



UMEÅ, SWEDEN

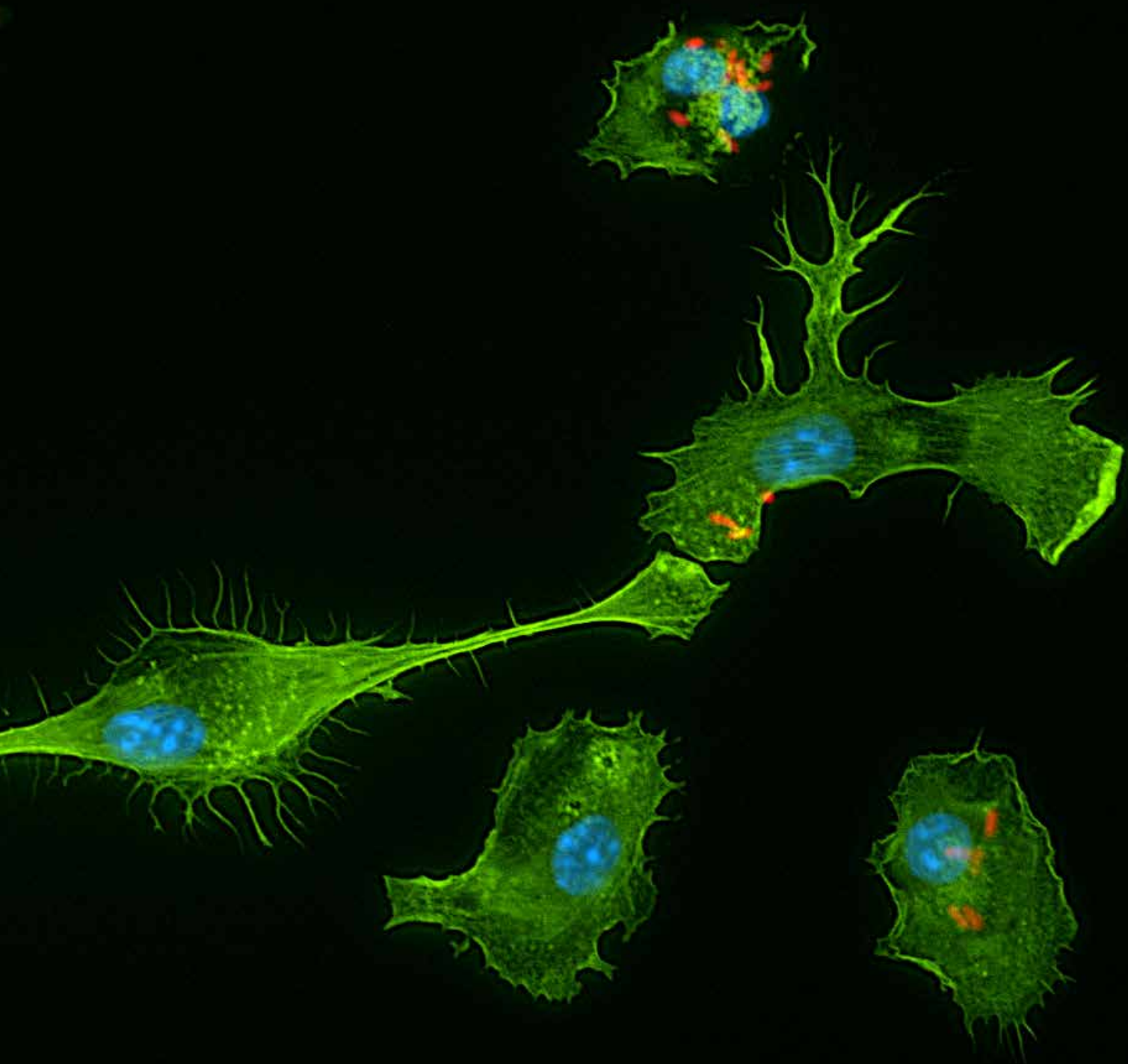
**A CENTRE OF EXCELLENCE
FOR ANTI-INFECTIVE
RESEARCH & DEVELOPMENT**



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Infectious diseases are one of humanity's greatest problems. Every year, millions of people die needlessly from infectious diseases which in most cases should have been preventable or treatable. The challenges include antibiotic resistance, the emergence of new infectious diseases and the re-emergence of old ones, as well as transmission issues exacerbated by increasing population density.

Vaccines and treatment with antibiotics have been so successful that it was thought that the battle against infections had been won. However, bacteria which are resistant to antibiotics have now become such a major problem that they constitute a threat to modern medical treatment. New types of antibiotics to tackle resistant bacteria are urgently needed yet there is an almost empty drug pipeline with only few early stage drugs under development. So far the industry has focused its efforts on combating Gram-positive

bacteria. In Europe, two thirds of deaths from bacterial infections are due to Gram-negative bacteria and with the emergence of superbugs resistant to all antibiotics on the market, the importance of developing Gram-negative therapies is paramount.

For global health there is an urgent medical need to discover and develop novel classes of anti-infectives with hitherto alternative modes of action.

Top research institutions and companies in Umeå are tackling these issues in new and unique ways, based on knowledge of pathogenicity and modes of action of many microbes, including Gram-negative bacteria.

ANTI-INFECTIVE EXPERTISE IN UMEÅ

Unique insight into the pathogenicity of microbes
and novel approaches to anti-infectives

Biotech Umeå is the growing life science cluster of northern Sweden, and houses two universities, academic and governmental research groups and organisations, many life science companies and a university teaching hospital.

A well-oiled innovation system and technology transfer system in the form of organisations such as Uminova Innovation and Umeå Biotech Incubator, drive the efficient translation and commercialisation of research projects into market viable solutions.

A centre of excellence for anti-infectives research and development, Umeå excels both scientifically and commercially in the fields of the pathogenicity of microbes, infectious diseases and the development of new antibiotics. The Umeå cluster offers significant resources in the research, development and commercialisation of discoveries through the following organisations:

2 UNIVERSITIES

with more than 36 000 students (Umeå University, and the Swedish University of Agricultural Sciences)

UCMR

Umeå Center for Microbial Research with research in infection and pathogenicity

MIMS

Laboratory for Molecular Infection Medicine, the Swedish node of the Nordic EMBL Partnership for Molecular Medicine

LCBU

Laboratories for Chemical Biology Umeå, offering high throughput chemistry and screening platforms

FOI

Swedish Defence Research Agency, one of Europe's leading research institutes within biological defence and security

NORRLAND'S UNIVERSITY HOSPITAL

the major hospital in northern Sweden, situated in Umeå and employing nearly 6000 people

BIOTECH UMEÅ

the region's cluster organization with approximately 70 life science companies

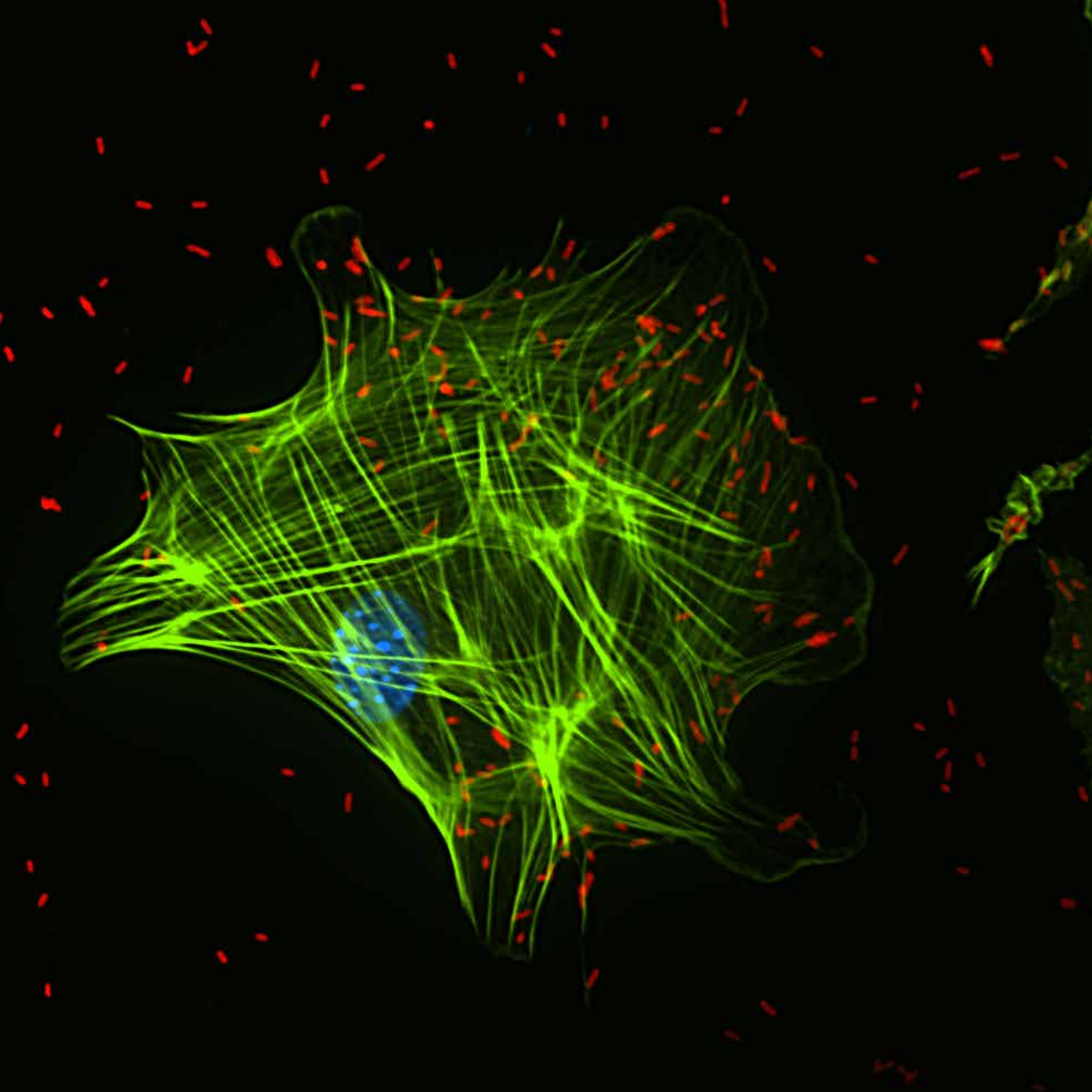
UMEÅ BIOTECH INCUBATOR

providing infrastructure to support spin-outs with lab facilities, seed financing and business development

UMINOVA INNOVATION

providing support to commercialise business ideas from researchers and students, and support to innovative companies in the region.





UMEÅ CENTRE FOR MICROBIAL RESEARCH (UCMR)

An academic interdisciplinary research centre established by a consortium of scientists devoted to top quality research and novel applications in microbial pathogenesis

UCMR is home to 170 scientists from 35 nationalities with expertise in chemistry, physics, medicine and biology. The main areas of focus are the pathogenic mode of action of microorganisms and the development of novel vaccines and anti-infectives. Target organisms of note being studied and researched at UCMR include:

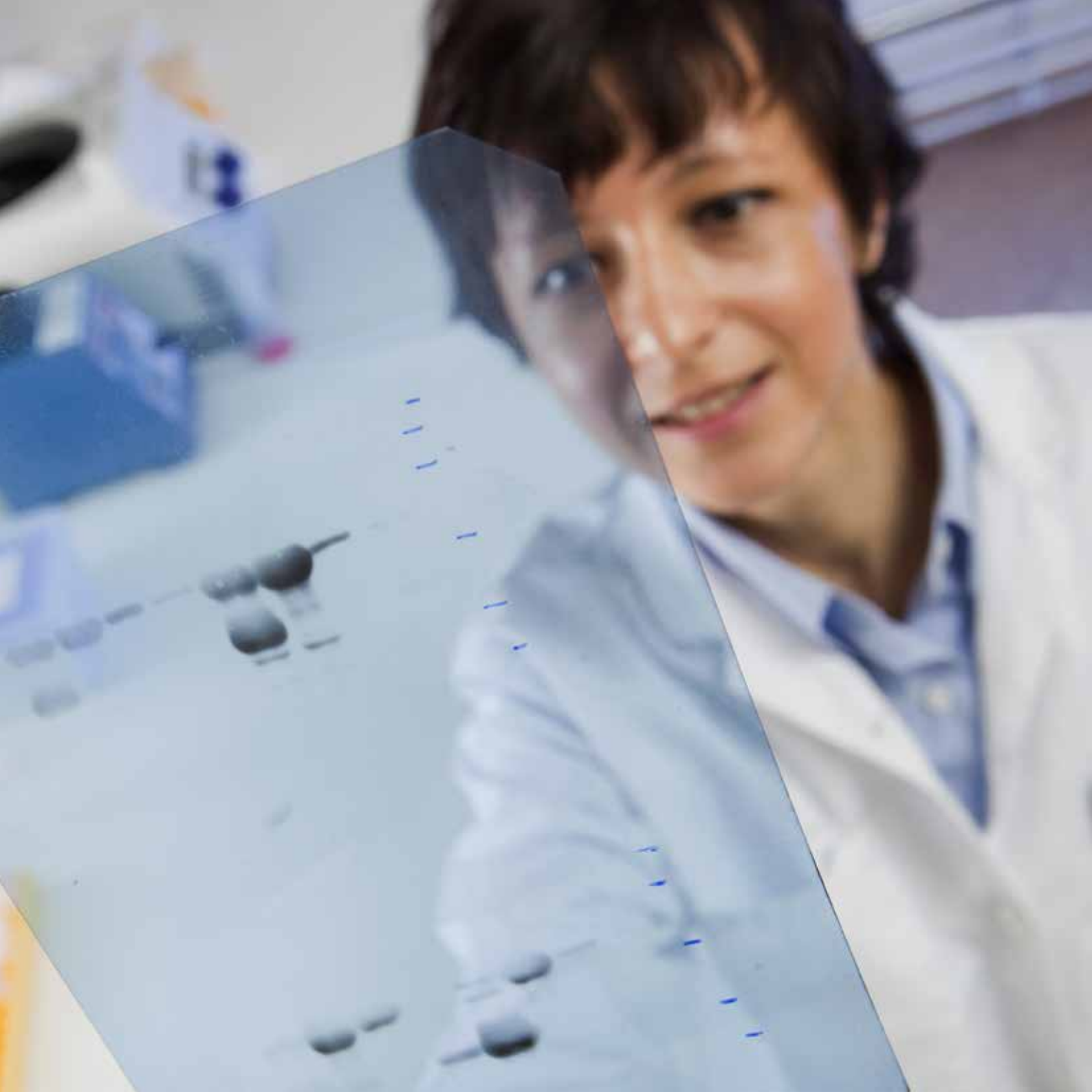
Adenoviruses, Borrelia, E. coli, Helicobacter pylori, Listeria monocytogenes, Pseudomonas aeruginosa, Rhinovirus, Staphylococcus, Streptococcus, Francisella tularensis, Trypanosoma brucei, Vibrio and Yersinia

Several UCMR research groups are actively investigating novel antimicrobials against important Gram-negative pathogens. Common to all these projects is that they focus on identification of small molecules that target different virulence mechanisms in these pathogens.

- **Secretion systems in Gram-negative bacteria**, such as Type III, Type VI and Tat secretion systems in *Yersinia*, *Pseudomonas aeruginosa* and *Vibrio* (5 groups).
- **Biofilm formation** in *Streptococcus* and uropathogenic *E. coli* infections, dental plaques and cholera. Coating for prevention of biofilm formation (4 groups).
- **Borrelia antigen and tick borne encephalitis virus (TBE)** - ecology and molecular virulence of Lyme disease and relapsing fever, and strain pathogenicity of TBE virus (2 groups).

- **Helicobacter pylori** - molecular mechanisms and dynamics in adhesin expression during persistent infection. Vaccine development (2 groups).
- **Mechanisms of innate immunity** - cellular interactions and signal transduction in innate cellular immunity in response to attacks from bacteria, fungi, viruses and parasites (2 groups).
- **New diagnostic tools for infectious diseases** - virulence mechanisms of *F. tularensis* and attenuated vaccines.

For details on the research at UCMR, please visit www.ucmr.umu.se



MOLECULAR INFECTION MEDICINE SWEDEN (MIMS)

MIMS is the Swedish node of the Nordic EMBL partnership in Molecular Medicine

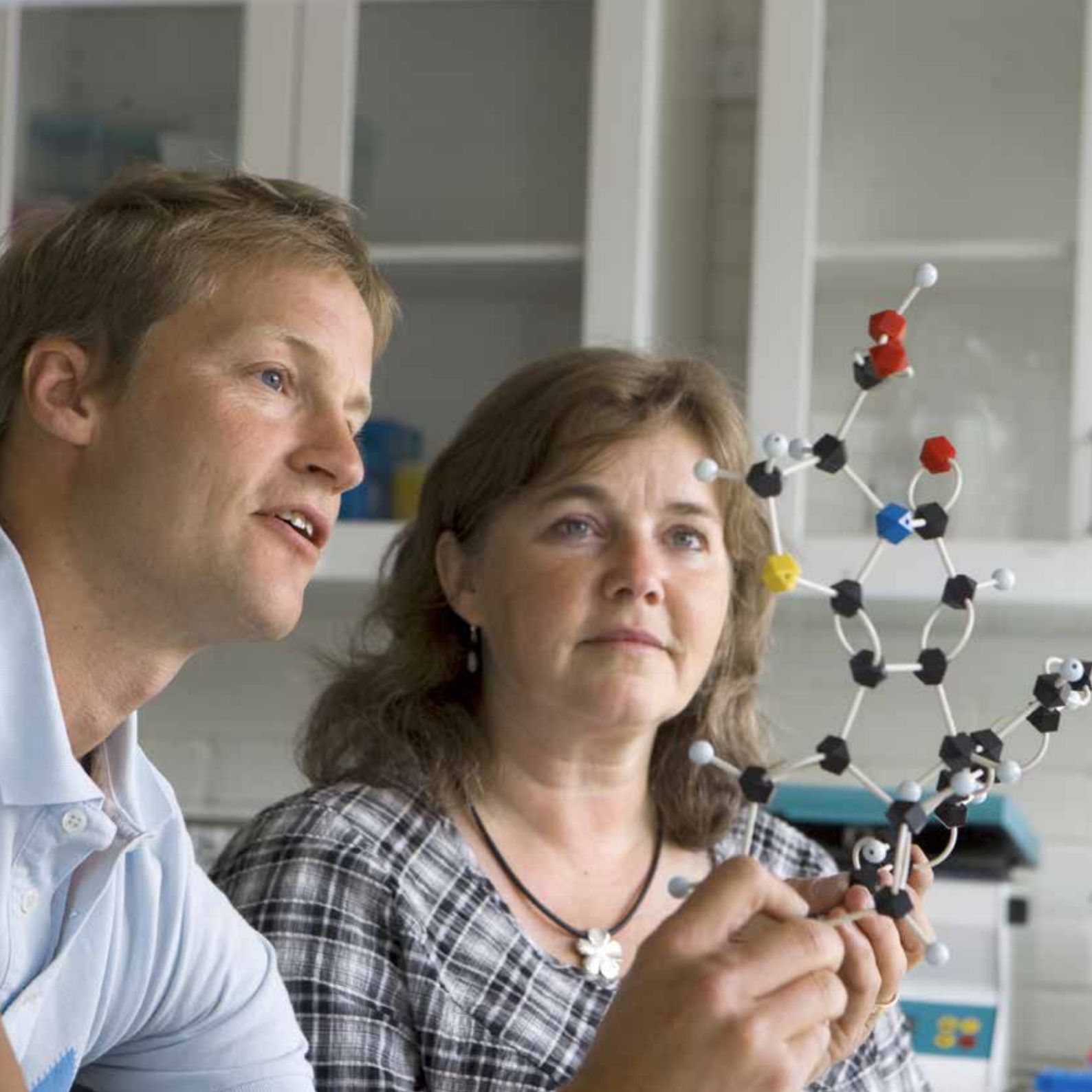
The Laboratory for Molecular Infection Medicine Sweden (MIMS) is the Swedish node of the Nordic EMBL partnership in Molecular Medicine. It is a joint venture between EMBL (European Molecular Biology Laboratory) and the Universities of Helsinki, Oslo and Umeå, dedicated to the investigation of the molecular basis of disease and development of new treatments.

MIMS incorporates 14 group leaders and over 60 PhD students running a wide variety of projects in infection medicine and infection mechanisms. MIMS also supports several core research facilities and platforms including the Laboratories for Chemical Biology Umeå (LCBU). Translational research is strongly promoted through “MIMS Clinical Research Fellows Program” to recruit physicians to the initiative. Projects run within the MIMS include:

- Virus binding mechanism to host cells: implication for tropism and treatment
- dNTPs as cellular regulators
- Molecular mechanisms involved in Gram-positive pathogenesis
- Signal transduction in host-microbial interactions and inflammation
- Listeria: a model system for studying RNA-mediated regulation of virulence of gene expression
- Mechanisms and dynamics of endocytic carrier formation during infection
- Interaction between the immune system and fungal pathogenesis (Candida)
- Tick borne encephalitis virus and meningoencephalitis
- Molecular virulence of Lyme disease and relapsing fever (Borrelia)
- Helicobacter pylori and glycobiology: protein-carbohydrate interactions during health and disease
- Protein secretion systems involved in Yersinia and Pseudomonas virulence
- Virulence mechanisms of the intracellular pathogen
- Expression of virulence by extra-intestinal pathogenic E. coli
- The structure and function of type III secretion system in Yersinia

For details on all projects please visit: www.mims.umu.se

MIMS attracts top international researchers in infectious diseases and puts Umeå at the forefront of infection medicine research.



LABORATORY FOR CHEMICAL BIOLOGY UMEÅ (LCBU)

LCBU offers an open access high throughput screening platform for academic research groups, research institutes, and companies

LCBU at Umeå University is home to a high throughput screening platform, that offers academic research groups and biotech companies the possibility to screen a compound library in order to validate their research or find chemical starting points for early stage drug development. The platform is directed towards the study of infectious diseases, an internationally acknowledged area of research strength of the Umeå life science cluster.

LCBU includes:

UMEÅ ORGANIC CHEMISTRY FACILITY

The Umeå Organic Chemistry Facility offers:

- Custom synthesis
- Compound optimization
- Design and synthesis of second generation compounds

The chemistry platform is also heavily involved in the Molecules for the Future project, a Swedish-Norwegian (Umeå-Tromsø) collaboration project. This project aims to construct a natural product compound library based on the unique extremophilic microbial flora in the Arctic Ocean.

COMPOUND COLLECTIONS

Currently, LCBU has access to the following collections:

Synthetic Library

17,500 of synthetic compounds available in both 96-well and 384-well formats selected to cover a large chemical space.

Fragment Library

A collection of 1000 fragments for fragment based screening by NMR.

Natural Product Library

Under the project name Molecules of the Future, LCBU is producing

a collection of substances derived from secondary metabolites from extremophiles living in the Arctic Ocean.

INSTRUMENTATION

The facility has instruments for liquid handling in 96- and 384-well format and plate readers for measurement of absorbance, fluorescence and luminescence. The instrumentation can perform a wide variety of assays dependent on user requirements.

For more information about LCBU, please visit www.cbcs.se/lcbu/

LCBU offers a powerful platform for the discovery, development and utilization of new compounds and molecules to treat infectious diseases.



FOI - SWEDISH DEFENSE RESEARCH AGENCY IN UMEÅ

Leading contract research and expertise in anti-infective research, development and testing in a high security setting

FOI (The Swedish Defence Research Agency) is one of Europe's leading research institutes for defence and security. The Agency's CBRN Defence and Security Division in Umeå is home to leading experts on chemical and biological issues relevant to defence and civilian crisis management. As a CRO, the division is internationally recognised as being unique in the field of in vivo molecular infection and houses a P2 animal facility. This latter facility, coupled with research expertise and sophisticated instrumentation in analytical chemistry, organic chemistry, toxicology, microbiology, medicine, physics and environmental chemistry, means that the institute offers one of the widest ranging spectrums of expertise available to the pharmaceutical and biotechnology industries. Some of the services that Umeå based FOI facilities offer are as follows:

- **In vivo imaging model for real-time disease monitoring** - allowing visualization of disease progression, migration and clearance
- **Models for lung diseases** - pre-clinical testing of early drug candidates in in vivo models for effects on lung mechanics respiration, inflammatory cells and mediators, histopathological changes, emphysema formation
- **Models for skin penetration studies** - penetration of active substances, effect of different formulations, toxicological evaluation, effects of decontamination and/or cleaning
- **Other in vivo infection models for preclinical evaluation of antimicrobial compounds and vaccines**
- **Synthesis of bioactive compounds for preclinical testing** - synthesis of highly toxic organic compounds as well as air sensitive substances. This facility can also be used for toxicological, analytical and various testing assignments

For more information, please email lage.jonsson@foi.se

The Swedish Defence Research Agency in Umeå offers outstanding facilities and know-how for disease and infection modelling.

UMEÅ COMPANIES ACTIVE IN ANTI-INFECTIVES

Umeå companies are taking breakthrough discoveries for treating infectious diseases to the market

The Umeå region, with its cutting-edge research, has become an exceptionally productive source of companies, many of which are international leaders within their fields. The Biotech Umeå cluster is well recognised as excelling in infectious disease research, and has leveraged this expertise to generate several exciting new companies active in developing anti-infectives with novel modes of action. With professional business development and tech transfer support from organisations such as Uminova Innovation and Umeå Biotech Incubator, discoveries and inventions can progress rapidly from the lab bench to early-stage, investment-ready companies.

Adenovir Pharma AB - developing treatments for viral eye infections

Adenovir Pharma AB is developing new topical treatments of infectious diseases affecting the eye - adenoviral conjunctivitis (epidemic keratoconjunctivitis - EKC) - with potential for treatment of other eye infections caused by different viruses using the same receptor. The company's proprietary multivalent

sialic acid technology causes the viruses to aggregate, thereby becoming inhibited from binding to and infecting human corneal cells. In contrast to most other antivirals, the product acts outside the human cells, so the risk of development of viral resistance is minimal.

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QureTech Bio AB - new antibacterial compounds against chlamydia

QureTech Bio is developing a potential new class of compounds that may have broad-spectrum activity against Chlamydia and other pathogens. Initial observations indicate a set of compounds that

are effective against Chlamydia but non-toxic to human cell lines. Improved antibiotics in this area are urgently required due to resistance development and increasing reports of treatment failure.

CONTACT

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HeliCure AB - potential first-in-class vaccine against Helicobacter pylori

HeliCure AB develops therapeutic vaccines for prevention of gastric cancer caused by H. pylori by active immunization in infected patients with persistent dyspepsia. Oral and nasal vaccines are under development, consisting of a proprietary cocktail of adhesion proteins unique to H. pylori as active immunizing agents, combined with an immune stimulating nasal

adjuvant. Studies using the multi-component vaccine have shown protective effects against H. pylori in animal models. This vaccine has first in class potential in addressing the pressing medical need for prevention of gastric cancer. The company has a strong patent portfolio covering the development, manufacturing and application of this and future products.

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YP III (p18/102 wt)
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Omnio Healer AB - breakthrough treatment for chronic wounds

Omnio Healer is developing novel biological drug candidates based on the discovery that plasminogen, the key protein in anti-coagulation, can treat diseases in which inflammation plays a beneficial role. It has been shown that plasminogen improves healing in in vivo wound models of burns, incisional and excisional wounds, diabetic wounds, ear drum wounds (tympanic membrane perforations, TMP) and periodontitis. Plasminogen can act as an

alternative to antibiotics in treating infection, addressing a further therapeutic area, namely combating antibiotic-resistance. Their lead candidate has generated promising preclinical results. Plasminogen has an enormous range of indications and has “true blockbuster” potential. Unlike present treatment of chronic wounds, which is palliative and based on dressing and pressure technology, plasminogen instigates a restorative healing process of wounds/ulcers.

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Probac AB - novel, stable and documented probiotics

Probac develops novel probiotics targeting three areas: bacterial infections of the ears-nose-throat, the gastrointestinal tract and the immune system. They market several probiotic strains for foods or dietary supplements based on *Lactobacillus rhamnosus* LB21 and *Lactococcus*

lactis L1A, shown to have positive effects on the GI tract. Probac’s newest product, Proactiv, is a novel probiotic which targets post-antibiotic recurrence of tonsillitis and otitis, and which could also be used for preventive care.

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Tanomed AB

Tanomed has developed a safe and effective compound that can help limit the effects of common cold. The product contains an enzyme found in several consumer products, safely used by millions of consumers

every day. It is intended to be delivered as a nasal spray that delivers an effective dose. The product will be ready for EU market launch as an OTC product in 2012/2013.

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Zovec AB – second generation *Borrelia* vaccines and diagnostics

Zovec AB is developing second generation *Borrelia* vaccines, vaccination regimes and diagnostics based on own extensive intellectual

property together with newly established gene maps of the bacteria.

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UBI - THE UMEÅ BIOTECH INCUBATOR

Developing great life science research into global business

UBI is Umeå's biosciences business incubator. It offers an extensive range of services to entrepreneurs and is the main vehicle for commercialisation of innovations from Umeå's life science research community. UBI has been established to meet the specific requirements of the biomedical sectors, where extensive and expensive laboratory equipment is needed to develop products to a marketable stage. Projects usually come to UBI at the proof-of-concept stage, before forming into a company to attract first round financing and investment partners. UBI can host up to 20 projects or companies in their facilities. UBI offers researchers and entrepreneurs a host of facilities and services including:

- Facilities and infrastructure for biotechnology development activities.
- Pre-seed financing to verify the business idea before starting a company.
- Business development knowledge to start-up biotech companies in the incubator.

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Infectious Diseases Projects at UBI

IDENTIFICATION OF RTX NEUTRALIZING NATURAL COMPOUNDS

Natural compounds that inhibit the virulence of the RTX protein leukotoxin, as expressed by *Aggregatibacter actinomycetemcomitans*, have been identified. This gram-negative bacterium is associated with localized aggressive periodontitis, an inflammatory disease affecting the tissues that surround and support the teeth leading to tooth loss. The focus of the project is to develop a prophylactic product to prevent and treat periodontitis, which is a global problem with a growing market. The compounds could be further developed to other indications, such as cholera, urinary tract infections, diarrhea and whooping cough, caused by various gram-negative bacteria with RTX proteins.

NOVEL PEPTIDE-BASED ANTIVIRAL DRUG AGAINST HERPES

Human herpes virus family members infect a majority of the population. They establish themselves latently in infected individuals and cause common clinical problems, sometimes with severe and life-threatening consequences. Development of antivirals targeted to herpes viruses began in the mid 1970s, but recently

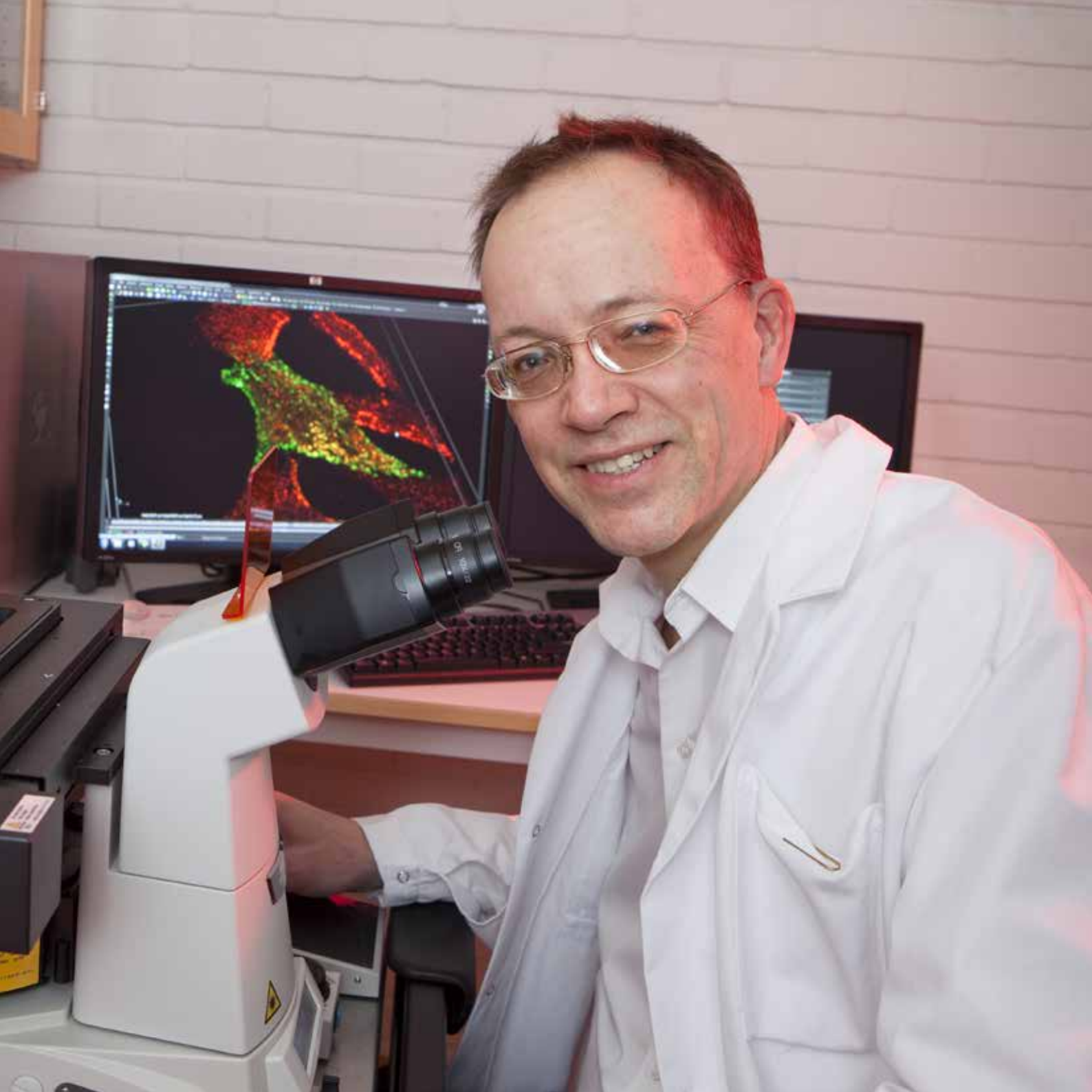
the problem of antiviral resistance has increased, currently 4-7% in immune-compromised individuals on long-term HSV treatment. Novel antivirals, targeting other facets of the infection/replication process are needed, especially for use in long-term treatment of severely immune-compromised patients, where the problem of resistance development is particularly evident. This project aims to develop a novel class of peptide-based antiviral drugs against herpes virus infection. The technology targets the early phase of viral infection and acts to block this.

NEW BACTERIAL AGENTS TARGETING SECRETION SYSTEMS IN G-PATHOGENS

The project develops a screening platform to identify inhibitors to type VI secretion system, present in several Gram-negative bacteria. Hits from the screen have been identified and are now being further developed to proof-of-concept stage, with potential of developing a new class of broad spectrum therapeutic agents.

NOVEL ANTI-ADENOVIRAL AGENTS

The project will develop specific antiviral compounds for treatment of severe adenovirus infections, e.g. in transplant patients, and drug-resistant herpes simplex virus (HSV) infections. There exists a large unmet medical need in these areas.



BIOTECH UMEÅ. A GREAT PLACE FOR LIFE SCIENCE INNOVATION

Biotech Umeå is the region's cluster initiative, created in order to support growth of the biotech and medical technology industry in the Umeå region. In the last five years, the number of life science companies in Umeå has doubled.

A strong and systematic interplay of life science research and commerce is at the heart of this growth process. Fuelled by innovative work and ideas stemming from Umeå's research community, a well-oiled and innovative tech transfer system supports the process of taking an idea from the lab bench to a marketable product.

BIOTECH UMEÅ GOALS ARE THREEFOLD

- to promote the cluster in order to create growth in existing companies
- to attract both foreign and national interest and finance
- the creation of new ventures

The cluster is now home to approximately 70 life science companies, and about 3000 people are employed in life science research and companies. The companies present in the cluster span all stages of size and maturity - from newly founded fledgling companies right through to major international players.

EXCELLENCE IN INFECTIOUS DISEASE RESEARCH

The Umeå cluster excels in infectious diseases and new anti-infectives research. The strong national and international collaborative spirit within the research community enables the pooling and sharing of the intellectual capital of Umeå's leading institutes, initiatives and organisations - the universities, the hospital, UMCR, LCBU, MIMS and FOI - to breed new ideas and potential therapies.

STRONG BUSINESS SUPPORT

With support from Biotech Umeå, UBI and Uminova Innovation to provide financing and business know-how, a number of projects have now entered into the commercial development process as incubator projects and companies, and promise to deliver exciting and successful future solutions to combat the growing global threat of infectious disease.

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Umeå is home to many growing companies, mainly in the fields of biotechnology, medicine, IT, the environment and energy, and modern forestry and engineering industries. The two universities, Umeå University and SLU, with 36 000 students, are purposeful, inquisitive and innovative.

The average age in Umeå is 38 and this is reflected in the townscape with its pubs, restaurants, cafés, discos and shops. Umeå is home to Norrlandsoperan and several international jazz, folk music and rock festivals.

Umeå has been appointed European Capital of Culture 2014. Preparations are in full swing. As the most northerly Capital of Culture ever, Umeå will treat audiences and visitors from all around Europe to a challenging and innovative year.

Investing in your future



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