activities.

Stockholm University

Stockholm University is Stockholm's largest university. Its researchers contribute to the development of public policy and political decision-making, as well as participate in Nobel Prize Committees and international expert bodies.

Swedish University of Agricultural Sciences (SLU)

SLU's mission is to develop the knowledge about how to use natural, biological land and water resources in a sustainable manner. The university's publications belong to the most cited in their scientific fields and its researchers contribute to around 1.400 scientific articles every year. SLU has a broad expertise in the field of infectious diseases and how to prevent the spread of infectious diseases, including antibiotic-resistant bacteria. Education, research and environmental monitoring and assessment are pursued at some thirty locations all over the country. The university management is situated in Uppsala.

Virology Section

The Virology Section at SLU is pursuing research on viruses of veterinary and public health importance and has the following main research activities: emerging viral diseases, transboundary viral diseases and viral diseases of small animals. The section is part of the Collaborating Centre of the OIE (World Organisation for Animal Health) for the Biotechnology-based Diagnosis of Infectious Diseases in Veterinary Medicine. Examples of current externally funded projects are the EU supported EPISEQ, Formas supported "Viral Metagenomics and Bioinformatics as powerful novel tools in veterinary infection biology"; and VR/Sida supported "Application of viral metagenomics to investigate circulating viruses in the wildlife-livestock interface for a preparedness of new emerging diseases".

The Stockholm School of Entrepreneurship

The Stockholm School of Entrepreneurship is an internationally acknowledged academic facility in the area of innovation and entrepreneurship. It is founded by the Royal Institute of Technology, The Stockholm School of Economics and Karolinska Institutet to develop an integrated teaching syllabus to meet the demands of students, faculty and industry. Today Stockholm University and University College of Arts, Crafts and Design have joined as member institutions.

SciLifeLab

SciLifeLab is a national resource and a joint endeavor, involving four universities in the Stockholm-Uppsala region; Karolinska Institutet, Royal Institute of Technology, Stockholm University and Uppsala University, to create an infrastructure for world-leading research in the fields of health science and ecology. SciLifeLab was established in 2010, with support from the Swedish government. Today more than 200 research groups are associated with the center. Two international research panels assessed the research center during 2015, on behalf of the Swedish Research Council. Amongst other things, they concluded that the project maintains very high scientific quality and that SciLifeLab has great potential to become a world leader in Life Sciences.

The European Centre of Disease Prevention and Control (ECDC)

The ECDC was established in 2005 and is an EU agency with the aim of strengthening Europe's defenses against infectious diseases. ECDC's mission is to identify, assess and communicate current and emerging threats to human health posed by infectious diseases. In order to achieve this mission, ECDC works in partnership with national health protection bodies across Europe to strengthen and develop continent-wide disease surveillance and early warning systems. It is seated in Stockholm.

The Medical Products Agency (MPA)

MPA is the Swedish national authority responsible for regulation and surveillance of the development, manufacturing and marketing of drugs and other medicinal products. MPA's task is to ensure that both the individual patient and healthcare professionals have access to safe and effective medicinal products and that these are used in a rational and cost-effective manner. MPA is seated in Uppsala.

4. World leading research creates possibilities

This region has a tradition of research, with extensive experience in registry studies and intensive cooperation between academia and the cluster of bio-/medtech and pharma companies. Furthermore, it's not the university but the researchers themselves who enjoy ownership of their patentable inventions.

Selection of current research projects

INFECT

This EU project aims to contribute to the systems understanding of the pathophysiology of highly lethal destructive soft tissue infections, i.e. necrotizing fasciitis and other necrotizing soft tissue infections (NSTIs). INFECT is based on a consortium consisting of 14 international partners, including clinicians, scientists, SMEs and a patient organization. The partners have joined forces to employ a new strategy to advance our understanding of the pathogenesis of NSTIs and improve identification and management of patients to promote novel developments in therapeutics and diagnostics. The project is divided into 9 different Work Packages. The Department of Medicine, Huddinge at Karolinska Institutet, under the leadership of Professor Anna Norrby-Teglund, is responsible for Work Package 5, 6 and 9.

NK cell response to infections

Professor Hans-Gustav Ljunggren's research group at Karolinska Institutet currently explores the function of human NK cells in health and in different disease settings including viral infections and cancer. Studies in the group involve phenotypic and functional characterization of NK cells in healthy humans as well as in humans in the context of primarily virus infections and cancer. A particular interest is focused towards the NK cell response to flavivirus infections, such as infections by Denguevirus, tick born encephalitis virus and hepatitis C virus (HCV). A focus is also directed towards Bunyavirus infections causing severe hemorrhagic fevers, including hantaviruses.

Cellular immune responses

Cellular immune responses play an important role in protecting from viral infections. These responses can, however, contribute to the immunopathogenesis of chronic viral infections such as human immunodeficiency virus (HIV)-1 and HCV infections. Professor Johan K. Sandberg and his research group at Karolinska Institutet's Dept of Medicine, Huddinge are particularly interested in HIV-1 infection, but also study aspects of other chronic viral infections such as HCV and herpes simplex virus (HSV) where immune evasion mechanisms are significant. Another layer of complexity is added by vaccines, antiviral and immunomodulatory treatments used today and in development.

The Viral Hepatitis Research Group

Viral hepatitis is a major health problem with approximately half a billion people infected worldwide. Professor Matti Sällberg's research group at the Department of Laboratory Medicine at Karolinska Institutet studies how hepatitis viruses cause disease and how the body reacts to the infection, and the factors that contribute to the cure and/or control of the disease. The group focuses both on basic research as well as development of new therapies. It has formed several national and international collaborations in both academia and in the pharmaceutical industry.

The translational research is conducted in collaboration with the Unit for Infectious Diseases, Karolinska University Hospital Huddinge and Linköping University Hospital.

Possible new malaria vaccine

Professor Mats Wahlgren's research group at the Department of Microbiology, Tumor and Cell Biology studies severe malaria and in particular the molecular pathogenesis of severe *Plasmodium falciparum* malaria with a focus on the surface molecules of the infected red cell. The team described rosetting and its association with severe malaria. An archetype anti-rosetting vaccine to combat against this severe disease is being developed as is a receptor-based drug, the latter together with Modus Therapeutics.

HIV-prevention

The HIV epidemic is still growing globally and the search for effective biomedical HIV prevention options is intense. Environmental factors including hormonal contraceptive use, genital infections and sexual intercourse affect the susceptibility to HIV infection, which has been shown in epidemiological and experimental studies. The molecular mechanisms behind these findings are however poorly defined. Professor Kristina Broliden's research group at the Unit of Infectious Diseases, Karolinska Institutet and Clinic of Infectious Diseases, Karolinska University Hospital, are studying how the human female genital tract is affected by these factors. The group hopes to contribute to the development of topical prophylactic compounds and to the prescription of optimal contraceptive methods to women.

ADVANCE

ADVANCE (Accelerated Development of Vaccine outcome research Collaboration in Europe) aims to help government agencies and decision-makers in the healthcare field to make quick and well-informed decisions regarding strategies for vaccinating the European population. ADVANCE is a collaboration between European researchers, public health, regulatory agencies and vaccine manufacturers. Researchers at the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet will participate in the scientific studies that are planned within the project and also contribute their expertise regarding the establishment of the framework. Project leader at Karolinska Institutet is Lisen Arnheim Dahlström.

Vaccines and antivirals against CCHF and Ebola

The world has recently experienced several outbreaks of deadly viral infections. Ali Mirazimi from the Department of Laboratory Medicine at Karolinska Institutet has spent the last 15 years studying how our immune system fights these deadly viruses. Currently, he is focusing on the Crimean-Congo haemorrhagic fever (CCHF) and Ebola viruses. These viruses cause high fever and headaches, followed by bleeding, organ failure, and death in 5-30% of CCHF and up to 90% of Ebola cases. Ali Mirazimi's research group has shown that the CCHF virus has mechanisms that help it avoid the antiviral activity of the innate immune system's primary weapon against viruses – the interferons. They have also developed new model systems that can be used to investigate interactions between viruses and host cells. The primary aim is to find a vaccine against CCHF and novel antivirals against CCHF and Ebola.

Detection of Airborne Viruses

The Micro and Nanosystems research group at the Royal Institute of Technology in Stockholm, headed by prof. Göran Stemme, is focused on Micro- and Nanoelectromechanical Systems and their applications. The group is exploring the possibilities of cost-effective detection of air-borne pathogens through the use of so called lab-on-chip devices. Thanks to ultra-sensitive electronic technologies, along with a novel and industrially compatible packaging platform developed within the group, it aims to bridge the gap between academic research and commercial products.

New method for detection of Tuberculosis

Tuberculosis is the leading cause of death from infectious disease, and one of the top ten causes of death worldwide. Yet, very little is known about tuberculosis bacteria in air, the transmissible form of the pathogen. This is largely due to the lack of adequate tools for sampling the bacteria from air. A recently started project at Karolinska Institutet's Department of Microbiology, Tumor and Cell Biology, led by Senior researcher Antonio Rothfuchs, aims to rectify this situation by developing an air-sampling device to detect and study the tuberculosis bacteria in air. Such a device can serve an unmet need in the development of new intervention strategies and the deployment of novel diagnostic approaches to tuberculosis. The project is funded by the Bill & Melinda Gates Foundation.

New biomarker for acute bacterial infection

The development of rapid and reliable biomarkers for early diagnosis of acute bacterial infections are expected to lead to a more rational use of antibiotics. A new biomarker for acute bacterial infection shows a higher accuracy than other clinical chemical analysis currently used in health care. This according to a study conducted by researchers under the leadership of Professor Per Venge at the Centre of Excellence, Inflammation at the Uppsala University Hospital and Uppsala University. The new biomarker, human neutrophil lipocalin (HNL), was better able to distinguish healthy people without infection from patients with infection, and patients with non-bacterial infection from patients with bacterial infection, than many of the established biomarkers which today exists as clinical chemistry analysis. The promising results of the research are expected to accelerate the development of a rapid test for clinical use.

Drivers of antibiotic resistance evolution

The research of Professor Dan Andersson's group at Uppsala University addresses the mechanisms and dynamics of evolution in bacteria and how various factors such as the extent and type of genetic variation, strength of selection pressures, compensatory mutations and population dynamics affect the tempo and mode of adaptive evolution. The research focuses on two different areas. One is to examine the major factors that influence the tempo and mode of bacterial evolution. The other is to understand how antibiotic resistance affects the fitness, virulence and transmission of various pathogenic bacteria.

Bacteria as the body's own vaccine factories

The mapping of the genome of bacteria is entering a new phase. The goal is to make it possible to design bacteria for entirely new tasks, like acting as the body's own vaccine plants. Siv Andersson is the Professor of Molecular Evolution at Uppsala University and one of the pioneers in Sweden in the mapping of genetic material. A project funded by the Knut and Alice Wallenberg Foundation makes it possible to study the genes coding for teamwork in bacteria, and how to design living vitamins or vaccines. The first step is to use the new technologies to complement the genome with genes for collaborative working and study social behavior. If the researchers in Andersson's group succeed, this could mean a whole new opportunity to create protection against infectious diseases such as malaria. The commercial applications are some way off, but the possibilities are staggering.

Viral Zoonoses

Most human infections are zoonotic, i.e. they occur mainly in animals but also have the capacity to cross species-boundaries and attack humans. The work of Professor Åke Lundkvist's research group at Uppsala University is based on an interdisciplinary approach between molecular virology, immunology, genetics, molecular epidemiology and diagnostic aspects of zoonoses, especially emerging zoonotic viruses. It's currently focusing on the following agents: hantaviruses, flaviviruses (TBE, Dengue and West Nile viruses), Sindbis virus, Rift Valley fever virus, and avian influenza virus. The Zoonoses Centre and Prof Åke Lundkvist also run the Zoonoses Seminar Series with the aim of learning more about diseases transmissible from animals to humans.

New generation vaccines against RS virus in calves

BRS is a virus that attacks the respiratory tract in cattle and paves the way for other infections. Today's vaccines give calves incomplete protection. But a new generation of vaccines are now on their way. These new vaccines are developed using modern genetic engineering and tests on calves have been very promising, according to a doctoral dissertation by Veterinarian Krister Blodörn at the Swedish University of Agricultural Sciences. The project is a collaboration between SLU, INRA French National Institute for Agricultural Research and The British Pirbright Institute. The next step is to assess the long-term protection of these new vaccines, and see if the effect can be further improved, for example by combined vaccination.

Bacteriology section at SLU

The research profile of the bacteriology section at the Department of Biomedical Sciences and Veterinary Public Health at the Swedish University of Agricultural Sciences includes pathogenicity and diversity of bacteria that are important in veterinary medicine. The section also works with the epidemiology of the corresponding diseases and zoonotic or potentially zoonotic bacteria. Its research activities are focused on pathogenicity mechanisms, antibiotic resistance, phylogeny and characterization of new and potentially important bacteria. Currently, bacteria of the following genera are being studied: *Bacillus*, *Brachyspira*, *Clostridium*, *Helicobacter*, *Nicoletella*, *Staphylococcus* and *Treponema*. This department is headed by Prof Ivar Vågsholm.

One Health Sweden

One Health Sweden is an integration concept including several universities and governmental organizations that want to contribute to a sustainable intellectual platform where veterinarians, physicians, molecular biologists, ecologists, environmental chemists who have an interest in zoonotic infections can interact and create synergies. The network was founded in 2010 by Björn Olsen, professor in infectious disease at Uppsala University and senior physician at Uppsala Academic Hospital. The collaboration is part of the worldwide One Health concept and the main partners are Uppsala University, National Veterinary Institute, SVA, Swedish University of Agricultural Sciences, SLU and Linnaeus University, Kalmar.

The Infections Tool

The Infection Tool (Infektionsverktyget in Swedish) is a national IT effort to document, store and re-connect information on healthcare associated infections and antibiotics use. The purpose of the tool is to prevent healthcare-associated infections, improve adherence to treatment recommendations and reduce the use of broad-spectrum antibiotics. A reporting tool can generate reports on nosocomial infections, antibiotic prescriptions, links to risk factors, etc. within individual organizations. This feedback will help caregivers identify problems, and provide a good basis for local improvement work.

The ENABLE project

ENABLE was launched in February 2014 within the framework of the Innovative Medicines Initiatives (IMI) program, "New Drugs for Bad Bugs" (ND4BB) with Uppsala University and the pharmaceutical company GlaxoSmithKline as principals. The project has the goal of developing antimicrobial drug candidates that can be tested in the clinic and thus increase the ability to develop new antibiotics against infections caused by gram-negative bacteria. The consortium consists of 39 different partners from all over Europe, coming from academia, research institutes, small and medium-sized biotechnology companies and large pharmaceutical companies. Anders Karlén, Professor in Computer-aided drug design, Uppsala University, is the leader of the Managing Entity and co-coordinator of the €85 million, six-year project.

The DRIVE-AB consortium

This project develops alternative economic models that can create incentives to discover and develop new antibiotics. Uppsala University is a partner and one of the leading institutions in DRIVE-AB. The public-private consortium is funded by the Innovative Medicines Initiative (IMI) and is the only global research project which develops and tests new, evidence-based and globally feasible reward systems to stimulate investment in antibiotic research and development which is also linked to the sustainable use and equitable access to antibiotics. Leading the work at Uppsala University is Professor Francesco Ciabuschi at the Department of Business Studies. However, the group is interdisciplinary and includes researchers from business studies, medicine, informatics and media, economic history, law, educational sciences and engineering sciences.

The AIDA project

A clinical study within the project investigates the benefits of adding the antibiotic meropenem for patients with serious infections caused by meropenem-resistant bacteria and treated with colistin, another antibiotic. Colistin has demonstrated in preclinical studies a capacity to influence the bacterial membrane and thereby restore susceptibility of bacteria resistant to antibiotics. With the help of mathematical models (pharmacometrics) the variability between patients can be characterized and thus contribute to individualized antibiotic dosing. Associate professor in Pharmacometrics at Uppsala University, Lena E Friberg is the principal investigator from Sweden for the AIDA project.

Joint Programming Initiative on Antimicrobial Resistance

JPIAMR is a so-called "Joint Programming Initiative" – a type of EU program in which member countries contribute funding to create international partnerships aimed at solving important social issues such as antibiotic resistance. This project is designed to streamline the development of antibiotic combinations and dosages that can overcome resistance and has a high probability to work clinically. This project is in progress during 2016-2018. Two other projects in progress during the period 2017-2019, aim to study the mechanisms for selection and transmission of resistant bacteria in humans and in the environment and how to slow the development of resistance by combinations of antibiotics. The Swedish Research Council, led by Director General Sven Stafström, has taken on a leading role for JPIAMR, managing the overall coordination (work package 1) and the dissemination (work package 2) of this endeavor. In addition, SRC contributes to the evaluation of the JPI as well as IPR and regulatory issues (work package 6). A JPIAMR secretariat has been established at the Stockholm SRC office to handle these tasks.

ReAct

Combating antimicrobial resistance at an international scale is a recognized high-priority task in Sweden. ReAct is an Uppsala-based international network that started with a small group of people, one of them being professor Otto Cars, internationally renowned specialist in infectious diseases at the Department of Medical Sciences, Infectious Diseases, Uppsala University. In recent years, ReAct has been a key international player in the approach as to how new antibiotics are to be developed. The network works with antibiotic resistance issues from a health system perspective. It seems that a new business model will have to be built where the public and private sectors work together to solve scientific problems while creating innovative incentives – both financial and other. It's not just research in antibiotic resistance, which is strong in Uppsala, but also the dissemination of information and advocacy.

Uppsala Health Summit

Is an international conference organized in collaboration between Uppsala University, the Swedish University of Agricultural Sciences (SLU), Uppsala County Council, the National Food Agency, the National Veterinary Institute (SVA), Uppsala municipality and The Swedish Medical Products Agency. In 2015, experts gathered to discuss future issues in the antibiotics field. The findings were

presented in a report containing a number of concrete proposals. For 2017, infectious diseases will be the theme for the Summit. The program focuses on how we can become better at preventing and controlling infectious diseases from a one-health perspective. The summit is chaired by Prof Anders Malmberg, Deputy Vice-Chancellor, Uppsala University.

Cell phone based diagnosis of infections

A new kind of affordable, 3D-printed microscope makes it possible for physicians to accurately diagnose cancer tumors and infections such as tuberculosis. The microscope works in conjunction with the camera of a regular cell phone and shows the DNA-sequence of a sample without the use of the expensive and cumbersome equipment used today. If produced in large numbers, the price of the microscope could fall to below USD500, and make DNA-sequencing available to many more physicians, not least in developing countries. When bacteria are viewed at the DNA-level it is easier to choose the appropriate treatment, making this new invention a useful tool in the fight against resistance to antibiotics. The microscope is the result of a collaboration between researchers at UCLA, who have built the microscope itself, and researchers at Stockholm University and Uppsala University and SciLifeLab in Stockholm under the supervision of Prof Mats Nilsson who have worked on the DNA-sequencing.

Other discoveries and innovations with significant impact on current infectious disease research, diagnostics and treatment

Discovering NK cells

During his doctoral studies in the 1970s at Karolinska Institutet, Rolf Kiessling discovered a hitherto unknown tumoricidal lymphocyte, which he named natural killer cell. These cells are an important part of the body's defense against tumor cells and viruses. As Professor of Experimental Oncology and chief physician at the Radiumhemmet, Kiessling conducts research on immunotherapy, including among other things, genetically modified T-cells and checkpoint antibodies.

ELISA

ELISA, the Enzyme-Linked Immunosorbent Assay, was invented in 1973 by Peter Perlmann and Eva Engvall at the Stockholm University. The ELISA uses antibodies and color change to identify a substance. High sensitivity and strong specificity are advantages that have made ELISA a popular and useful tool with many applications, either in scientific research or clinical diagnosis of diseases or conditions. In infectious diseases ELISA can be performed to evaluate either the presence of antigen or the presence of antibody in a sample, it is a useful tool for determining serum antibody concentrations (such as with the HIV test or West Nile virus).

5. Unique biobanks and data registers

Samples from the healthcare sector have been registered in Sweden since the 1920s. Today approximately 600 biobanks contain several hundred million of samples that can be traced to a specific person or research sample.

Some of the region's biobanks and registries

The world's largest twin registry

Karolinska Institutet has the world's largest twin registry. It was established in the 1960s and contains information about 85,000 identical and fraternal twins.

The PKU registry covers almost all Swedes born after 1975

As Sweden's largest biobank, the PKU Registry at Karolinska University Hospital includes almost all Swedes born after 1975, i.e. about 3 million individuals.

LifeGene - one of the largest health studies in the world

The project is a prospective cohort longitudinal study intended to provide knowledge on how genes, environment and lifestyle affect health. LifeGene was started in 2010 and a half million Swedes will regularly provide samples and information for at least 20 years. The study will use high-tech tools within e-epidemiology to perform measurements and data collection. The project is being run by Professor Nancy Pedersen and Professor Jan-Eric Litton at Karolinska Institutet.

The Human Protein Atlas - a database of the human proteome

Mathias Uhlén, Professor of Microbiology at the Royal Institute of Technology, has been the leader of the Human Protein Atlas consisting of 13 million images of the proteins of the human body. Fredrik Pontén, Professor of Clinical and Experimental Pathology at Uppsala University, has also taken part in the project which was completed in 2014. An unexpected discovery in the work with the Protein Atlas was that almost half of 20,000 human proteins are base proteins that exist in all of the cells of the body. In addition, researchers found that very few proteins are unique to their respective tissues. This is of great significance for the pharmaceutical industry, since drugs affect proteins. If a drug targets a specific protein in the liver and the same protein also exist in the kidneys and brain, unexpected side-effects may occur. Approximately two scientific articles based on the Protein Atlas are published each day.

BBMRI.se - a national biobank for research

Stockholm BioBanking and Molecular Resource Infrastructure of Sweden, BBMRI.se is a national infrastructure for saving and analyzing biobank samples from patients and healthy volunteers. The infrastructure provides possibilities for discovering diseases at an early stage. Karolinska Institutet, the host university for BBMRI.se, and a further eight universities are partners in this collaboration. In 2014, BBMRI.se was selected as one of the four nodes in a European BBMRI-ERIC center for ethical and legal issues regarding biobanks.

6. Commercialization of innovations

The region has more than 600 biotech, medtech, pharma and platform companies. There are about 30 Life Science incubators and innovation facilitators. For example, in 2015 The Uppsala Innovation Center was ranked as the world's 10th best business incubator with a university connection by UBI Global. In 2015, Johnson & Johnson Innovations established a satellite office at Karolinska Institutet. Here, Nordic researchers and companies have access to the company's expertise and other resources that can contribute to commercializing discoveries and innovations within the life sciences.

Projects in clinical trials

According to SwedenBIO's report, "The Swedish Drug Development Pipeline 2016", there are currently 22 projects in the field of infectious diseases in preclinical and clinical development. Of these projects, 14 are being undertaken by companies in the Stockholm-Uppsala region, and 5 of those have reached the clinical phase (phase I-III).

Some of the region's companies within the field of infectious diseases

Abera

Offer: Abera has developed next-generation bacterial and derived Outer Membrane Vesicles (OMV) vaccine delivery platforms that combine high-level multivalent antigen presentation with strong stimulation of the immune system.

Problems they solve: The Abera platform enables cost effective and fast production. Abera can produce a vaccine that is ready to use within 14-30 days. The company currently has vaccine candidates against Tuberculosis, Streptococcus pneumoniae, Chlamydia and Therapeutic Cancer under development.

Annexin Pharma

Offer: Annexin Pharmaceuticals develops new therapeutic approaches for inflammatory cardiovascular diseases and infection. The concept for the therapy is based on the anti-inflammatory properties of Annexin A5 that acts simultaneously against several key pathogenic mechanisms of cardiovascular diseases.

Problems they solve: Viruses causing Viral Hemorrhagic Fevers (VHF) attack and damage our vascular system. Annexin Pharma has demonstrated that their compound Annexin A5 protects the vasculature from damage by inflammation. Annexin A5 has the potential to act at several levels in the pathogenesis of VHF such as Ebola and Dengue Fever.

Apodemus

Offer: Apodemus is a pharmaceutical company focused on the development of antiviral treatments and diagnostic tools for viral infections.

Problems they solve: Apodemus has discovered a new virus group. This group has been found in clinical material from patients with various diseases including neurological, metabolic and pregnancy related diseases and furthermore in animals with symptoms of these diseases. The observation that the same virus group affects both animal and man will facilitate the development of both pharmaceutical treatments and diagnostic tools.

Aprovix

Offer: Aprovix's product Qvintip® is a self-sampling kit that includes analysis for high-risk HPV.

Problems they solve: 65% of women afflicted by cervical cancer have not been smear tested, making testing for high-risk HPV important. Qvintip can detect the causes of cervical cancer before cell changes occur, giving patients the best prospects of starting treatment early to avoid unnecessary suffering and deaths.

Bactiguard

Offer: Bactiguard's technology is based on a thin layer of noble metals, referred to as the "Bactiguard coating", which is applied to the surface of medical devices and prevents bacteria from adhering and forming biofilm.

Problems they solve: Bactiguard wants to prevent healthcare associated infections caused by medical devices. By avoiding unnecessary infections and prolonged hospital care, Bactiguard could help reduce the use of antibiotics and thereby prevent the spread of multiresistant bacteria, and ultimately reduce healthcare costs.

Boehringer Ingelheim Svanova

Offer: The company develops and manufactures test kits to detect antibodies against viruses, bacteria, parasites and mycoplasmas in various animal species.

Problems they solve: BI Svanova brings diagnostic solutions to market by combining their knowledge about diagnostic assays with their research group's experience in the field of epidemiology and infectious diseases caused by different agents such as viruses, bacteria and parasites.

Bioimics

Offer: Bioimics develops innovative low-molecular weight antibiotics targeting bacterial RNase P – an RNA enzyme (ribozyme).

Problems they solve: RNase P is essential for cell survival, without functional RNase P protein synthesis is blocked and the bacteria will die. Bioimics has developed molecular biology tools and established a technology platform for fast evaluation of small molecules' potential to block RNase P activity and to inhibit cell growth in a variety of bacteria.

Cavidi

Offer: Cavidi is a leading supplier of viral load for HIV monitoring and also provides tools and kits for virus research.

Problems they solve: Cavidi's products facilitate efficient management of anti-HIV drugs (ARV therapy) enabling people living with HIV to live close to normal lifespans. Cavidi's diagnostics reduce the cost of treatment and the spread of HIV.

CytaCoat

Offer: CytaCoat has developed a technology platform for prevention of hospital acquired infections associated with the use of medical devices.

Problems they solve: Multiresistant bacteria are a growing serious threat to society. The CytaCoat platform technology provides a universal and covalently coupled antibacterial coating technology active against several clinically relevant bacterial strains including multi drug resistant bacteria such as MRSA and ESBL.

DexTech Medical

Offer: DexTech develops candidate medications with applications within urological oncology and infection.

Problems they solve: DexTech Medical's candidate medication for instillation therapy of superficial bladder cancer, CatDex, has proved to have antibacterial properties. This is now being further studied with focus on treating urinary tract infections and as an oral antibacterial medication, e.g. a mouth wash, and as an additive to toothpaste.

Diagnostics Development

Offer: The company produces and sells antibodies, antigens and sensitive immunoassays for the study of inflammatory processes in human disease. It also provides services to other companies in their development and analytical and clinical validation of their diagnostic assays.

Problems they solve: The focus of Diagnostics Development is in the research and development of reagents and assays for the clinical and research markets.

Disruptive Materials

Offer: The company has discovered a new material, Upsalite[®], with unique water adsorption characteristics, pore structure and biotechnological properties.

Problems they solve: Upsalite shows promising performance as a drug delivery vehicle. It can increase the solubility of poorly soluble drugs and also adjust their release rate. Furthermore, Upsalite has been shown to inhibit growth of, *Staphylococcus epidermidis*, bacteria associated with acne and hospital acquired infections.

Eurocine vaccines

Offer: The company uses its clinically validated technology Endocine[™] to develop a nasal influenza vaccine, Immunose[™] FLU, for children.

Problems they solve: Because today's flu vaccines are considered to have limited efficacy in children there is a need for an effective new vaccine that also provides protection for children. Immunose[™] FLU is a nasal inactivated influenza vaccine adjuvanted with, Endocine[™], an adjuvant systems composed of endogenous lipids found ubiquitously in the human body.

Gradientech

Offer: Gradientech is developing, QuickMIC[™], an in vitro diagnostic solution for rapid antibiotic susceptibility testing (AST) of positive blood culture samples.

Problems they solve: Millions of people contract sepsis every year. To avoid high hospital costs and mortality rates a rapid diagnostic AST solution is essential. Adequate antibiotics administration is

also essential to combat the constantly increasing antibiotic resistance. QuickMIC™ can be applied in parallel with, or following, bacterial identification and generates phenotypic AST results in only 2 hours.

Instagraft

Offer: Instagraft has developed an innovative skin grafting device which makes autologous skin grafting simple.

Problems they solve: Skin grafting is usually performed as sheet grafts – a complicated procedure requiring a surgery room, specialized staff and frequently also putting the patient under general anesthesia. Using Instagraft, skin can be harvested safely in all types of health centers, directly in micro size and without causing new wounds.

Kibion

Offer: Kibion offers solutions for rapid Urea Breath Tests for diagnosing the stomach ulcer bacterium *Helicobacter pylori*.

Problems they solve: The solid dosage system of Kibion's tests eliminates the need for a test preparation or a test meal. The patient simply swallows a capsule or tablet.

Modus Therapeutics

Offer: Modus Therapeutics is developing Sevuparin – a candidate drug in clinical development.

Problems they solve: There are about 10 million severe falciparum malaria cases every year, which despite optimal antimalarial treatment, result in nearly one million deaths, most of them children. Sevuparin, the company's chemically modified heparin, is a potential new adjunctive treatment of severe malaria that acts by preventing and reversing the infected cells' ability to block blood vessels.

Molecules of man

Offer: The company develops human monoclonal antibodies for treatment or protection against hepatitis C.

Problems they solve: The Hepatitis C virus (HCV) affects an estimated 170 million people worldwide. Molecules of Man uses antibodies against the HCV surface proteins, which have recently shown potent and broad antiviral effects against HCV of all known subfamilies.

Novavax

Offer: Novavax is a vaccine company, whose Novanax technology platform produces recombinant nanoparticle vaccines that can be applied to a wide variety of infectious diseases.

Problems they solve: Its product pipeline targets a variety of infectious diseases with vaccine candidates currently in clinical development for respiratory syncytial virus ("RSV"), seasonal influenza, pandemic influenza, and Ebola virus ("EBOV"). It also has additional preclinical-stage programs for a variety of infectious diseases.

Q-linea

Offer: Q-linea develops procedures, instruments, and systems for protein and nucleic acid analysis, particularly with applications in the field of microorganism detection and identification for in vitro diagnostics.

Problems they solve: Millions of people contract sepsis every year, and the mortality rate is very high. To address the need for more rapid diagnosis of potential pathogens causing sepsis or septic

shock in patients, Q-linea is developing a fully automated, high-throughput diagnostic platform, ASTriD. The system will perform both molecular pathogen identification and phenotypic antibiotic susceptibility testing, directly from whole blood, delivering ID after four hours and AST in an additional six.

Scandinavian Biopharma

Offer: Scandinavian Biopharma is a research based biotech company, which is also a distributor of vaccines and immunoglobulin's to the Nordic market.

Problems they solve: Travelers' diarrhea is the leading cause of illness among international travelers to developing countries. Enterotoxigenic Escherichia coli (ETEC) bacteria are the primary cause of this disease. ETEC is also a major cause of diarrheal disease in children living in countries endemic for ETEC, leading to over 400 million diarrheal episodes and approximately 300,000 deaths every year. Scandinavian Biopharma's vision is to successfully develop a vaccine to prevent and control ETEC-related illness and mortality among infants and young children living in ETEC-endemic areas, as well as to prevent ETEC-associated travelers' diarrhea occurring among international travelers.

Sensabues

Offer: Sensabues has developed, ExaBreath, an exhaled breath biomatrix platform test for drugs, metabolites and biomarkers.

Problems they solve: Drug detection, health monitoring and medical diagnostics is usually intrusive and relies on medically trained staff. Sensabues offers cost-effective and non-invasive collection, detection and identification of substances such as performance enhancing drugs used in sports (stimulants), drugs of abuse (narcotics), therapeutic drugs (antibiotics) as well as metabolomics, biomarkers. and bacterial infections such as tuberculosis.

SinSa Labs

Offer: The SinSa program is translationally oriented with the goal of helping patients suffering from infectious disease, with a special focus on orphan drug indications with high unmet medical need.

Problems they solve: SinSa Labs has designed small peptides and organic molecules that kill bacteria and fungi. These novel molecules are proven effective in destroying Gram-negative and Gram-positive bacteria such as CREs, MRSA, VREs, Mycobacterium Tuberculosis, as well as the so-called ESKAPE organisms.

SymCel

Offer: SymCel develops and markets analytical instrumentations for real time cellular bioenergetic measurements.

Problems they solve: Many assays require labelling and provide endpoint data. SymCel's calScreener™ is a label free assay which monitors the metabolic response in biological systems using calorimetry. The assay can be used in a variety of applications such as antibiotics development, drug testing on parasitic worms or malaria infected red blood cells and to monitor bacterial load in food and water.

Vidilab

Offer: Vidilab has created a parasitological faecal sample kit and accepts parasitological faecal samples from companies and private consumers, as well as being the service laboratory for the Swedish Animal Health Service. The company performs more parasitological faecal samples than any other laboratory in Scandinavia.

Problems they solve: If suspicion exists that an animal suffers from worms or parasites it should never be treated without first being tested. With the use of Vidilabs tests, animals are spared from unnecessary suffering, fewer toxic substances end up in the environment, and antibiotic resistance issues are averted.

Vironova

Offer: Vironova offers a range of products and services which can be used in development of particles for vaccines, drug delivery and gene therapy as well as viral safety testing and material quality control.

Problems they solve: By combining expertise in electron microscopy, virology, mathematics and image analysis, Vironova has developed a unique offering of services, hardware and software products. Today it has GLP-certified cell and virus facilities in that include equipment for advanced electron microscopy, image analysis, nano-characterization and viral clearance testing.