

At the cutting edge



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2018 in brief

During 2018, Karolinska University Laboratory has continued to develop in many ways, not only for the benefit of patients in the Stockholm Region and other parts of Sweden, but also for the benefit of patients abroad. We do this because being at the forefront raises considerable interest and instils confidence. Colleagues, from both Sweden and abroad, who have spent time with us on study visits, have been inspired by our continuous development efforts. During the year we were hosts for two Swedish National Programme Areas, Rare Diseases and Medical diagnostics. We arranged several conferences, with a mention to the Diagnostic Forum in Stockholm. The Diagnostic Forum, a meeting point for Biomedical Scientists, focusing around the theme – Together We Create the Best Care.

One of our greatest challenges has been staffing issues and the high staff turnover rate, not least within complex and 24-hour activities that are essential for emergency medical care. Our joint venture on the

serology. Faster test results in cases of suspected sepsis may be crucial to treatment and disease progression.

To meet the need for advanced clinical laboratory diagnostics within highly specialised university affiliated healthcare, the laboratory works with the development of precision medicine and the introduction of cell therapies. Biobank samples are an important prerequisite for precision medicine and now that Stockholm Medical Biobank is a part of the Karolinska University Laboratory, the potential for research and university affiliated healthcare are further improved. The continued work with Genomic Medicine Center Karolinska has led to the establishment of new methods for individualised patient treatment, an exciting and expansive field that revolutionises healthcare. In an enhanced collaboration with the Cancer theme, the Department of Clinical Genetics has taken over certain activities within the framework of hereditary cancer.

“KUL accommodates current and future patient diagnostic needs.”

“Attractive Employer KUL 24Sju” project has been a success and reversed the trend surrounding the tough staffing situation. Ensuring we have a highly skilled workforce remains the most critical issue for Karolinska University Laboratory in the long-term, and we continue to work on increasing our attractiveness as an employer.

Within the framework of the New Karolinska University Hospital in Solna, parts of our division have also been relocated to the unique hospital building. This has meant we have received access to modern facilities for sampling and transfusion medicine, a much awaited improvement for both employees and patients. At the same time, the work of our multidisciplinary KUL 24Sju laboratories has continued to meet patients’ needs for higher accessibility to laboratory analyses. During the year we also launched both blood culture and infectious

Within the Division of Pathology, digitalisation has begun and, in combination with artificial intelligence, algorithms have been developed to recognise patterns in tissue sections. This raises the quality and resources can be focused on activities adding the most value to the patient. In the highly specialised field of university affiliated healthcare, clinical decision support will become more important in the future: Clinical pharmacology is the leader in this development, and, in the longer term, artificial intelligence will likely become a valuable support.

Together, we further develop Karolinska University Laboratory's activities to accommodate current and future patient diagnostic needs. Our annual report, “At the cutting edge”, highlights parts of Karolinska University Laboratory's operations and shows our ambition to be at the forefront!



Andreas Matussek,
Managing Director



PHOTO: ISTOCK

Regional mandate: highly specialised analysis services

Karolinska University Laboratory has assumed the Stockholm Region's mandate and is responsible for so-called highly specialized analysis services within transfusion medicine and genetics. This responsibility entails

- Maintaining 24-hour operations if necessary
- Acting as a "back-up" if capacity problems occur, such as in the case of prolonged operational disturbances that may affect patient safety
- Being responsible for maintaining competencies and being responsible for development within the field
- Acting as consultants with respect to the regional mandate
- Assuming primary responsibility for developing infrastructure solutions within the mandate for new diagnostic services and new fields of activity.

We are expanding in North Stockholm

Karolinska University Laboratory re-establishes laboratory service in Solna, Sundbyberg, Sigtuna and Sollentuna starting in spring 2019.

We answer when you call us

Last year our customer service department received over 90,000 calls. If you want to contact us, then call **08-517 71 999** or send an e-mail to universitetslaboratoriet.karolinska@sll.se

Follow us on LinkedIn #laboratorietiframkant

On the Karolinska University Laboratory website you will find links to our current job vacancies, as well as news related to us and information about research currently being carried out at our laboratory.

Course program for health care staff

Each year, Karolinska University Laboratory arranges several training initiatives for healthcare staff. We offer advanced courses in subjects such as newborn screening (PKU), congenital metabolic diseases, blood transfusion, blood culture, drug test specimen collection and Medical Review Officer (MRO) training for occupational medicine doctors. The full list of courses offered is found on our website.



Popular with students

149 students from the Biomedical Laboratory Science Study Programme completed various parts of their courses at KUL in 2018.

More services available in our webshop

We continue to expand our web service. You can now order newborn screening (PKU) referrals, mailing labels and information material about the newborn screening test through our webshop.

If you would like to become a customer in our webshop, then you will find all the information you need on our website www.karolinska.se/lab





Early diagnostics are decisive in Alzheimer's disease

Despite many years of research, no medication for Alzheimer's disease currently exists. The hunt continues around the world for the missing piece of the puzzle, so the course of the disease can be fully understood, and a treatment found.

Cognitive disorders are rapidly on the rise, and this is primarily due to an ageing population. Alzheimer's disease is most prevalent and includes some 60 percent of patients with a cognitive impairment diagnosis.

The BioClinicum Research Centre at Solnavägen is one of Karolinska University Hospital's newest research environments. The building plays a key role in the work with strengthening real world evidence and to quickly be able to translate this into new treatment methods. At BioClinicum, some 100 research groups are gathered

in one location, which is interconnected with the new hospital building on one side of the road and Karolinska Institutet with the ultramodern BioMedicum laboratory building and preclinical research on the other side.

Lars Tjernberg, who is one of the researchers conducting intensive research into Alzheimer's disease and part of the research theme of Ageing, works on the 9th floor. Lars is an Associate Professor at Karolinska Institutet and has a so-called joint employment position. This means that he shares his time between the BioClinicum



Researcher Lars Tjernberg, divides his time between the BioClinicum Research Centre in Solna, the Clinical Chemistry Laboratory and KUL24Sju at Karolinska University Hospital in Huddinge.

Research Centre in Solna and the Clinical Chemistry and KUL 24Sju Laboratory at Karolinska University Hospital in Huddinge.

Lars Tjernberg has worked with Alzheimer's disease throughout his research career. His research focuses on amyloid β -peptide, $A\beta$, which is a small piece of a protein that clumps together and is the primary component of the typical plaques formed in the brain in Alzheimer's disease. The idea is that the research will lead to a better understanding of the factors affecting the production of $A\beta$ and how the plaque occurs.

"We have discovered a number of proteins that affect the production of $A\beta$ in the brain. We have then studied and selected those with the greatest impact on the $A\beta$ of the brain neurones. With the help of a new revolutionary microscopic method, we have made it possible to take a closer look at the process in the smallest detail, which was not previously possible."

One of the challenges with the disease is that the disease begins much earlier than the symptoms. Therefore, reliable and early diagnostic markers are required, something which Lars Tjernberg looks for in his work.

"What I want to achieve is to find even earlier indications of Alzheimer's disease. I study, for example, glycans, which are sugar molecules assembled in a certain way. By looking at them individually or together with other

"What I want to accomplish is to find even earlier indications of Alzheimer's disease."

biomarkers, we might be able to detect the disease long before it starts to produce symptoms. The advantage of my joint employment is that in my work at Karolinska University Laboratory I have the support of the research development at Karolinska Institutet, which can be implemented in practice at the hospital."

Lars Tjernberg believes that it is important to diagnose Alzheimer's disease as early as possible for many reasons. Not least because, soon, there will probably be medicines to prevent the disease if they are used at an early stage. In addition, an early and safe diagnosis would improve clinical trials of drugs for the disease.

"We want to understand the mechanisms behind the disease and be able to diagnose it better. Of course, the best thing would be if people with an elevated risk of developing Alzheimer's disease could take a simple blood test at their GP, and based on the result, either be written





Lars Tjernberg wants to find even earlier indications for the detection of Alzheimer's disease. The aim is to be able to detect the disease before it begins causing symptoms.

off or remitted to a centre for cognitive medicine. They will be able to investigate the disease further and if the results indicate the presence of Alzheimer's disease, then treatment can begin promptly.”

A major step in the process of early and rapid diagnosis is the highly specialised Cognitive Medicine Clinic at

“From time to time I have something to add and I notice that there is an interest in my perspective on healthcare.”

Karolinska University Hospital in Solna, which opened in late April 2018. The clinic, which primarily caters to patients up to 70 years of age, has a new concept with significantly shorter investigations. Instead of dementia investigations that can take up to three months, patients at the clinic receive results within 10 working days.

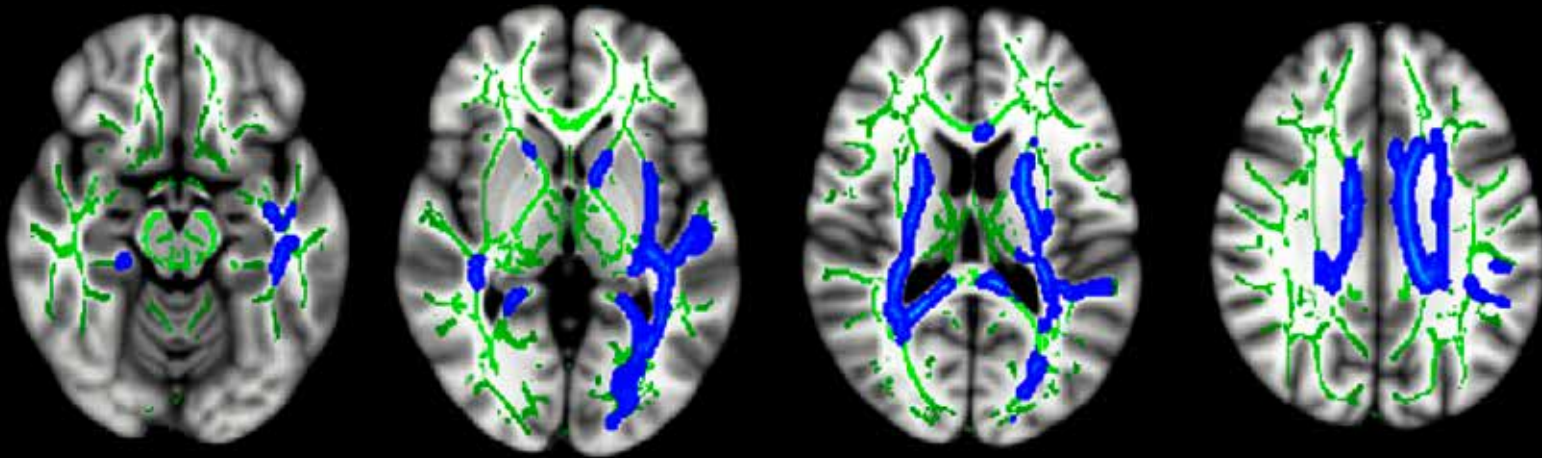
Marie Rydén is a specialist and responsible physician for the new clinic. She maintains that a long investigation creates unnecessary concern in both patients and



Marie Rydén is responsible for the highly specialised Cognitive Medicine Clinic at Karolinska University Hospital in Solna.

relatives. In addition, a suspected cognitive disorder should be investigated as soon as possible because other treatable causes of the symptoms are sometimes detected. The treatment currently available for Alzheimer's disease is symptomatic and primarily works in the early phases of the disease. An early diagnosis also facilitates the planning of care and gives both patients and relatives time to approach the disease.

“We work closely with the Karolinska University Laboratory, which is a precondition for our activities. Our goal is to be able to complete the investigation in five days instead of ten. Therefore, we are currently discussing



In Alzheimer's disease, changes occur in the brain that are visible via magnetic resonance imaging (MRI).

the possibility of further shortening the response times to dementia markers,” says Marie Rydén.

Just over a year has passed since **Mikael Hesse** – only 50 years old – was told he has Alzheimer's disease. He felt the first symptoms of the disease one year earlier. It was when Mikael, who worked as a pilot both in the Swedish Air Force and at Scandinavian Airlines, was going to begin his training on a new type of aircraft in France, when he noticed he had a tough time taking on new knowledge. After a doctor's appointment, sick leave and a new, but unsuccessful, attempt at his training, Mikael was referred to the Cognitive Medicine Clinic at Karolinska University Hospital in Huddinge. An investigation was started, and Mikael received a diagnosis.

“Naturally it came as a shock. Alzheimer's is a terrible disease, not least because there still isn't a cure. Now the family and I take one day at a time. We have started living for the moment, and tackle problems as they arise.”

Today, Mikael's life is very much about staying physically active. He runs, goes to spinning classes, works out at the gym, and pampers the family dog with long walks. He and his wife Karin have been appointed as ambassadors for the Swedish Alzheimer Research Foundation where they work in numerous ways to visualize the disease and show that it also affects younger people. Mikael is also a patient representative at the Karolinska University Hospital patient flow table for cognitive impairment and dementia, whose purpose is to develop healthcare with a focus on the patient's best interests.

“I mainly listen to what is said at our meetings and think it's exciting when representatives from different hospital departments discuss what is in the works. From time to time I have something to add and I notice that there is an interest in my perspective on healthcare,” says Mikael. •



Mikael Hesse a patient representative at the Karolinska University Hospital patient flow table for cognitive impairment and dementia.

FACTS: JOINT EMPLOYMENT

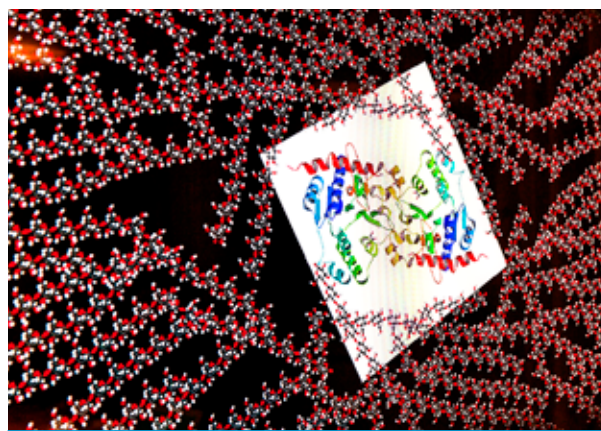
Joint employment facilitates valuable collaboration between the Karolinska University Laboratory and Karolinska Institutet. The form of employment enables research to take place within healthcare and contributes to the development of knowledge and specialist knowledge that is beneficial to all disciplines within clinical development.

Porphyria Centre Sweden – a matter of national importance

The Centre of Inherited Metabolic Disorders, CMMS, is a specialist laboratory comprised of a few expert teams working with various rare diseases and groups of diseases. One of these teams is Porphyria Centre Sweden, which is a national centre of expertise on Porphyria Metabolic Disorders.

Porphyria is the collective name for a group of hereditary disorders caused by enzyme defects in the eight steps of heme synthesis. Heme is a component of hemoglobin, where it transports oxygen in the blood, and in several enzyme systems that metabolise certain drugs and hormones. When the formation of heme does not work as it should, substances are accumulated in the body that can lead to the symptoms from the nervous system and/or the skin, depending on the substance that has accumulated. The diagnostic process is based on analysing the preliminary stages of the heme, which provide information about where in the synthesis chain the fault lies.

The Porphyria Centre Sweden, which was formed back in the 1980s, is part of the Centre of Inherited Metabolic



FACTS: PORPHYRIA – ONE NAME, MANY DISEASES

The three most commonly occurring forms of porphyria in Sweden are acute intermittent porphyria, porphyria cutanea tarda and erythropoietic protoporphyria, which constitute three completely disparate diseases. Sweden has the world's highest prevalence of acute intermittent porphyria and the disease affects 10 of 100,000 inhabitants. There are also more forms of porphyria that are only represented by isolated cases. Most forms of porphyria follow a so-called autosomal dominant inheritance. This means that there is 50% risk of a child inheriting porphyria if any of the parents have the disease. •



Eliane Sardh is responsible for the medical operations at Porphyria Centre Sweden.



In a porphyria investigation, it is important to prevent the porphyrins from being broken down by exposure to light. Therefore, some analyses are carried out in a darkroom environment with red light.

“The challenge is to remember that a laboratory investigation is always needed to confirm the diagnosis.”

Disorders, CMMS at Karolinska University Laboratory. The Centre is a national laboratory and the only facility in the country that investigates and follows up Porphyria Disorders.

Clinically, Porphyria Disorders are divided into two main groups, acute porphyria, and cutaneous porphyria. It is often difficult to detect acute porphyria. This is due because the symptoms may resemble many other acute conditions and because it is a rare disease that many doctors do not have much experience with.





Pauline Harper, Eliane Sardh and Daphne Vassiliou at Porphyria Centre Sweden.

“Many of the acute symptoms are common in our emergency wards and the challenge is to remember that a laboratory investigation is always needed to confirm the diagnosis,” says **Eliane Sardh**, researcher and consultant, who is responsible for medical operations at the Porphyria Centre Sweden.

In addition to the laboratory operations, since 1994, The Porphyria Centre Sweden has been commissioned as a national centre of knowledge for diagnostics and treatment of porphyria disorders. The commission includes consultation concerning treatment and follow-up of all porphyria disorders, drug information relating to acute porphyrias, maintaining a register of patients with confirmed porphyria diagnoses and of their relatives. The Porphyria Centre Sweden is also tasked with carrying out research and development.

The Swedish family register of all patients in the country diagnosed with porphyrias is a cornerstone of the operation. Using these, the laboratory can search for mutations and tailor its analysis methods. Based on the results of the analyses, the investigation can also be supplemented with genetic diagnostics. When the diagnosis is made, it is important that the family is offered, it is important that the family is offered genetic counselling, which includes information about the disease and how it is inherited.

“Working with illnesses that are serious and yet so rare that they are often missed and mistreated is very special,” says Specialist **Daphne Vassiliou**.

The Porphyria Centre Sweden has considerable international renown and is part of the European Porphyria Network, or EPNET. The Centre also maintains a close co-operation with the Swedish patient organisation. It also cooperates closely with the Swedish Patient Organisation Riksföreningen mot Porfyriskjukdomar, RMP,

concerning the design and dissemination of information on porphyria disorders

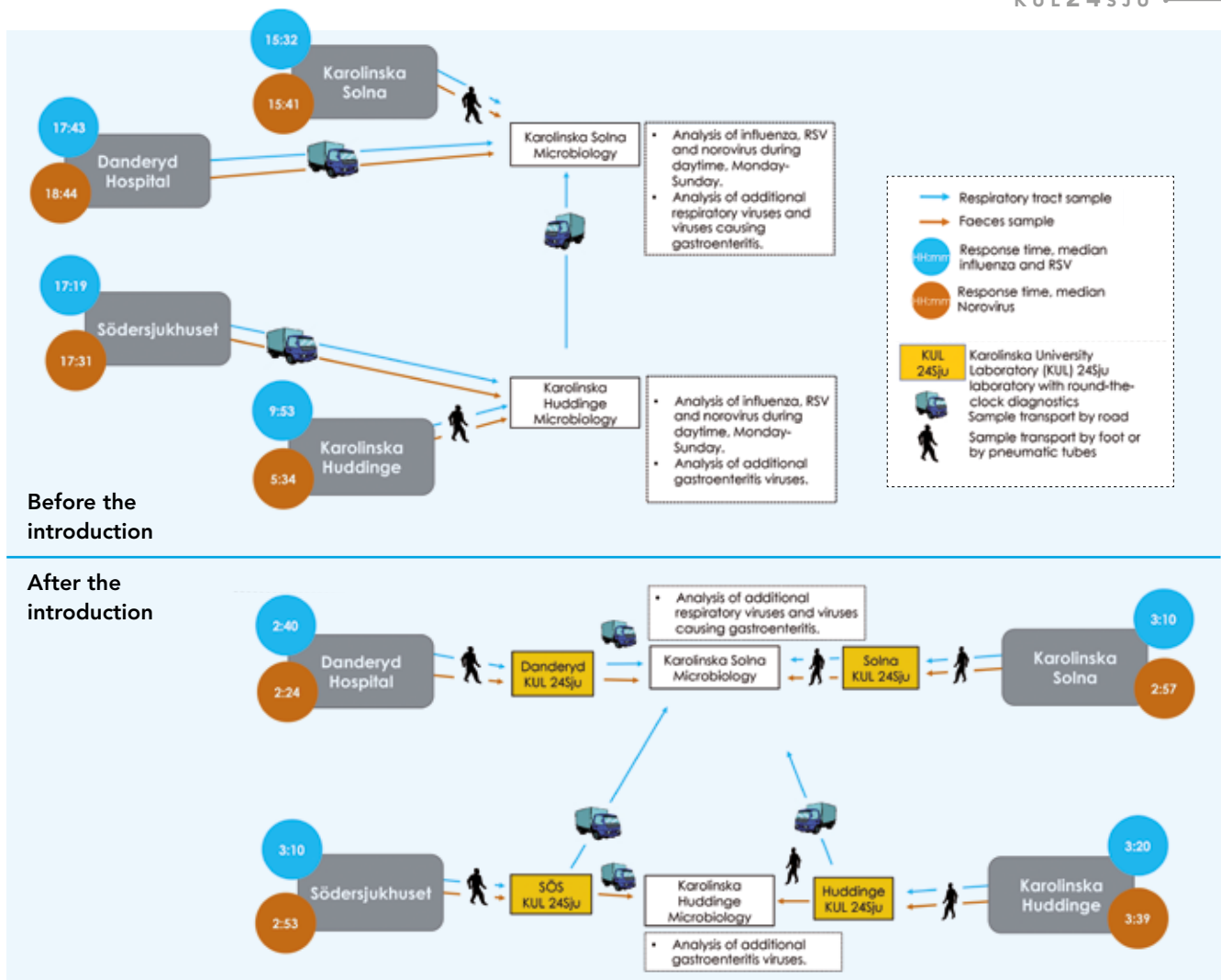
“Patients are extremely committed. This, together with the laboratory's high international standard and our dedicated employees, means that we have participated in several clinical trials in a way that is globally unique and means an incredible amount to us,” says Consultant and Associate Professor **Pauline Harper**.

Acute intermittent porphyria is the most usual form of acute porphyria. Patients who suffer from acute attacks are treated with a form of heme called chloroheemin. For the most severely ill patients with recurrent attacks, liver

“If we had not been able to deliver in the way we have, then the development of a drug would not have progressed this far.”

transplant is the only curative treatment. Now, however, a new candidate drug shows promising results in a Phase 1 clinical study conducted in close collaboration with the Porphyria Centre Sweden who also recruited most patients. The candidate drug is based on so-called RNA interference, which is a natural method of inhibiting a particular gene expression, in this case the first step of heme synthesis in the liver.

“In principle all attempts to find a new drug for acute porphyrias have been done in collaboration with us at Porphyria Centre Sweden and CMMS. If we had not been able to deliver in the way we have, then the development of a drug would not have progressed this far. There is really a direct link to the laboratory, the cooperation with our patients and our knowledge,” concludes Eliane Sardh. •



The illustration describes the sample flow and response times before and after the introduction of round-the-clock diagnostics.

Faster results lead to faster decisions

The recurrent influenza season puts additional pressure on the emergency departments. A quick response within just a few hours, helps the hospital to plan the use of hospital beds and provides better patient care.

Karolinska University Laboratory has been analysing the influenza, RSV and norovirus round-the-clock at Danderyd Hospital, Södersjukhuset and Karolinska University Hospital in Huddinge and Solna since December 2017. The response times for the analyses have been able to be reduced, which is both due to shorter transport routes and because they are processed round-the-clock.

The automated round-the-clock diagnostics were first implemented at Södersjukhuset in February 2016. They have subsequently been introduced at other hospitals during late autumn 2017, starting at Danderyd Hospital followed by Karolinska University Hospital in Solna and Huddinge. The goal was to stay one step ahead and be up and running before this year's flu season.





“In the past we had a response time of up to 24 hours, which is a long time for these types of analyses. Not least because the results are used as a basis for both treatment and placement of the patient,” says **Mattias Karlsson**, who is a molecular biologist at the Department of Clinical Microbiology and project manager for the introduction of round-the-clock diagnostics.

The work took place in two stages where the first involved testing the diagnostics locally at Södersjukhuset, from which transport was established to and from other hospitals. As the response times were still regarded as being too long, in stage two we chose to move diagnostics

“Now those boundaries are not delineated, and we have found the right forms of cooperation so we can develop further.”

from clinical microbiology to the 24-hour laboratories in clinical chemistry and KUL24Sju, which are located at Karolinska University Hospital in Solna and Huddinge, Södersjukhuset and Danderyd Hospital. Large-scale training schemes were carried out, procedures were clarified

Mattias Karlsson is project manager for the introduction of 24/7 diagnostics.

and developed, including through new job descriptions to ensure quality and simplicity when carrying out analyses.

“To facilitate the communication and decision-making processes, we have created a management group comprised of representatives from the two specialist laboratories. We meet once a month to follow up the activities of the different units.”

Mattias Karlsson wishes to particularly highlight the excellent cooperation between functions as being decisive to the implementation of round-the-clock diagnostics. A partnership that constitutes a good basis for future development projects and future diagnostics.

“Traditionally speaking, strict boundaries have existed across the functions. Now those boundaries are not delineated, and we have found the right forms of cooperation so we can develop further. Naturally, our hope is to offer care providers even faster answers, both for these types of analyses and others,” concludes Mattias Karlsson. •



Sepsis – A lifethreatening condition



Sepsis occurs when the immune response overreacts to an infection in the body. The rapid progression means that the patient's condition can become life-threatening within just a few hours. Therefore, fast and safe diagnostic methods are crucial to the patient receiving correct treatment.

In Sweden, more than 40 000 people are diagnosed with sepsis every year. This makes the condition more common than both Myocardial Infarctions and the four most common forms of cancer combined. Sepsis is extremely serious and occurs when an infection has spread to the entire body and affects vital organs. The infection is often a consequence of, e.g., pneumonia, urinary tract infection or skin infection.

During sepsis, the body's immune system overrides and produces substances in excessive concentrations that cause blood vessels in the organs function worse and may also cause fluids to begin leaking from the blood vessels. This causes blood pressure to drop to a dangerously low level and the body has difficulty in supplying oxygen to vital organs. In septic shock, the vital organs stop working. Today, it is known that the chances of surviving septic shock decreases by around 5 percent for every hour without proper treatment.



Volkan Özenci has developed new methods for the rapid diagnosis of sepsis.





One of the challenges in treating sepsis is that at first you do not know which microorganism is causing the infection, or which antibiotics would be best for the patient.

“The time between the sepsis diagnosis and correct treatment is the main determining factor of survival. Therefore it is important to diagnose and receive laboratory results as early as possible,” says **Volkan Özenci**, Associated professor and Consultant at the Laboratory for Clinical Microbiology at Karolinska University Hospital in Huddinge.

“The time between the sepsis diagnosis and correct treatment is the main determining factor of survival.”

Back in 2006, Volkan Özenci and his research colleagues developed a method that could identify the bacteria causing sepsis in just four hours. This was a vast improvement in comparison with earlier test methods where results were first obtained after 24 hours.

“The method is now part of our routine diagnostics and is used worldwide, from the US to Japan. In Europe, four out of ten major EU laboratories use the method

in daily routines. Response time is now two hours for Gram-negative bacteria and between four and five hours for Gram-positive bacteria,” says Volkan Özenci.

More lives can also be saved via the sepsis alarm routine, which was introduced at Karolinska University Hospital in Huddinge in September 2017. Thanks to the alarm routine, patients with symptoms of sepsis can now be treated much faster than before.

The alarm means that the nurse who makes the primary assessment of the patient can press a special alarm button if the patient exhibits symptoms of sepsis. The alarm goes to both the infectious disease doctor, the emergency physician and intensive care doctor who work together and carry out a joint assessment of the patient. Optimal treatment is then introduced at an early stage.

Since the introduction of the sepsis alarm routines in the autumn of 2017, the alarm has been activated when treating more than 650 patients, thus corresponding to 1.3 sepsis alarms per day. Approximately 70% of the patients the alarm was sounded for proved to have sepsis and because the alarm was activated, they were able to receive timely and correct treatment. A preliminary evaluation shows that for those patients for whom the sepsis



Kristoffer Strålin has been involved in introducing the new sepsis alarm routine.

alarm was triggered received antibiotics after an average wait of 1 hour and 14 minutes. However, in situations where there alarm was not triggered, the average wait time for the patient to receive their first dose of antibiotics was 4 hours and 7 minutes.

Kristoffer Strålin is a Consultant and heads the sepsis patient group at Karolinska University Hospital. He has been involved in developing the new routine and is also the primary author of the Stockholm Region Sepsis Care Programme, which is now being introduced at emergency care hospitals in Stockholm.

“The sepsis alarm routine makes it possible to optimise initial patient care, which we believe is important for survival in cases of sepsis,” says Kristoffer Strålin..

FACTS: SEPSIS

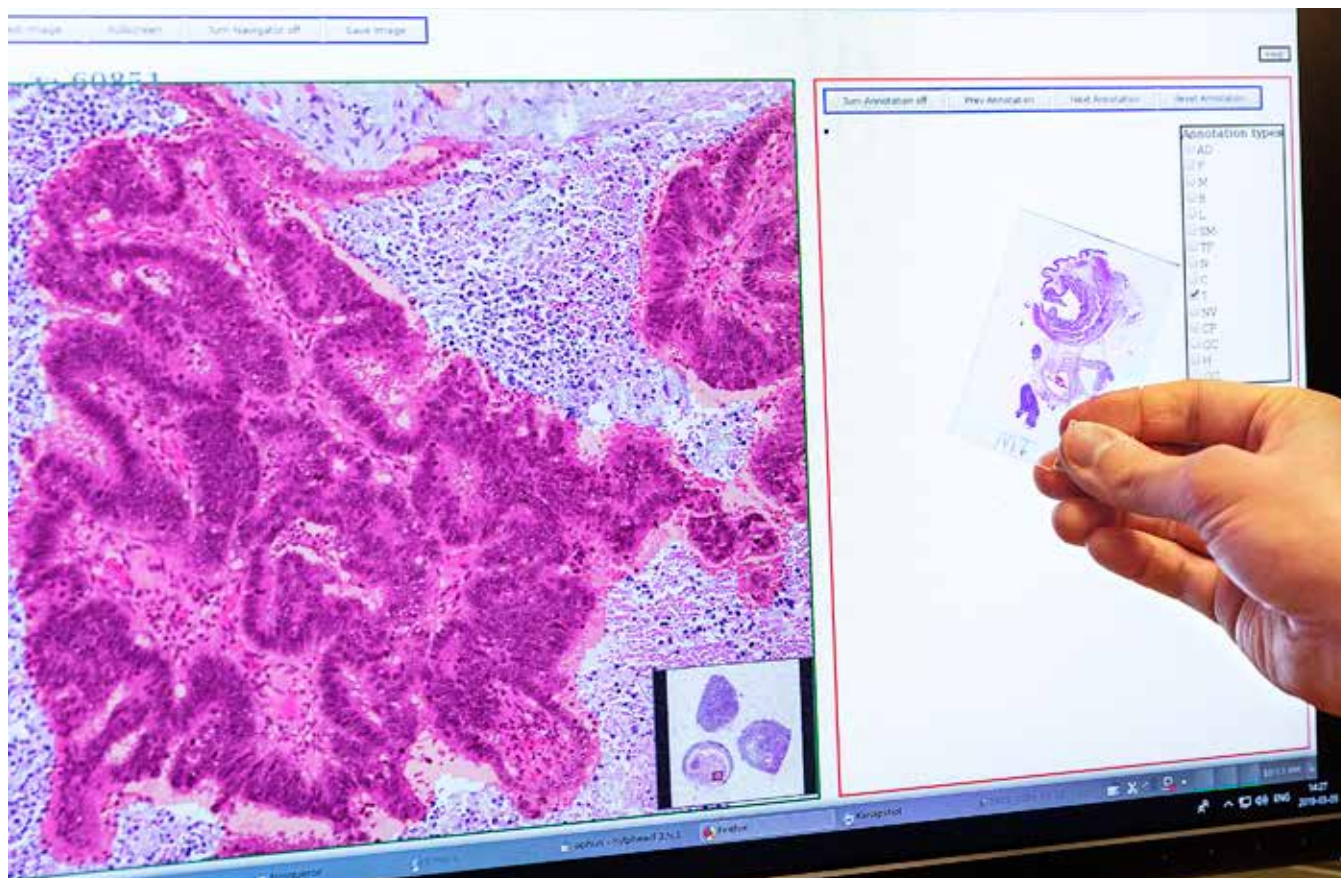
In the past, sepsis was commonly referred to as blood poisoning, however, bacteria are only present in the blood in 20-30% of cases. Approximately 9 out of 10 cases of sepsis in the Western world are caused by a bacterial infection, but the condition can also be caused by fungal or viral infections. A total of 19 million people suffers from sepsis globally every year.

Following the introduction of the sepsis alarm routine at Karolinska University Hospital in Huddinge, the emergency departments at Danderyds Hospital, Södersjukhuset and S:t Görans Sjukhus have also implemented the sepsis alarm routine.

“**Blood cultures prior** to administration of antibiotics are an important quality indicator for sepsis because positive blood cultures provide a sound diagnosis. However, one problem with blood cultures is that they are quite often negative despite the patient having sepsis. We are working on the development and assessment of more sensitive methods, especially those that show bacteria DNA in the blood. There is much to be gained from fast, safe and sensitive diagnostics, not only for the patient but also to society. In addition to saving lives, we can free up beds in our intensive care units faster and we can also avoid the overuse of antibiotics,” says Kristoffer Strålin.

With the introduction of sepsis alarm routine, Volkan Özenci and his colleagues designed a study focusing on the preanalytical part of blood culturing to simplify and improve the sampling itself. New sampling routines are now being discussed.

“I notice that there is a great deal of confidence in clinical microbiology and that the laboratory has a changed role. We have gone from being a support organisation to becoming much more clinically oriented,” concludes Volkan Özenci. •



Artificial intelligence in the future of pathology

Digital Pathology and artificial intelligence, AI, are rapidly growing areas that change how a tissue sample can be investigated and analysed. The technology assists pathologists who can then utilise their competence more effectively, which improves the quality of care and benefits the patient.

Today, pathologists devote quite a bit of their time to microscopic examination of samples. Investigation of certain common forms of cancer may involve up to 80 tissue samples per patient. Now a new tool is being developed for faster and more accurate diagnosis in the laboratory, by utilising AI in the form of self-learning image analysis. The new digital technology can provide support to pathologists, so they are able to utilise their competence more effectively and focus on samples requiring advanced analysis.



Attila Szakos, to the left, and Carlos Fernandez Moro, above, view the new digital technology as aid in their work as pathologists.

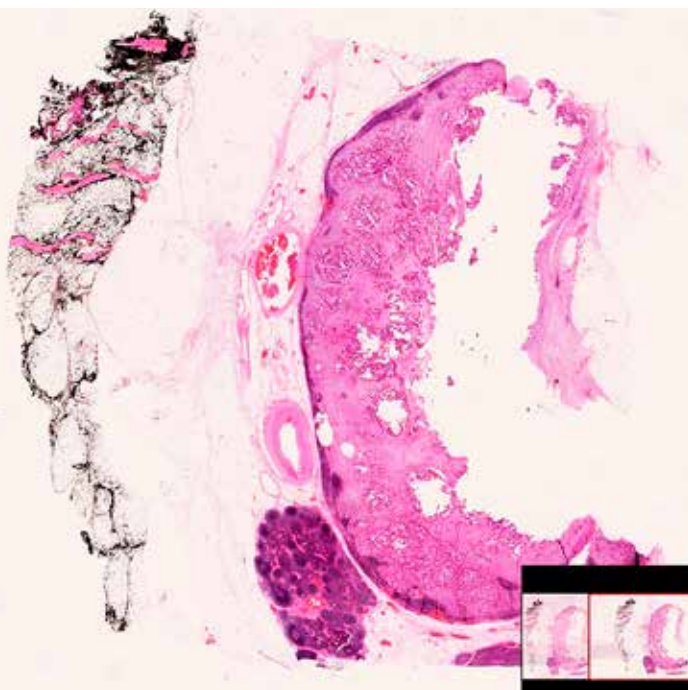
“We want to be able to come closer to a diagnosis and help clinicians to become even better at working to treat their patients in the best conceivable way.”

“The modern technology won’t make pathologists less necessary. Instead, we will be able to focus on increased volumes and reporting requirements. AI supports us, so that our work will become smoother and more efficient,” says **Attila Szakos**, Consultant at the Laboratory for Clinical Pathology and Cytology and Director of the Function Unit.

Over the past two years, the Laboratory for Clinical Pathology and Cytology at Karolinska University Hospital in Huddinge has been part of a collaborative project with Saab to develop the future of digital pathology with the support of AI. The project was funded by Vinnova and coordinated by the Innovation Center. The Centre is a part of Karolinska University Hospital that works with innovation as a tool to address the challenges faced by healthcare and to create the best possible care. Also collaborating on the project were Semmelweis Universität in Budapest and the Queen Mary University of London.

“We have, among others, supplied a large number of samples that were scanned at Karolinska Institutet and generated over 600 digital images. These have since been





forwarded to Saab for development of the algorithm in the image management model, says **Carlos Fernandez Moro**, Consultant and Researcher at the Laboratory for Clinical Pathology and Cytology.

During phase 1, an AI system was developed to automatically detect metastatic lymph nodes from colorectal cancer. This system was advanced further during phase 2, as images were extracted, and AI algorithms, evaluative metering and data visualisation tools were developed. The project has also grown with an added image analysis and visualisation tool for the detection of metastatic lymph nodes from malignant melanoma in sentinel nodes and quantitative analysis of colorectal cancer and liver metastases. Phase 3 has now started where the system is to be tested in a clinical routine setting.

“The image management model shows that the algorithm has a potential to provide support in the analysis of pathological preparations.”

“The image management model shows that the algorithm has a potential to provide support in the analysis of pathological preparations. A complete solution may mean much of our monotonous work with manually analysing samples under microscopes will be done automati-

cally instead,” says Carlos Fernandez Moro.

The laboratory already utilises automated processes where, for example, dehydration, embedding, sectioning and staining can be performed automatically.

“We want to be able to come closer to a diagnosis and help clinicians to become even better at working to treat their patients in the best conceivable way,” states Attila Szakos, who also believes that this type of innovation and research project is of immense importance to increasing interest in the laboratory as a workplace. •

FACTS: ARTIFICIAL INTELLIGENCE, AI

Artificial intelligence works based on algorithms, which are mathematical instructions to be able to learn a task through practice. In many ways, the technology resembles the way the human brain learns by processing information in a network of cells. In pathology, algorithms can be trained to recognise structures and patterns, process all information and find suspicious structures.



Catarina Pommer, COO of health care company Tiohundra, Peter Graf, CEO of health care company Tiohundra and Ingrid Engström, Marketing Assistant at Blodcentralen Stockholm.

Next Stop Norrtälje Hospital!

In November 2018 the blood bus stopped at Norrtälje Hospital for the first time. The aim was to recruit new donors from among healthcare company Tiohundras employees who are permitted to give blood during working hours.

Norrtälje Hospital is the largest employer in the municipality. It is a small hospital, but provides all basic emergency medical care, except for childbirth. Here they are keen on doing their part to significantly increase the number of blood donors. The hospital allows employees to give blood during working hours, and it also allows them to book their appointments in advance, which enables them to get away from their jobs for a while. In November 2018, the Transfusion Medicine Department at Karolinska University Laboratory expanded its service and a blood bus stopped at the hospital.

Just one month later, in December 2018, the blood bus had some 50 visitors during the day, both established blood donors and those who had samples

taken to be able to give blood in future. Due to the positive response, Norrtälje Hospital is now among the regular stopping points for the blood bus.

"Tiohundra is committed to allowing employees to give blood during working hours and to the dissemination of information, which makes it possible," explains Ingrid Engström from Blodcentralen who hopes that the stream of donors will continue to flow.

The blood bus makes regular visits to Norrtälje, Rimbo and Hallstavik. The new stop at Norrtälje Hospital is primarily intended for Tiohundras employees, but other donors are also welcome, subject to availability.

Karolinska University Laboratory strives to make giving blood easy. There are currently three blood centres (blodcentraler) in central Stockholm and four blood buses that regularly visit about 140 locations in the county. Each day approximately 100 litres of blood are used in the county of Stockholm.

Specialists working together for the good of the patient

For over a decade, clinical pharmacology has been a unique collaboration between the allergy and dermatology clinics at Karolinska University Hospital. Here, patients with suspected drug hypersensitivity can see an allergologist or dermatologist together with a specialist in clinical pharmacology.

The collaboration between clinical pharmacology and the dermatology clinic began in the early 2000s. The concept of allowing patients with suspected drug hypersensitivity to be investigated by two specialists at a common reception point proved to be a success factor. After a few years, the Lung and Allergy Clinic also decided to start up the same type of cross-disciplinary drug clinic.

Eva Wikström Jonsson is a Consultant and Associate Professor in Clinical Pharmacology, and Director of Drug Information at the Division of Clinical Pharmacology. One half day a week, together with an allergologist, she receives patients referred to the allergy clinic for suspected drug hypersensitivity with immediate reaction.

“While the allergologist focuses on symptoms, diagnostics and the general treatment of the patient, my role is specifically focused on the drug that may have triggered a hypersensitivity reaction. This may involve complex situations where the patient has been exposed to many drugs during a brief time. Perhaps there is a complicated primary disease that requires comprehensive drug treatment. Many patients have been treated for complicated infections.

Diana Rydberg is a Consultant at Clinical Pharmacology at Karolinska Institutet and has a corresponding role together with a dermatologist at the Dermatology Clinic where together they handle patients with suspected drug hypersensitivity involving delayed skin reactions.





Sjuksköterska
K Karin Sanden
Leg. sjuksköterska
PD, Ung och Allergipoliklin



Eva Wikström Jonsson, together with an allergologist, receives patients referred to the allergy clinic.



Diana Rydberg handles patients at the skin clinic together with a dermatologist.

She states that her work is often about removing the suspicion that the problem is due to a hypersensitivity reaction.

“We work a bit like detectives, and it is not always possible to explain the original reaction. The important thing is to be able to find a safe alternative that the patient can be treated with.”

Before Eva and Diana meet with patients at the respective allergy and skin clinics, they perform a thorough literature review based on the query raised in patients’ referrals. Among other things, they look at what is known

about the suspected drug and how similar investigations were carried out before. At the patient visit, there is then the opportunity to ask supplementary questions and carry out further testing and investigations. The clinical pharmacologists are also involved in preparing the recommendation in the final statement of opinion.

FACTS: DRUG HYPERSENSITIVITY

The term drug hypersensitivity is used when someone reacts to drugs at doses that normally do not usually cause problems. Following this, the divisions allergic hypersensitivity, which is immunological, and non-allergic hypersensitivity are used. Allergic reactions can be immediate or delayed. Drug hypersensitivity is differentiated from other types of reactions, such as dose dependent adverse reactions.

“We are a small, but close-knit team that has drug clinics where input from the nurses is also important. One of their responsibilities is patient skin testing, which is a rather special task and a bit of an art,” explains Eva Wikström Jonsson.

Both Eva and Diana believe that this type of collaboration between a clinical specialism and clinical pharmacology could include more areas where there are complex issues concerning drugs.

“It’s stimulating to work cross-professional and allow different specialisms to complement each other. Helping each other contributes to a more comprehensive assessment that will benefit the patient.” •



Breast Centre – a coherent care pathway

Clinical Pathology and Cytology at Södersjukhuset has a key role to play in the cohesive care process that characterises the activities at the hospital's breast centre. Here, the pathway through care is fast and smooth – from screening and diagnostics, via treatment to rehabilitation and follow-up.

The Södersjukhuset Breast Centre is one of Europe's largest centres for diagnosis and treatment of breast cancer. It is also one of Stockholm's three breast centres where the basis for the centre is a clear patient focus with increased accessibility and better conditions for real world evidence. Each breast centre has an overall responsibility for patients with breast cancer, from diagnosis and investigation to treatment and rehabilitation. This means that the Clinical Pathology and Cytology Laboratory at

Södersjukhuset has a large volume of samples coming from activities at the breast centre.

In February 2017 SöS Bröstcentrum (mammography) opened in new premises located at Södra Station. Women between the ages of 40 and 74 are provided mammography screening appointments here to detect breast cancer as early as possible. For suspected breast cancer, several different specialists work together to make the most detailed and complete diagnosis possible. Triple diagnos-





tics mean that the clinical examination is combined with mammography/ultrasound and biopsy/cytology.

The Clinical Pathology and Cytology Laboratory at Södersjukhuset recently opened a fine needle aspiration biopsy clinic in association with Bröstcentrum Mammografi. The clinic helps to create a better flow within the division and makes it easier for patients, as they are often

“The fact is that we would be extremely unsuccessful without the Clinical Pathology and Cytology Laboratory.”

able to have cell or tissue sampling done in conjunction with their mammography examination.

The laboratory is involved in several stages of the breast cancer process. Here, an initial diagnosis is made based on a cell or tissue sample the patient has taken at

the fine needle aspiration biopsy clinic. Most often, the analysis shows benign changes and the patient can be given some reassuring results. If the investigation indicates there is breast cancer, then the diagnosis forms the basis for further treatment.

Marjan Delavaran-Shiraz is head of unit for the division and describes the laboratory as being more of a specialist department than a traditional laboratory.

“What we provide is much more than a test result, it is a diagnosis and a prognosis. The investigations we carry out are a prerequisite for being able to give the patient the correct treatment.

Linda Nigard is a consultant and surgeon at the Breast Surgical Unit at Södersjukhuset. The unit investigates breast symptoms and is responsible for the surgical treatment of breast cancer. She and her colleagues operate on an average of 30 patients per week. The laboratory is frequently interacted during operations. During breast preservation surgery, the specimen is X-rayed in the laboratory to ensure the whole cancer tumour is removed and with a good resection margin. The images are then sent for interpretation by the mammography department, and they respond directly to the surgical department. In cases



“We are proud to be able to contribute to a fast and efficient flow in the breast cancer process.”

where a sentinel node is removed, it is sent to the laboratory for a frozen section procedure while the operation is being carried out. The results give the surgeon guidance as to whether the cancer has spread, and if they need to go ahead and remove additional lymph nodes.

FACTS: BREAST CANCER

Breast cancer is the most usual form of the disease among women. Each year, approximately 8,000 women and about 100 men in Sweden are affected by the disease. Breast cancer accounts for approximately 30% of all cancer in women. The risk of breast cancer increases with age. A slight increase in the number of cases of newly diagnosed breast cancer is seen every year. At present, approximately one in ten women in Sweden will suffer from breast cancer at some point during their lifetime.

View the film *The role of pathology in the care chain – an important part of the team* <https://www.youtube.com/watch?v=AWixSC1jndw>

“Correct diagnostics are crucial, so we don’t miss anything, but also so that we don’t overtreat patients and operate unnecessarily. The fact is that we would be extremely unsuccessful without the Clinical Pathology and Cytology Laboratory,” states Linda Nigard.

After surgery, the laboratory investigates exactly what type of breast cancer the patient has. They also find out whether all the cancer is gone and perform supplementary investigations that form the basis for the oncologist’s decision concerning continued treatment. Multidisciplinary conferences with surgeon, oncologist, radiologist and pathologist are also included for a correct assessment of each new breast cancer patient, both before and after surgery.

“We have access to the surgery schedule and can see how many patients are booked for surgery. This means that we can prepare ourselves in terms of resources. Every Tuesday our employees stay a little longer to assist the surgeons who then have operations late in the afternoon. We are proud to contribute to a fast and effective flow in the breast cancer process with a focus on continuous improvements and the patient’s best interests,” concludes Marjan Delavaran-Shiraz. •

A quality mark that shows competence

Accurate laboratory diagnostics are crucial to a patient being able to receive a correct diagnosis and treatment. Karolinska University Laboratory is regularly reviewed by supervisory bodies and authorities such as the Swedish national accreditation body Swedac.

Accreditation is based on internationally recognised standards, which means that analytical results from an accredited laboratory are accepted in the 34 countries included in the European Committee for Standardization, or CEN, which have approved the standard. More advanced diagnostics and the demand for specialist competence increases the necessity to seek out cross-border cooperation, which is why the broad acceptance is important.

“The accreditation gives us a formal recognition of our competence and our way of working. Swedac reviews whether we carry tasks impartially, at an elevated level of quality, and that all the elements in an analysis are correctly executed,” elaborates **Suzanne Sallander**, who is Quality Manager at Karolinska University Laboratory.

In the Stockholm Region, suppliers of laboratory diagnostics are required to have accreditation. Accreditation provides regulators and authorities with an independent evaluation by a third party. Swedac plans its work so that the entire division is reviewed in four years. The accred-

itation is not limited-time but is valid on a continuous basis provided that the requirements are met.

“Karolinska University Laboratory has an exceptionally large mandate covering all of Region Stockholm. As we have a common accreditation and a standardised way of working, samples and analyses are handled in the same way regardless of where in the region the patient had the sample taken. This is important for patients who are monitored via laboratory analyses,” continues Suzanne Sallander.

Becoming accredited is a long-term commitment. Parts of Karolinska University Laboratory were already accredited at the beginning of the 1990s. Today it has grown to be Sweden’s most extensive accreditation for medical laboratories.

During the first weeks of February 2019, 18 inspectors from Swedac visited Karolinska University Laboratory. Discussions were held with representatives from across the business, including medical management, technical management, quality coordinators, plus other managers and employees.

Birgitta Jonsson, Quality Manager at Clinical Chemis-



“The accreditation gives us a formal recognition of our competence and our working methods.”

try and KUL24Sju was one of many who were involved during Swedacs visit.

“There is extensive preparatory work before an inspection. The management system’s documentation must be submitted to the inspectors in appropriate time, logistics for the visit must be planned, including offices, transportation, and all persons involved must be in the right place at the right time,” says Birgitta Jonsson and continues:

“In the business, Swedac visits are a welcome opportunity to discuss our own routines and to have the opportunity to enter into a discussion with subject specialists about methodological issues.”

At a well-attended closing meeting, Lead Assessor Helene Johansson summarised the results of audit. She specifically highlighted the company’s competent and committed employees, whom she believed are well versed in their quality management system and are extremely committed to continuously improving processes. •





The Karolinska University Laboratory management team is comprised of 17 persons. The following persons appear in the photo below, from the left: **Mikael Björnstedt**, Director of Clinical Pathology and Cytology. **Andreas Matussek**, Managing Director Karolinska University Laboratory **Matti Sällberg**, Head of Department, KI. **Marja-Liisa Dahl**, Director of Clinical Pharmacology. **Joachim Lundahl**, Assistant Managing Director **Carina Ritzmo**, Director of Laboratories for Community Healthcare and Preliminary Analysis **Tobias Allander**, Director of Clinical Microbiology. **Helena Dybeck-Lundmark** HR Manager. **Joakim Dillner**, Director of R&D. **Eva Hendig**, Executive Assistant. **Cecilia Odelsparr**, Director of Operations. **Margareta Sten-Linder**, Director of Clinical Chemistry and KUL24Sju. The following are missing from the group photo: **Anna Wedell**, Director of the Center of Inherited Metabolic Diseases. **Maria Matl**, Director, Clinical Immunology and Transfusion Medicine. **Maria Johansson Soller**, Director of Clinical Genetics **Robert Nilsson**, Director of Controlling **Lisa Wiklund**, Head of Nursing Development

FACTS

Function areas: Clinical Pathology and Cytology, Clinical Chemistry and KUL24Sju, Clinical Microbiology, Clinical Immunology and Transfusion Medicine, Clinical Pharmacology, Clinical Genetics, Center of Inherited Metabolic Diseases, Laboratories for Local Care and Pre-analysis.

Number of employees: (2018) 2137

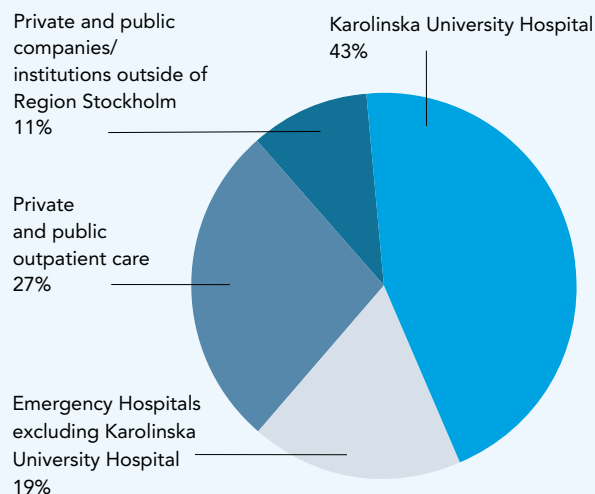
Production (thousands, including analyses, sampling, patient treatment, blood sampling, etc.): (2016) 25,600, (2017) 26,900, (2018) 27,500

Revenue (SEK million): (2016) 2,400, (2017) 2,500 (2018) 2,600

Quality and patient safety: Karolinska University Laboratory is accredited according to ISO 15189 "Medical laboratories – Requirements for quality and competence in medical laboratories". The accreditation comprises all hospital and local care laboratories with relevant operations. Our quality and management systems also meet the requirements of the quality standards ISO/IEC 17025, ISO 9001, WADA, EFI, CAP, GMP, GLP, JACIE.

Environmental work: Karolinska University Laboratory is environmentally certified according to ISO 14001.

TURNOVER 2018



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Karolinska University Laboratory

We offer laboratory medicine with good service, high quality and a complete selection of clinical analyses and laboratory services. On a scientific foundation, we develop the laboratory medicine of the future.