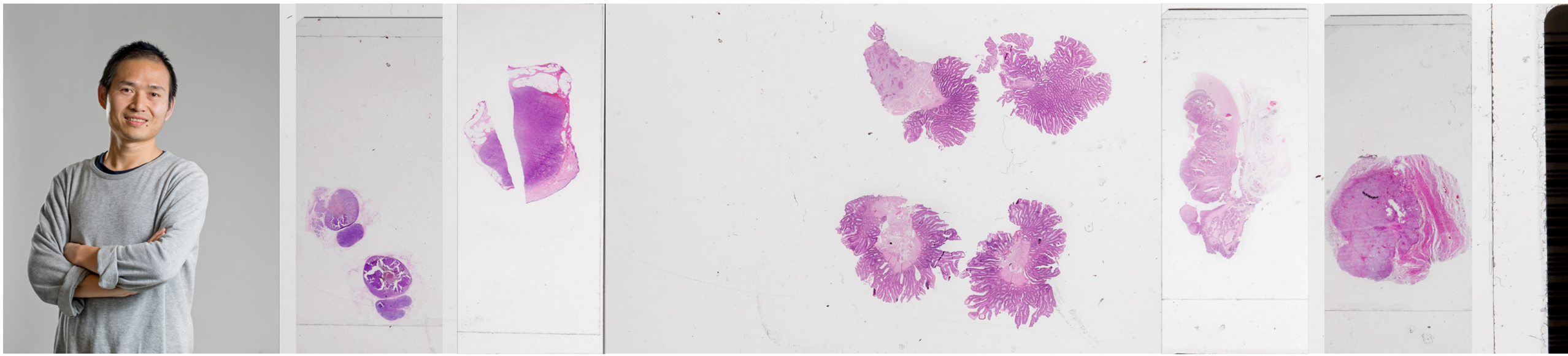


CANCER SOLUTIONS: Researcher Xisong Ke, Department of Clinical Science, Faculty of Medicine and Dentistry, University of Bergen (UiB). ALL PHOTOS: EIVIND SENNESET

Attacking the command centre of cancer

Researchers at the Centre for Cancer Biomarkers in Bergen analyse cancer stem cells to find solutions for the disease. TEXT KIM E. ANDREASSEN

> **“We have recently developed promising drugs that affect cancer stem cells’ signalling system.”**

Cancer cells in a tumour contribute unequally to the disease, with a small population of cells driving the tumour growth and metastasis of cancer stem cells. Now, researchers at the University of Bergen (UiB) have conducted successful trials of a new type of chemotherapy.

“We have recently developed promising drugs that affect cancer stem cells’ signalling system, which is the command centre for the creation of new cancer cells,” says Researcher Xisong Ke at the Department of Clinical Science at the University of Bergen (UiB). “In both laboratory and animal testing the drugs have shown tumours to stop growing, to be reduced or even to disappear.”

Using purified Chinese herbs

Over the past few years, Ke and his colleagues in the research group of Professor Karl-Henning Kalland have tested thousands of small molecules in the cancer’s stem cells and examined how they affect the signalling pathways in the cells. Some of these small molecules are drugs approved by the United States’ Food and Drug Administration (FDA) and others were purified from Chinese herbs, which the researchers have received from partners in Shanghai.

“Traditional Chinese medicine is based on 5,000 years of trial and error. Through this process, the Chinese have found the plants with the best medical effects and have discovered new biologically active substances along the way,” explains Professor Kalland.

The research group from Bergen has signed contracts with Chinese research groups to test such substances in the cell model.

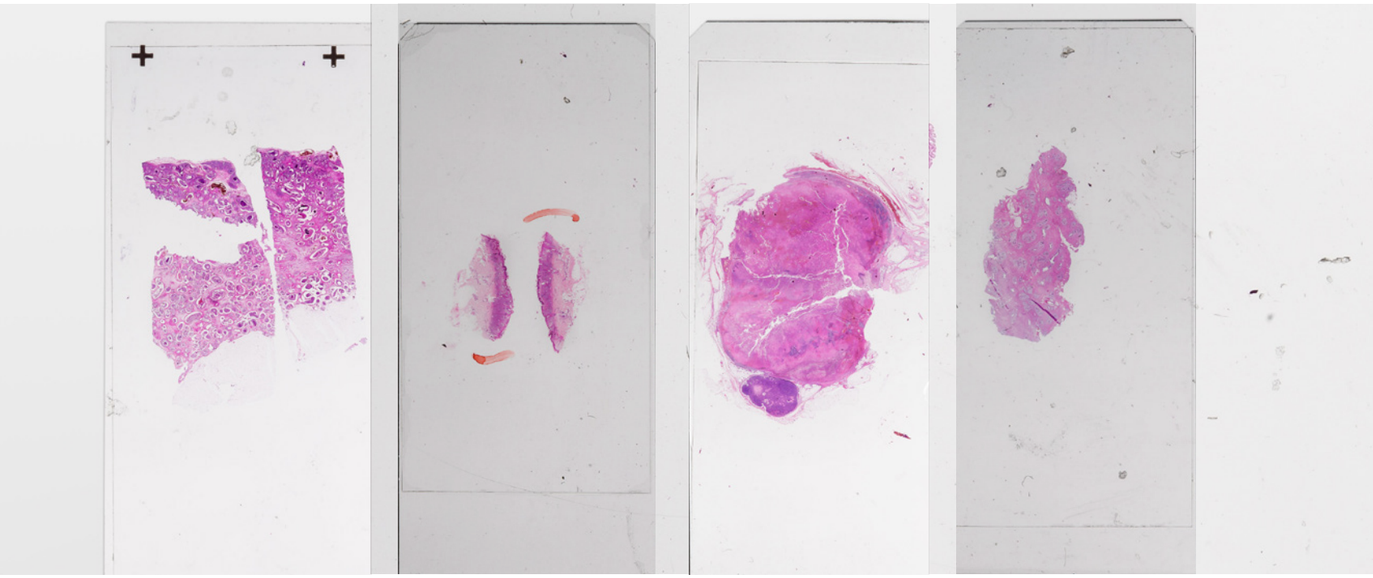
Tracking cancer step-by-step

Ke arrived at UiB in 2006. Since then, he has received funding from the Bergen Medical Research Foundation (BMFS) and Helse Vest (the Western Norway Regional Health Authority). Whilst working as a post-doctoral fellow at UiB, he developed a model showing step-by-step how cells change from normal cells into aggressive prostate cancers. Prostate cancer is the most common form of cancer among Norwegian men. Each year, the disease affects 5,000 men, of whom around 1,000 do not survive the cancer attack.

“The model shows how prostate cells are transformed, step-by-step, into aggressive cancer cells. We have found molecular mechanisms that are essential to how prostate cancer is spreading,” says Kalland.

The UiB researchers have managed to frame the signalling system that the stem cells use to command other cells.

“These mechanisms are more or less the same for several types of cancer, such as prostate cancer, colorectal cancer and breast cancer,” Kalland says.



Professor Karl-Henning Kalland, Department of Clinical Science, Faculty of Medicine and Dentistry, University of Bergen (UiB).

“We have found molecular mechanisms that are essential to how prostate cancer is spreading.”

“We found some signalling pathways that are essential for the transformation of normal cells into cancer cells. We have also observed that only a few cells can turn into cancer cells and form tumours,” adds Ke.

The problem of drug-resistant cells

Compared to previous studies, the researchers can now observe which cancer cells are spreading earlier in the process. By identifying the points of attack as the disease progresses, it is easier to develop medication for each phase of the cancer’s spreading. In future, this will enable the researchers to develop treatment that is tailor-made for each patient.

“We test how substances with mapped chemical structure affect the signalling pathways the cells use to switch genes for reprogramming on and off. The main goal is to find substances that knock out these pathways,” explains Kalland.

Currently there are medicines and therapies that can reduce tumours. However, one of the main challenges is that some tumours may grow and spread repeatedly. Growing cancer cells in the laboratory, the researchers have been able to observe how cancer cells reprogram and shelter in different shapes as they spread.

Another problem is that some cancer cells become drug resistant. Ke has found examples of cancers resilient enough to grow outside of the optimal environment that other cells require, or even without nourishment.

Targeted therapy

Kalland and his team constantly work to create forms of therapy targeting both resistant and aggressive cells, to prevent these from growing back and spreading anew.

“If we succeed, this is reason for optimism for future cancer patients. But, this would only represent one part of multiple contributions to treating resistant cancer types,” says Xisong Ke. “With cancer cells as resistant as the ones we try to fight, it will be necessary to combine new forms of chemotherapy with immunotherapy also in the future.”

”I don’t think there is only one solution in the fight against cancer. Cancer has to be attacked from various angels, with a combination of strategies. If we find a substance that is effective, this doesn’t necessarily mean we have found a solution for all types of cancer. It will most likely be just one of several angels of attack,” says Karl-Henning Kalland. ●

FACTS

Centre for Cancer Biomarkers

- The Centre for Cancer Biomarkers (CCBIO) is a research centre that opened in May 2013.
- Headed by Professor Lars A. Akslen.
- This is one of four Norwegian Centres of Excellence (SFF) at the University of Bergen (UiB).
- This is the second national cancer research SFF, along with the Centre for Cancer Biomedicine at the University of Oslo.
- The centre is working to identify mechanisms that control the interaction between cancer cells and their micro-environment, identify diagnostic characteristics of this interaction, and conduct clinical trials with tailor-made treatment.
- The centre consists of researchers from a number of cancer research groups at UiB: Department of Clinical Medicine (previously at the Gade Institute), Department of Biomedicine, and Department of Clinical Science.
- The centre collaborates closely with colleagues at, among others, Harvard University in Boston and Karolinska Institutet in Stockholm.
- The centre’s work ranges from basic biological research to developing diagnostic tests and targeted treatments.
- For more information, visit the CCBIO home page: uib.no/en/ccbio

SFF at UiB

The Centres of Excellence (SFF) scheme is a national programme administered by the Research Council of Norway. The goal is to establish time-limited research centres characterised by focused and long-term research efforts of a high international calibre, including researcher training. High scientific quality is the main criterion for selection of centres. The Research Council provides the basic source of funding for the scheme, and SFF centres normally receive extensive funding for a 10-year period.

The first centres under the SFF scheme were announced in 2002, when three SFF were established at UiB: Bjerknes Centre for Climate Research, Centre for Medieval Studies, and Centre for Integrated Petroleum Research. Their SFF status expired in 2012. At present, four research environments hold SFF status at UiB, one of which is the Centre for Cancer Biomarkers. The other three are:

Centre for Intervention Science in Maternal and Child Health (CISMAC)

The centre opened in October 2013. CISMAC conducts intervention studies on maternal and child health, whereby the effectiveness of preventive or treatment measures is examined. The centre has 12 specific projects on its agenda, ranging from implementation of new vaccine trials to studying the effect of organisation of health care. CISMAC collaborates with the World Health Organisation and seven partners in India, Nepal, Uganda, Ethiopia, Zambia, and South Africa. National partners are the Norwegian Institute of Public Health and Chr. Michelsen Institute. Professor Halvor Sommerfelt at UiB’s Department of Global Public Health and Primary Care is centre director.

Birkeland Centre for Space Science (BCSS)

How is earth connected to space? This is one of the questions the researchers at BCSS are trying to answer. Professor Nikolai Østgaard from UiB’s Department of Physics and Technology is centre director. BCSS opened in March 2013 and has set out four prime areas of research:

1. Asymmetric Aurora: When and why are the aurora in the two hemispheres asymmetric?
2. Dynamic Ionosphere: How do we get beyond the large-scale static picture of the ionosphere?
3. Particle Precipitation: What are the effects of particle precipitation on the atmospheric system?
4. Gamma-ray flashes: What is the role of energetic particles from thunderstorms in geospace?

Centre for Geobiology (CGB)

The centre was established in June 2007 and officially opened in March 2008. CGB’s research focuses on extreme environments of the deep seafloor, the deep biosphere, and remnants of ancient crust. The centre brings together geologists, geochemists, microbiologists, and molecular biologists to study life in extreme environments, early Earth, and the roots of life. The centre is a hub for international research and researcher training, and undertakes interdisciplinary studies to generate new, fundamental knowledge about the interactions between the geospheres and biospheres. Professor Ingunn Hindenes Thorseth is centre director. Read about our Arctic expedition with CGB on **pages 14–15**