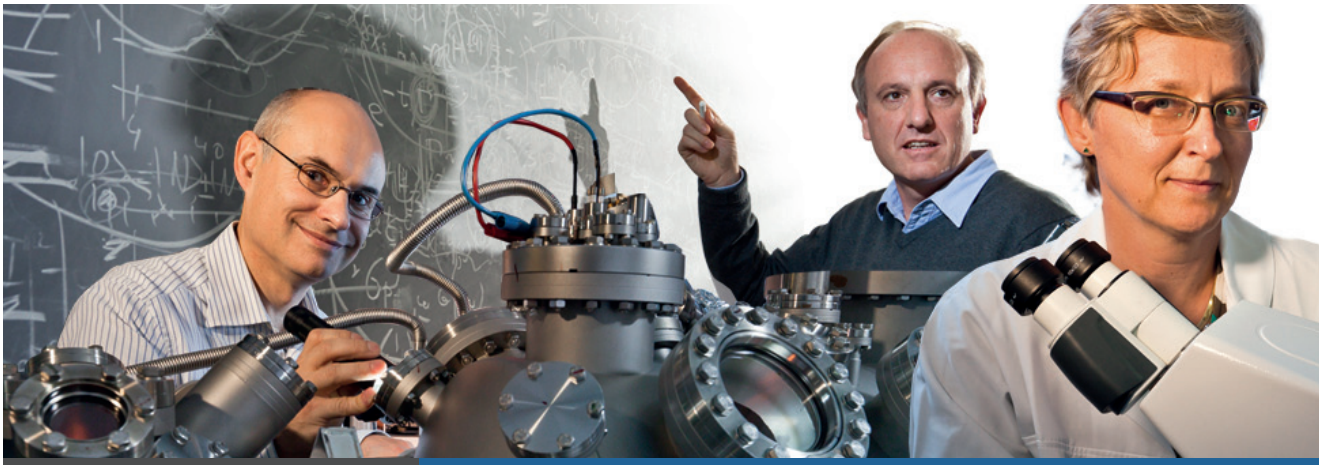


SNI
SWISS NANOSCIENCE INSTITUTE
EINE INITIATIVE DER UNIVERSITÄT BASEL UND DES KANTONS AARGAU

SNI update December 2012

Editorial

Dear colleagues

The year 2012 is almost over, the next holidays and the turn of the year are just a couple of days ahead. Before we spend our well-deserved holidays, we would like to inform you about the latest news.

In November, the University of Basel presented its new strategy. Within this strategy, the nanoscale sciences are tightly anchored as a focus area. "The creation of this broad area of strength is advised in the light of its success and potential," the paper states. We are glad the University of Basel appreciates our achievements of the previous years taking this measure.

2012 was a special year for the Swiss Nanoscience Institute, as we had to deal intensively with the planned finalization of the NCCR Nano and as we have initiated essential activities for the continuation of the SNI. Since the last issue of *SNI update*, we have made considerable progress:

For the planned graduate school, we have selected the first fifteen projects and the announcement of the positions is running. We are excited to receive the applications and will invite the first candidates for interviews in January. In addition, we have finalized the raw version of the final report for the NCCR Nano. Another activity that keeps us busy is the planning for the Swiss NanoConvention here in Basel from 23. – 24. May 2013. We will host SNC 2013 and will organize the final Review Panel Meeting for the NCCR in parallel. I am glad that we could engage a premium selection of international speakers for the event. Learn more about SNC 2013 in this issue of *SNI update* and do not forget to register soon.

All these activities will be resting a bit in the next couple of days until we all start again with new impetus and energy in January. I wish all of you a happy Christmas and holiday season and a good start on an exciting new research year. Additionally, I would like to thank all colleagues and co-workers for their support and collaboration in 2012. I am already looking forward to 2013 and the continuation of our various joint projects.

Best regards

Director Swiss Nanoscience Institute, University of Basel

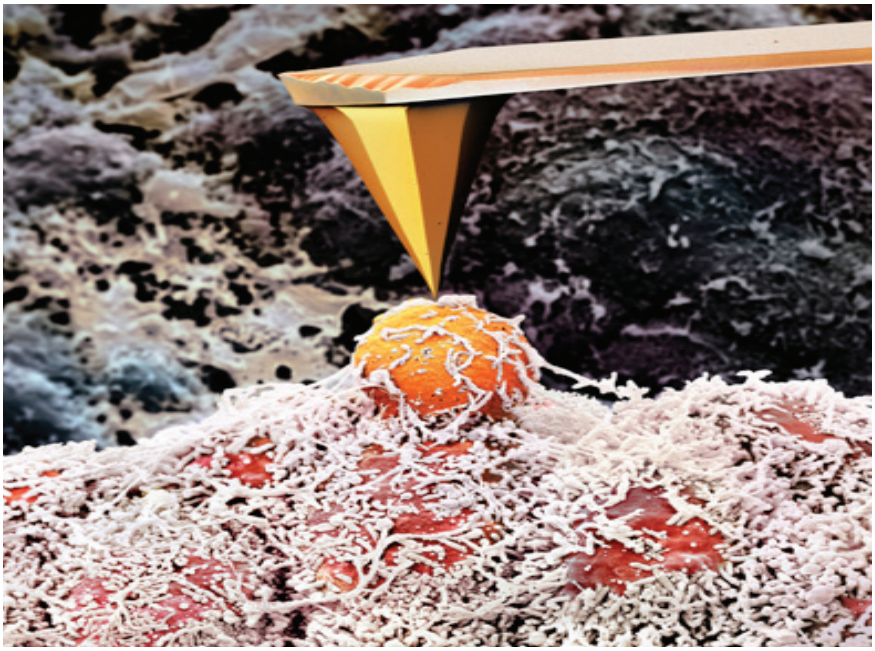
Coverstory

Hard shell and soft core

The anxiety that follows from the first detection of a lump in the breast to finally verifying if it is benign or malignant sounds all too familiar for thousands of women around the world. Yet, despite the agonizing wait that can take many days for a biopsy to be diagnosed, it often remains unclear whether a cancer has spread to form metastases in other organs. With metastases being responsible for most cancer-related deaths, it would be of significant benefit to have a fast and objective diagnostic method that could even provide information about the aggressiveness of the tumor. This forms the motivation behind the team of researchers led by Prof. Dr. Roderick Lim who is the Argovia Professor for Nanobiology at the Swiss Nanoscience Institute and the Biozentrum at the University of Basel to develop an innovative diagnostic tool based on atomic force microscopy (AFM) called ARTIDIS ("Automated and Reliable Tissue Diagnostics") to measure the local nanomechanical properties of tissue biopsies.

Result of a joined effort

ARTIDIS is the brainchild of Dr. med. Marko Loparic, Dr. Marija Plodinec and Lim, which works by quantifying local nanomechanical properties correlated across the biopsy to generate a universal fingerprint that differentiates between malignant tumors and healthy or benign tissue. This has led to a major breakthrough in cancer research as the team reports in the November issue of *Nature Nanotechnology* – against conventional wisdom - that a malignant tumor is not necessarily stiffer than healthy tissue. Surprisingly, a malignant tumor possesses a soft, compliant core although its exterior may be stiff. It is this nanomechanical heterogeneity that allows for the distinction between healthy and benign tissue. As their work now suggests, it is the "softness" of cancer cells that largely populate the central core, which plays an essential role in cancer metastases from the primary tumor to other sites in the body.



Using ARTIDIS to feel the tissue structure of a tumor biopsy by a nanometer-sized atomic force microscope tip (Project: Roderick Lim, Image: Eva Bieler/ ZMB, Artwork: Martin Oeggerli/ Micronaut 2012).

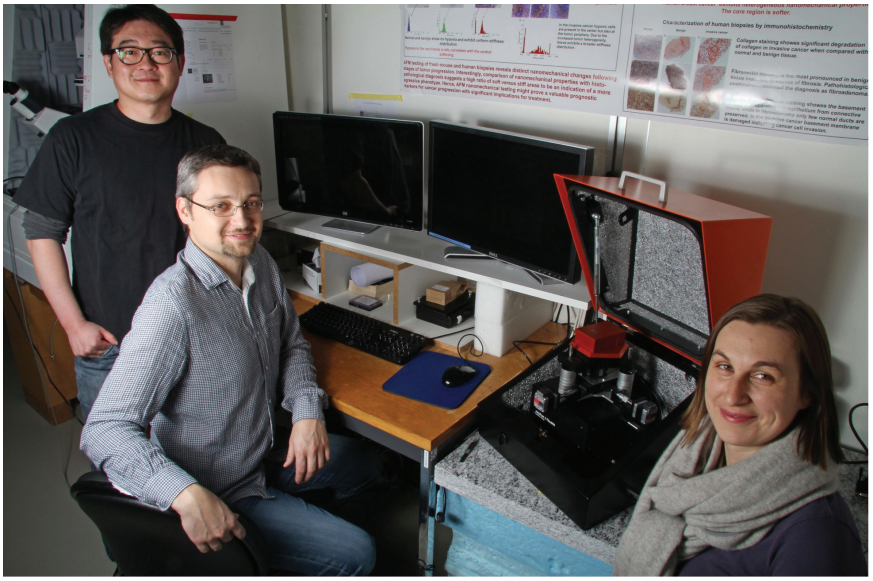
Research for many years

As a key "battle zone" in the fight against cancer, conflicting views persist because efforts to understand cancer biomechanics are largely polarized between tumor level and single cell experimentation. This led Plodinec, who is the first author on the paper, to want to scrutinize the similarities (or differences) in the mechanical responses of single cancer cells (i.e., on a petri dish) in comparison to their responses within tumor tissue. Nevertheless to do so in a meaningful manner prompted Loparic – a medical doctor specializing in tissue diagnostics - to adapt the AFM in ways that would allow for local nanoscale stiffness measurements to be collected and correlated across entire biopsy samples several millimeters in size. As the technology developed, the science also gained depth and momentum. The key collaborators of the project by now included cell biologist Dr. Cora-Ann Schönenberger from the Biozentrum, cancer biologist Dr. Mohamed Bentires-Alj of the Friedrich Miescher Institute in Basel, and from the University Hospital gynecologist Dr. Rosanna Zanetti-Dallenbach and pathologist Dr. Ellen Obermann.

Prototype as first goal

Riding on the promise of their first results, the Swiss Commission for Technology and Innovation (CTI) in 2010 approved a grant of 700 kCHF to Lim in partnership with the Swiss company Nanosurf AG to develop ARTIDIS into a research prototype. Now complete, the prototype is being tested across different tissue types. This is based on a key invention that allows ARTIDIS to operate over unadulterated tissue samples that can be extremely rough – an area where conventional AFM systems falter. In the process of the examination, the ultra-sharp, several nanometer wide tip of the microscope records tens of thousands of local nanomechanical measurements across the entire sample. The outcome of which is a universal fingerprint that characterizes and comprises of all the various cellular and extracellular components that make up the biopsy as a whole. Plodinec explains how different these look according to the state of the tumor: "In healthy tissue the stiffness of the sample is homogeneous. Benign tissue exhibits a larger variability and malignant tissue shows a unique, very heterogeneous profile. Here soft and stiff parts alternate. In the core of the tumor, soft cells are frequent, whereas stiff structures dominate the edges of the tumor."

Currently, the scientists are mainly interested in how these very soft cells at the centre of the tumor escape and spread, since they possess a similar fingerprint as lung metastasis of transgenic mice. These similarities between primary cancer cells and metastatic cells suggest that their compliance might play an important role in how cancer cells disseminate and invade other parts of the body. "Being a transport process, our working hypothesis is that mechanical compliance provides a means for cancer cells to squeeze through their surroundings into the blood and then invade other organs", explains Lim. The challenge now is to characterize the nanomechanical changes that accompany cancer progression and to correlate these to the complex biochemical and structural changes that occur in cells and the surrounding tissue environment.



"This project is interdisciplinary in the most authentic sense of the word, where our diversity is most definitely our strength. Our work ranges from uncovering new fundamental science to improving medical research and developing technology; it encompasses nanomechanics, cancer biology, cellular transport, nanomedicine and diagnostics, instrument design and engineering, etc. Yet, it is these challenges taken together with the potential societal impact of ARTIDIS that makes this project intellectually meaningful and deeply satisfying across many levels," says Lim (in the back). Foto: Ingrid Singh

Up till now, researchers from the SNI and Biozentrum have analyzed more than 100 biopsies of patients from the University Hospital in Basel. The nanomechanical results showed near 100 % agreement with histological studies. Moreover, an advantage ARTIDIS has over standard procedures is one of time. Whereas a patient has to wait up to one week for the histological result, it takes ARTIDIS approximately three hours to deliver the nanomechanical fingerprint. Running costs for ARTIDIS are also expected to be much lower than for histological analysis. "Importantly, the promise of ARTIDIS entering the clinic increases with the number of tissues (i.e., breast tissue, cartilage, retina) we can successfully assess," comments Loparic who is the project manager on ARTIDIS. Indeed, the first ARTIDIS demo-lab was just established at the University Hospital Eye Clinic to collect data on retinal diseases with the goal of improving patient treatment strategies.

In the future directly during surgery

Since July 2012, the CTI awarded an additional 1, 2 million CHF to Lim to take the project with Nanosurf into its next phase. Over the next two years, ARTIDIS will be further streamlined and optimized so to offer an easy-to-use device aimed for the clinic. If the method gains acceptance, patient-waiting times for diagnosis could be drastically reduced. In parallel, the team plans to dig deeper into understanding the nanomechanics of cancer and what its role might be in influencing the metastatic potential of cancer cells and their aggressiveness. On this note, the researchers all but decline comment except by noting that we should "watch this space".

We introduce...

Prof. Dr. Daniel J. Müller,

Professor of Biophysics at the Department of Biosystems Science and Engineering at the ETH Zurich in Basel

Since April 2010, Daniel Müller has been at the ETH Zurich and has led the Biophysics group at the newly founded department of Biosystems Science and Engineering at the ETH Zurich in Basel. Such a start on a recently founded institute or department is nothing unusual for him, as he has experienced start-up phases a couple of times during his career. He was involved in the founding phases of the Max-Planck-Institute for Molecular Cell Biology and Genetics and the Biotechnological Center in Dresden und founded one of the largest bionanotechnological start-up companies in Germany. Although he has changed his job a few times, he always remained true to his research area.

From physics to biology

Daniel Müller grew up in Brussels and Heidelberg. For his studies in physics, he moved to Berlin, which at that time was still separated and allowed him to experience history firsthand. He chose physics, as he was fascinated by the quantitative aspects and was eager to combine experimental methods with theoretical models. Not until he began with experimental work did he develop his passion for science. During his studies, he also got more and more interested in biology. He became aware of the fascination of complex biological processes and learned that their physical basics were poorly studied. Soon, it became clear for Daniel Müller that his PhD thesis should be on a biological topic. And he already knew what he wanted to study: Purple membranes examined with Atomic Force Microscopy (AFM). These special bacterial membranes have been interesting for scientists for some time because they contain the protein Bacteriorhodopsin. This protein works like a light-driven nanomachine that pumps protons to the extracellular side of the cells and herewith converts energy.

From PhD student to group leader

Müller got a scholarship and looked for the experts for his planned thesis. In Basel, Prof. Andreas Engel of the Biozentrum was eager to support him in respect to the application of high-resolution AFMs for the analysis of bacteriorhodopsin. In Prof. Georg Büldt from Jülich, Müller found an expert for purple membranes. Since his PhD, which was awarded the best thesis in Life Sciences at the University of Basel in 1997, membrane proteins have shaped the scientific work of Daniel Müller. He continued studying membrane proteins for his habilitation, which he finalized in 2000 at the Biozentrum of the University of Basel, and later during his time at the newly founded Max-Planck Institute (MPI) for

Molecular Cell Biology and Genetics in Dresden. After examining isolated proteins for several years, he realized that it is necessary to examine proteins in the living cell to understand their function. At the newly founded MPI, he found the best conditions for this undertaking. "The MPI in Dresden followed an innovative approach," Müller comments. "We were relatively many young group leaders and all received excellent working conditions, so that we were able to effectively start our scientific careers in a short time." Müller is still convinced that this concept should be applied more often. "There are excellent young talents, who can contribute to the scientific and societal innovation. Industrial countries like Switzerland are critically dependent on innovation. Therefore, we should provide the best working conditions to these talents and offer the best opportunities for their personal development."

From professor to entrepreneur

Following this exciting time at the MPI, Daniel Müller accepted a full professorship for Cellular Machines at the Biotechnology Center of the University of Technology in Dresden in 2002. Even then, the foundation of start-up companies by scientists of the university was fully supported in Dresden. As a consequence, Müller soon was able to put his plan to build up a bionanotechnological company into action. He began to look for coworkers and investors. In 2006, he founded the company *nAmbition* with the goal to build a fully automated robot for the measurement of interactions between single molecules. Already 3 years later, he and his team had reached their goal, and *JPK Instruments* from Berlin bought *nAmbition*. "That was an energy-sapping but interesting time," Müller remembers. "I had the double work load of my professorship and the company. However, all important positions at *nAmbition* were held by excellent people who significantly contributed to its success." Nowadays, Müller uses his invention – like colleagues all over the world – for his own research. "JPK has further developed our robot. Whereas our model rather looked like the Starwars robot R2D2, it is nowadays much more fancy and only weighs 3 kg."

From Dresden to Basel

After all this buzz around *nAmbition*, Daniel Müller was longing to return to science. And he was also looking for a new challenge, as he had been in Dresden for eight years. So he successfully applied for the Professorship of Biophysics at the Department of Biosystems Science and Engineering at the ETH Zurich. This is the first department the ETH established in Basel. Currently, the location close to the Badische Bahnhof is not ideal, as the researchers are pretty isolated. With the planned move to the Schallemättli area, closer to the university campus, collaborations with scientists from the University of Basel will get easier. "We all have contacts with our colleagues from the University of Basel and the local life sciences industry, but these collaborations can be expanded from both sides", Müller remarks. "In any case, the NCCR Nano and the SNI have been very positive for us. My colleagues at the SNI have welcomed with open arms. The NCCR Nano and the SNI contribute to the provision of fuel – our common research projects. I hope that in the future, we will be able to get more NCCRs, so that excellent research at the University of Basel and the ETH is further supported."

A vision becomes reality - the robot for single cell experiments.

From research to spare time

It is primarily science that drives Daniel Müller. Talking to him, one realizes how he is burning for his research, although these days, he himself does not work in the laboratory very often. Still, the membrane proteins keep him engaged. They contribute to important processes of the cell like signal transduction. However, our understanding of their functionality is still limited. Their regulation is more complex and they exist in more functional states than previously thought. Daniel Müller´s team studies the interactions between these membrane proteins and the cells. Applying various methods, the scientists measure forces that affect different positions of the proteins.

By doing this, they can draw conclusions about the proteins´ functionality. These results are relevant for the pharmaceutical industry, since membrane proteins are often considered as drug targets. Thanks to modern research, we know nowadays that proteins within the living cell function differently than in their isolated from. Therefore, many of the currently applied *in vitro* assays do not provide reliable information about the function of a substance in the body. "It is likely that we will have to work more often *in situ* or with artificial organs to obtain a better understanding," Müller assumes. At the beginning of his career, he would not have expected to have to work more and more like a cell biologist to reach his goals. But in any case, in Basel he is at the right place to collaborate with experts from the University of Basel and the local industry on crucial facts about membrane proteins.

Additionally, it is important for Daniel Müller that Basel became home. He enjoys the morning walk from his apartment in the old part of Basel to his work and having the university campus so close to downtown. He is often travelling, but when he is around, he appreciates the open-minded and culturally interested people in Basel, the theatre, exhibitions and vernissages or he just likes sitting in one of Basel´s many cafes, reading, meeting friends and for once not talking about membrane proteins.

Register your poster now

The Swiss NanoConvention (SNC) 2013 will take place from 23rd – 24th May 2013 in Basel. All PhD students, PostDocs and Project leaders who register now for a poster do not have to pay the registration fee of 200,00 CHF.

With the SNC2013, the NCCR Nano will be finalized. Therefore, each NCCR project should contribute with at least one poster at the poster session and should present the project at the Review Panel Site Visit. The poster session at the SNC2013 offers a unique chance to discuss different research approaches with internationally renowned experts here in Basel.

Please register your poster with title and abstract by January 15th with Tibor (tibor.gyalog@unibas.ch).

SNC 2013 in Basel

From 23rd – 24th May, the third Swiss NanoConvention will take place in Basel. The meeting will bring together nanoscientists from various research areas and will enhance the knowhow transfer between university and industry. On both days, internationally renowned scientists will present their latest research highlights. Keynote lectures will be held by:

- Benedetto Vigna, Executive Vice President at STMicroelectronics, Geneva, Switzerland
- James Heath, Professor of Chemistry at the California Institute of Technology in Pasadena, USA
- David Awschalom, Professor of Physics at the University of California, Santa Barbara, USA
- Cees Dekker, Professor of Biophysics at the TU Delft, Netherlands
- Hari Manoharan, Professor of Physics at Stanford University, Palo Alto, USA
- Harald Lauke, President of the Competence Center for Biological & Effect Systems Research, BASF, Ludwigshafen, Germany
- David Weitz, Professor of Physics at Harvard University, USA
- Michelle Bradbury, Director at the Memorial Sloan-Kettering Cancer Center, New York, USA
- Helmut Dosch, Director DESY, Hamburg, Germany

The program will be complemented by satellite symposia covering topics like Life Sciences, ICT, Materials and Imaging, and poster sessions that will provide optimal chances for discussions with colleagues. At the 23rd May, the NCCR Nano will have its last Review Panel Meeting with the Swiss National Science Foundation. At 24th May, a SATW conference takes place in parallel to the satellite symposia. In the afternoon, the Eurocafe offers information about the diverse funding opportunities within the EU for everyone interested.

Promotion of research in the canton Aargau

Under the lead of the SNI, an information event on research promotion in the canton Aaargau took place on November 22nd at the University of Applied Science in Windisch. During the event, Regierungsrat Urs Hofman presented the high-tech strategy, which was recently approved by the cantonal parliament. This strategy aims to increase advantages of site to locate small and medium-sized businesses in the canton Aaargau. The SNI and especially the Nano-Argovia program are an important part of the strategy. The program is supplemented by a high-tech center and a technology park located close to the Paul Scherrer Institute (PSI).

Industry representatives proved that collaborations between industry and academia already function well. Murray Height, founder and CTO at HeiQ, demonstrated the development of functional textiles. He showed a hygienically protecting fabric based on nanomaterials and a water repellent material that absorbs oil and therefore might be useful for the cleaning of oil-fouled beaches. Michael Hug from Credentis presented a new healing approach for dental enamel. Within this Argovia project, researchers study the healing mechanism and try to expand the current application. Jan Stifter, CEO of Medivation AG in Windisch, demonstrated a software for the precise three-dimensional modeling of knee prothesis. The software automatically models the implant from CT data. Within a project of the Aargauer Forschungsfond, the scientists aim to use MRI data as well. Martin Fierz from Fierz presented a new device to measure nanoparticles, which currently is being optimized and miniaturized so that it can be applied as a dosimeter for nanoparticles.

Well informed

During the next information day of the University of Basel, the SNI will again introduce the nanocurriculum. The information event will take place on January 10th, starting at 9.30. More information at: www.unibas.ch under Infotag 2013.

PhD students wanted

As already announced in the previous issue of *SNI update*, the SNI is planning to introduce a doctoral school in 2013. The program is intended as a continuation of nanoscale science research in Basel after the finalization of the NCCR Nano and aims to provide a diverse and highly qualified base for the education of young nanoresearchers.

Recently, the projects that will be supported in a first phase have been selected. "I am excited to see that we could choose fifteen excellent topics that reflect the strength of the SNI. From Nanobio to Quantum Science – everything is represented," SNI director Prof. Christian Schönenberger comments.

The registration period for the PhD grants is running up until end of December. Based on the submitted applications, the project leaders will suggest suitable candidates who then will be invited for interviews by the SNI management. Presumably, these will take place in February and March so that the selected PhD students are able to start their projects in March or April. The program will not only be provide scientific education, but other topics like recognition of their own strengths and important aspects of intellectual property rights will also be covered.

Projects and application at gradschool.nanoscience.ch.
For questions contact Michel Calame (michel.calame@unibas.ch).

Recent press releases and uninews

Basel, 29.11.2012. Targeted release of antibiotics by nanoreactors

Chemists at the University of Basel have developed tiny nanospheres that produce and locally release the frequently used antibiotic Cephalexin. If researchers succeed in building these nanoreactors into medicinal implants, bacterial infections could be targeted without distributing the active ingredients in the whole body. These findings were recently published in the science journal *Chemical Communications*.

Basel, 26.10.2012. Chemists from Basel create the first artificial metalloenzyme

By combining chemically and genetically modified building blocks, chemists from the University of Basel have created an artificial enzyme, which catalyzes an important chemical reaction highly selectively and efficiently. The researchers report in the journal *Science* that the enzyme can be used as catalyzer for the synthesis of important structure elements due to these properties.

Basel, 22.10.2012. Feeling the force of cancer

The spread of cancer cells from a primary tumor to other parts of the body remains the leading cause of cancer-related deaths. Researchers from the Biozentrum and the Swiss Nanoscience Institute at the University of Basel reveal in the

journal *Nature Nanotechnology* how the unique nanomechanical properties of breast cancer cells are fundamental in the process of metastasis. Using a technique based on atomic force microscopy, the scientists discovered a specific fingerprint for breast cancer.

Basel, 11.10.2012. New method for the examination of atomic steps

Atoms at the steps and edges of surfaces exhibit an increased reactivity that leads to more efficient chemical reactions. Physicists from the University of Basel, together with colleagues from Finland, have now managed to examine the chemical forces of these step atoms and to move the atoms using an atomic force microscopy probe. Results of these studies have been published recently in *Physical Review Letters*.

Please contribute

Please give feedback and submit ideas, success stories and news that might be of interest for the SNI community to the editorial team:

Dr. Christel Möller (c.moeller@unibas.ch) and
Dr. Tibor Gyalog (tibor.gyalog@unibas.ch).