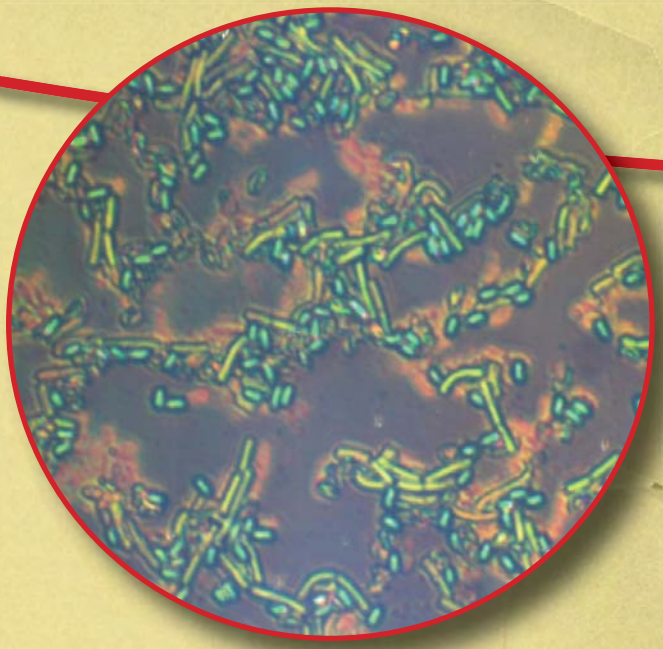
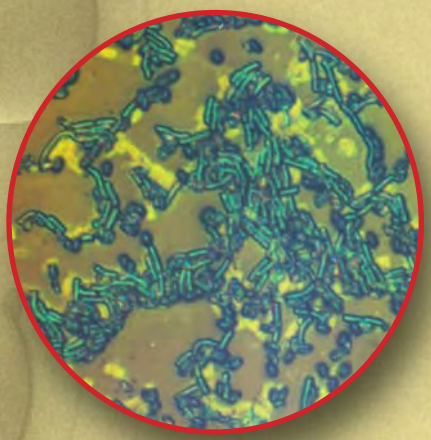
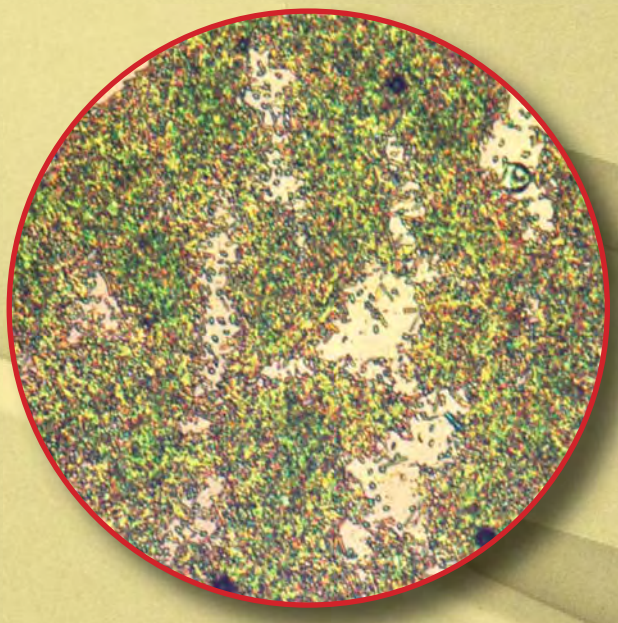
KIST Europe

Korea Institute of Science and Technology



Annual Report 2011





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01/2012

Preface - Greetings of the Institute Director

Dear readers,

I am very pleased to present the annual report of KIST Europe research institute. Again, it covers the most notable events in 2011, along with a number of scientific highlights, an overview of our research outputs and the publications in international scientific journals.

KIST Europe was established as a research institute abroad in 1996. The main objectives of KIST Europe are to contribute to the globalization of Korean R&D activities in the fields of mutual interests and to set up a platform for the promotion of science and technology cooperations between European and Korean partners.

KIST Europe has made a large progress in the research fields including Microfluidics, Clinical Diagnostics, Nanomedicine, Bio-MEMS and Cellular Immunotheraphy. In addition, KIST Europe has performed many activities to build a cooperation network between Korea and EU. For this purpose, we have managed many seminars and joint workshops on R&D issues so far.

I recognize that all our members have done great jobs and made great contributions to build up this KIST Europe, under sometimes difficult circumstances. I would like to extend my appreciation to them for their great effort and devotion. I am extremely proud of all members of KIST Europe for their continued and tireless effort in pursuing our mission.

And I also acknowledge the Korean government and KIST Korea for their continued encouragement and support. I am grateful to the Saarland government and Saarland University for their kind interest and support. I will do my best and devote myself to return these hitherto efforts and supports.

KIST Europe has the opportunity to publish our activities thanks to our researchers' efforts. The major goal of the publication of this annual report is to show our current activities and suggest some research ideas to our potential collaborative partners. We really welcome any collaborative idea from EU research organizations or industrial sectors. We are always open to any suggestion on collaboration between EU and Korea. I am sure that such collaboration will also promote the economical relations between Korean and European partners, as well as the advancements in science and technology research.

I hope you enjoy reading this report.

Prof. Dr. Kwang Ho Kim
Institute Director
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Greetings of the Head of Research

Dear readers,

I am very pleased to present the research activities of KIST Europe during 2011. The year was dominated by planning our longer term research future, by focusing our project portfolio and by implementing steps to achieve these ambitious goals. The vision is to develop technology and biotechnology for the detection and quantification of microorganisms, particularly to help prevent spreading of pandemic diseases in the future. A branch lab at KIST Seoul was opened and started work on biomimetic microfabrication. Finally, we started planning a high-safety biological laboratory unit for the handling of infectious microorgansims in-house.

We are all very proud of the wonderful opportunity we got here at KIST Europe, and try to do our best to promote collaborations between Korea and Europe, to establish independent high-quality research in our laboratories, and to get involved in university education.

I would like to acknowledge the generous funding by the Korean government, our host county Saarland, all my co-workers and everybody else involved in or supporting our research.

Prof. Dr. Andreas Manz
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Contents

KIST Europe - a summary

Aerial photo of the institute taken on May 2011

The Korea Institute of Science and Technology Europe Forschungsgesellschaft (KIST Europe) was established in 1996 in Saarbrücken, Germany, as an overseas branch of the KIST in Seoul, Korea.

A decade ago, at a time when the globalization of science and technology was a new concept, the KIST Europe was the first and only Korean government commissioned R&D institute abroad with R&D capability in its own right.

Since then, the KIST Europe has endeavored to build global S&T networks with prominent EU research institutes in the field of basic and application oriented researches.

Its partners are research institutes and industrial companies in Europe and Korea. Together with its partners, the KIST Europe solves problems and develops technologies which can be utilized on both continents. Its vision is to be the core of scientific and technological cooperation between Korea and EU countries.

The KIST Europe has grown from the small seed sown 13 years ago, and is now preparing for another powerful leap forward with the construction of a 2nd research building.

Over the next 10 years, the KIST Europe plans to further accelerate cooperation between Korea and EU countries.

By the end of the next decade, KIST Europe aims to be one of the most respected and top-quality R&D institutes recognized by EU community.

Facts & News

17.01.2011 - The first teaching lab course (bachelor, mechatronics) "Lab on Chip / Microfluidics" starts at KIST Europe under responsibility of Prof. Dr. Andreas Manz.

15.2.2011 - On Site Lab Meeting

Prof. Dr. Man Young Sung, a Dean of college of engineering at Korea University, visited KIST Europe for a meeting concerning opening of an on-site-lab.

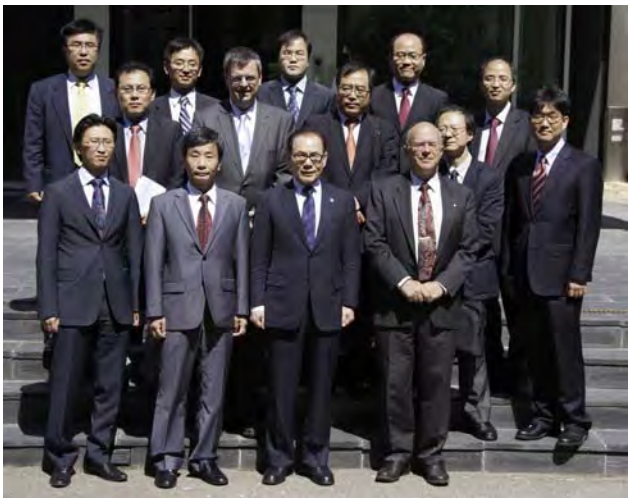
16.02.2011 - The 3rd Symposium ´Metabolites in Human Breath´was organized from KIST Europe and the Ruhrlandklinik, University Hospital at the University Duisburg-Essen. Clinical aspects of human breath analysis were discussed with respect to lung transplantation and early recognition of lung cancer.

08.04.2011 - Professorship Award

Institute director, Dr. Kwang Ho Kim was granted the title of a honorary professor by the Saarland government, a partner of long time cooperation with KIST Europe.

08.04.2011 - Offshore Hub Center Opening

In the presence of Prof. Dr. Joon Yung Park, Governor of Jeollanam-do, and Prof. Dr. Seokgyu Go, President of Mokpo National University, the opening of the offshore hub center in KIST Europe was celebrated.



25.05.2011 - Visit of the First Vice Minister

Dr. Dong-Geun Seol, First Vice Minister (Ministry of Education, Science and Technology), accompanied by delagates came to visit with the concern of development strategies of KIST Europe.

09.06.2011 - Memorandum of Understanding

A Memorandum of Understanding was signed by Karlsruhe Institute of Technology (KIT), KIST Europe and KIST Seoul.

All institutes agreed to pursue a long-term cooperation in microfluidics fields.

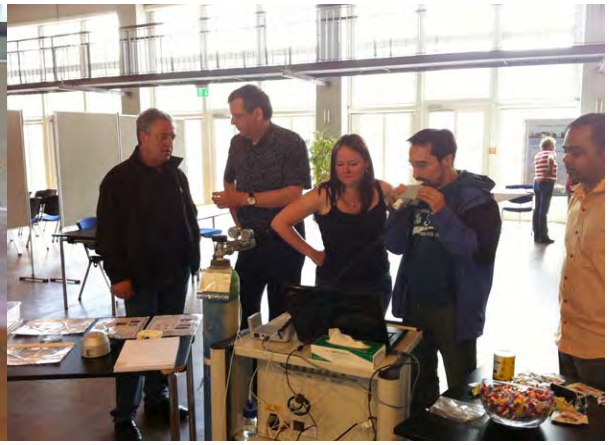
09.06.2011 - Branch Lab Opening Ceremony

A branch lab was opened by Andreas Manz at the KIST Seoul site. The laboratory consists of several visiting fellows from Europe, and PhD students for research in biomimetic microfabriation.

Microfabrication based on self- assembly and soft matter, or based on cell cultures for the excretion of solidifyable materials form the main focus of the activities. Currently, Dr. Stefan Giselbrecht (KIT Karlsruhe) and Dr. Maike Windbergs (HIPS Saarbrücken) are active as visiting fellows.

18.06.2011 - Open day at the Saarland University

For the first time KIST Europe take part on the open day of the Saarland University. Prof. Dr. Volker Linneweber visited the booth of KIST Europe.



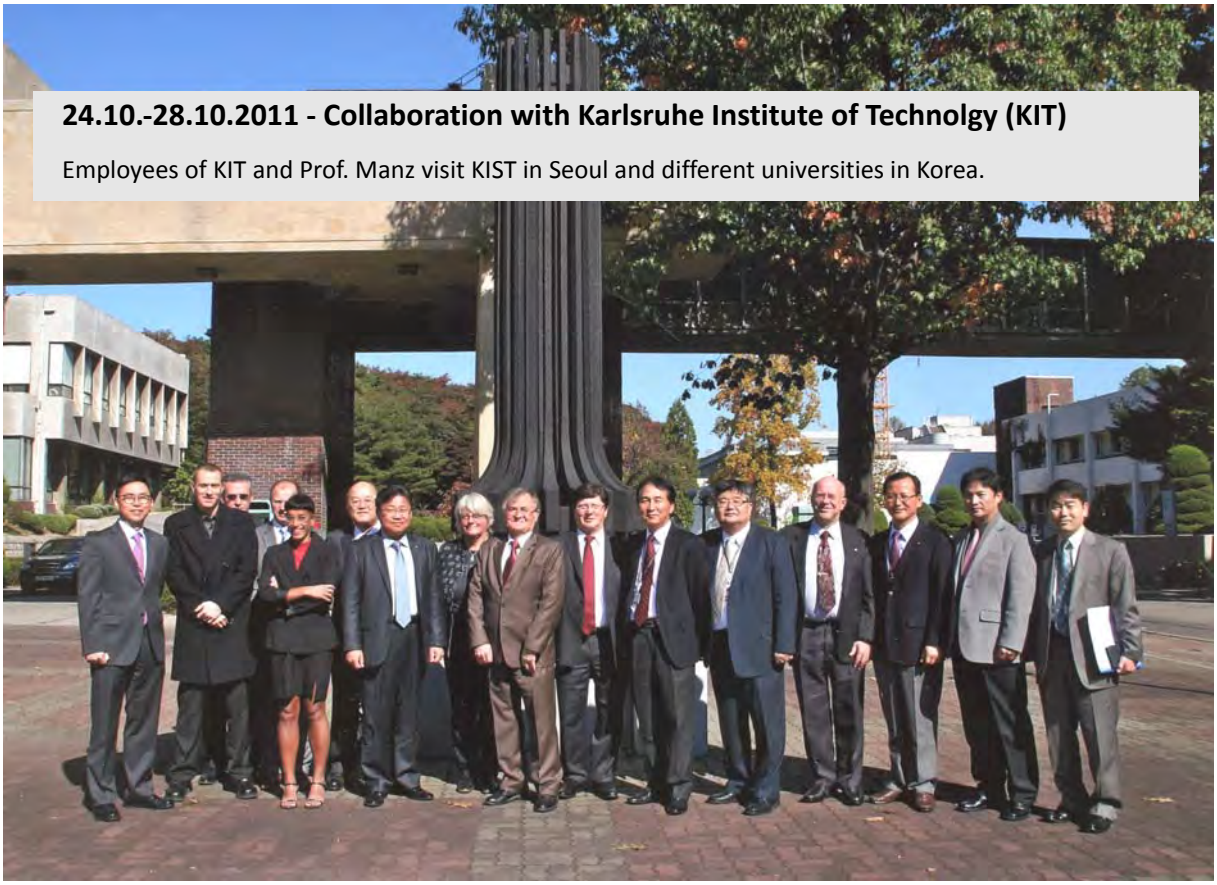
13.07.2011 - Delegation from Korean Ministry of Agriculture

20.07.2011 - Visitors from NRF National Research Foundation of Korea

17.10.-18.10.2011 - Bubble Tech to Bio App "LAB-ON-A-CHIP"

KIST Europe organized an international workshop "Bubble Tech to Bio App", the 2nd Korea - EU Workshop on Microfluidic Technology for Chemical, Biological and Medical Applications. It was held on October 17-18, 2011 at the KIST Europe Saarbrücken facilities, and attracted 28 speakers and 106 attendees from 14 countries.

26.10.2011 - The 4th Symposium ‚Metabolites in Human Breath' was organized at KIST Europe, Saarbrücken. More than 25 participants from university hospitals, medical doctors and scientists using ion mobility spectrometry to identify and quantify human metabolites in breath discussed latest results and ideas for further progress.



24.10.-28.10.2011 - Collaboration with Karlsruhe Institute of Technolgy (KIT)

Employees of KIT and Prof. Manz visit KIST in Seoul and different universities in Korea.

28.11.-01.12.2011 - PD Dr. Jörg Ingo Baumbach joined the state secretary Peter Hauptman from Saarland government during his stay in Korea. Peter Hauptmann visited Wonju Medical Industry Techno Valey and KIST Seoul. The delegation was welcomed at MEST First Vice Minister Dong-Geun Seol in Seoul.

Self-assembly of wild type phages with APTES-phage as a scaffold

Bacteriophage, Phage networks, APTES (3-Aminopropyltriethoxysilane)

Chemical modification of recombinant phages is able to assemble with wild-type phage that can be used as highly cross linked biomaterials. In this study, we show that genetically modified phage could be conjugate with APTES chemical on serine of p8 protein to form a positively charged phage, which could trigger the self-assembly process with negatively charged wt-phages. These properties of electrostatic bond have potential nanostructure or biopolymer. Furthermore, it provides the tuning of their functions in three dimensional structures.

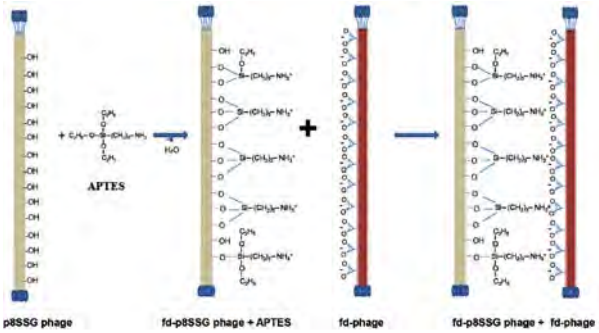


Figure 1: Schematic illustration of constructing APTES coated filamentous phage particles and fabrication of assemblies with wt- and APTES coated phages

Designing a surface via either protein or peptide absorption for bioactive biomaterial is one of the most critical issues for the development of new materials at the nanoscale. Recently, viruses have served as multifunctional nanoscale building blocks for organization of materials that have demonstrated a potential use for high-performance memory and computing devices and energy storage material and tissue engineering. The functional versatility of viruses is organized by their shape, charge, and peptide display, all of which can be changed through chemical or genetic modifications. These allow the virus to form high ordered structure. Therefore, phage can be assembled into a nanostructure or biopolymer itself. As illustrated in Figure 1, APTES substrate used as a silane coupling agent was selected to modify to conjugate with N-terminal of a hydroxyl group of serine. It is well known that positively charged amine group of APTES can laterally assemble protein by cross linking neighboring negative charged regions of protein. It can form a monomeric saline structure by the formation of Si-O bond. Subsequently, phage has positively charged amine group (NH3+) of APTES on the exterior p8 coat protein (APTES-phage). These positively charged fd phages were cross linked with three negatively charged N-terminus of amino acids (Glu, Asp, Asp) of p8 coat protein on a wild-type fd phage (wt-phage) in order to create the phage networks. To investigate the morphology of self-phage assemblies, we analyzed the mixture of APTES-phages and wt-phages by a fluorescence microscope shown in figure 2. Wt-phages and APTES-phage mixtures were incubated at three hours at 25 °C Fluorescence images show a scattered individual wt-phage in figure 2a and 2b whereas, Figure 2c and 2d show that APTES-phage with wild-type phages (1:1) initiates fibrillation and crosslink to form phage networks, indicating that the cationic ammonium from APTES -phage is acting like counter ion interacting with three anionic carboxylate from amino acids (E, D and D) of wt-phage particles. In summary, our results demonstrated that incorporating chemically engineered phage with wt- phage can result in the formation of fine tuned filamentous network assemblies which can further be applied in biotechnology such as in stem cell alignment and differentiation studies.

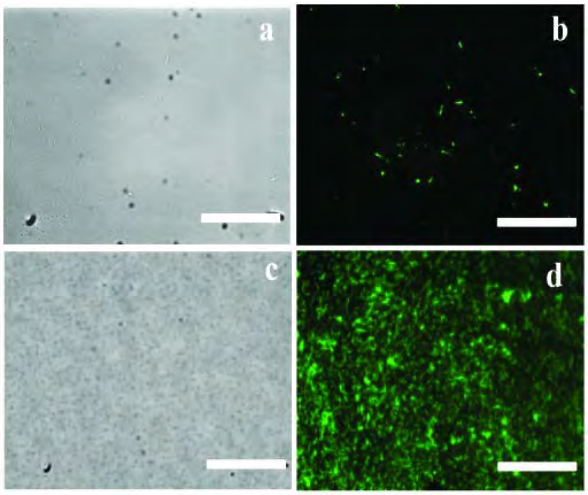


Figure 2: Bright field and fluorescence microscopic images of wild-type phages (a,b) and mixtures of APTES treated p8-SSG with wild-type-phages after 16 hours incubation (c,d). All fluorescence images were taken after incubating the antibody treated phages with cy3 conjugated streptavidin molecules. Scale bar= 10 µm

Conclusion

In this study, we present phage cross linking technique that can potentially be used as a scaffold to mimic certain features of natural ECM and increasing initial cell attachment on a phage assembly prior to implantation. Furthermore, display of bioactive molecules of phage could lead to a better formation of the tissue, including tissue growth, diseases and repair.

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Divalent counterion mediated phage bundle formation

bacteriophage, fd-SN, bundle, counterion condensation, AFM, nanobiotechnology

fd-SN phage was engineered by replacing flexible 5 amino acid (aa) N-terminus region (AEGDD) of the major coat protein p8 with the sequence SSGDD. Effect of surface charge densities on phage bundle formation in the presence of Ca^{2+} and Co^{2+} counterions was studied at various salt concentrations and pH values. fd-SN phages with more negative surface charges formed thicker and less dispersed structures than fd-p8SSGDD type phages. Phage constructs failed to form bundles at pH 3 but bundle formation was induced as the pH was elevated to pH 7.

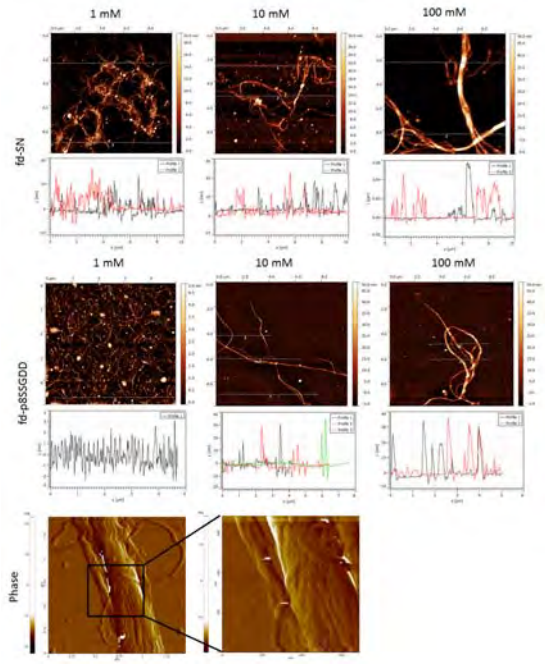

Figure 1: (a-f) AFM topographic images and height profiles of fd-SN and fd-p8SSGDD phages (1012 cfu/ml) treated with various concentrations of CoCl2 solutions (1 mM, 10 mM and 100 mM). (g) AFM phase images of one fd-SN phage bundle induced with 100 mM $CoCl_2$ solution. Measurements were performed in air at ambient conditions.

fd-SN phages formed highly branched structures after 1mM $CoCl_2$ treatment with an average thickness of ~ 10 nm (Fig 1a). As the $CoCl_2$ concentration was increased, structures got thicker and less branched. The average thicknesses of phage bundles with 10 mM and 100 mM $CoCl_2$ were around 15 nm and 32 nm respectively (Fig 1b&c). The thickest detected points on phage structures were ~ 17 nm, 23 nm and 58 nm for 1 mM, 10 mM and 100 mM CoCl2 correspondingly (Fig 1). AFM phase images for one of the fd-SN bundles formed with 100 mM $CoCl_2$ are seen in Fig 1g. The widest body part and one of the side chains of the phage bundle are composed of aligned and intertwined phage filaments induced by Co^{2+} counterions. fd-p8SSGDD phages failed to form assemblies with 1 mM $CoCl_2$ in contrast to fd-SN phages (Fig 1d). Due to the reduced surface charge density of fd-p8SSGDD phages, a decrease in counterion concentration on phage capsids is inevitable. Most probably less negatively charged fd-p8SSGDD phage particles interacted with fewer Co^{2+} ions resulting in a decreased interaction level between the oppositely charged phage molecules. Thus, we only observed randomly distributed phage particles with thicknesses less than ~ 4 nm (Fig 1d). As the $CoCl^2$ concentration was increased to 10 mM, phage bundle formation was induced. Resulting phage

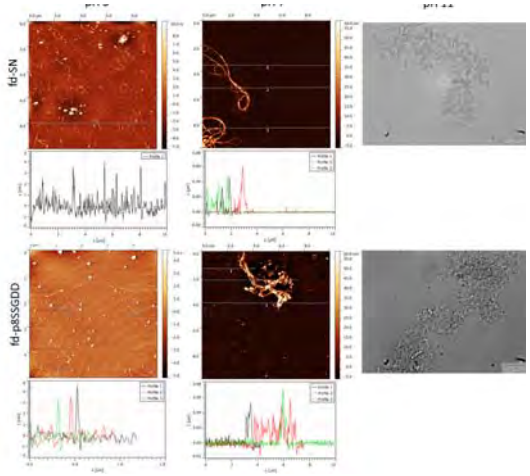

Figure 2: AFM topographic and light microscopy images of fd-SN and fd-p8SSGDD phages (1012 cfu/ml) treated with 100 mM $CoCl_2$ solution at various pH values (pH 3, pH 7 and pH 11). AFM measurements were performed in air at ambient conditions. Scale bar = 20 µm

structures were less branched than $CaCl_2$ case with an average thickness of ~ 22 nm (Fig 1e). Further increase of $CoCl_2$ concentration to 100 mM showed more compact and thicker phage structures with an average thickness of ~ 25 nm (Fig 1f). The maximum thickness detected on the phage bundles was ~ 40 nm. Moreover, 100 mM $CoCl_2$ treatment formed more looped and aggregated fd-SN and fd-p8SSGDD filamentous structures than 100 mM $CaCl_2$ (Data not shown).

Effect of electrostatic interactions on phage bundle formation was investigated by conducting the self-assembly experiments with 100 mM $CoCl_2$ at pH 3, pH 7 and pH 11 (Fig 2). Phages failed to form any network or bundle like structures at pH 3 which is lower than the pI value of p8 coat protein (pI 7) (Fig 2a&d). As the pH was raised to pH 7, bundle formation was induced (Fig 2b&e). Further increase to pH 11 caused reduction of cobalt ions (Fig 2c&f).

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Analysis of expression of specific DNA region in patient with AS

ankylosing spondylitis (AS), Q-PCR (quantitative PCR), CD40L (CD40 ligand)

To confirm the research about Ig unique rearrangement in AS patients, qPCR of expression level of specific DNA regions from cDNA samples of 23 controls, 18 RA, 9 SPA and 17 AS patients was conducted. To get more data, another qPCR was performed with 50 controls and from 50 with RA and 50 with AS. CD40L level was measured. CD40L is known as a Ig class switching regulator. Results demonstrated that unique rearrangements were exclusively occurred in AS and increased level of CD40L might reflect that Ig rearrangement can affect the AS pathogenesis.

the rheumatology clinic at Eulji University Hospital and further quantitative PCR were performed. PB was collected into sterile and cDNA was synthesized by Maxime™ RT PreMix (Oligo(dT)15 primer) Kit (Intron Biotechnology,Korea) following manufacturers' instructions. The amplification condition was 95°C for 30 sec, 50-60°C for 1 min, and 72°C for 1 min for 30-40 cycles. The relative amounts of $VH2^{ab}$ gene expression detected by PR1 (Healthy donor: 1.52, RA patients: 3.10, AS patients: 33.99). Produced gene product by PR1 was approximately 33 fold higher in AS patients

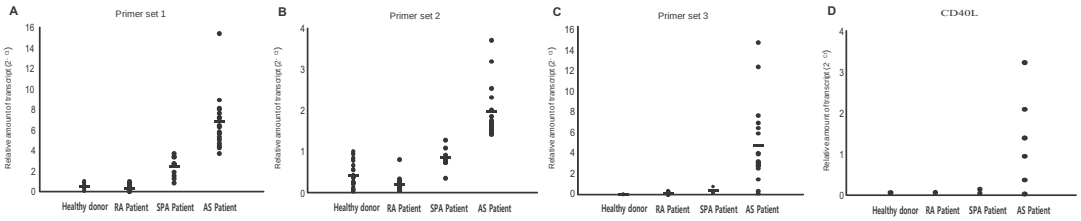

Figure 1: Q-PCR was performed with cDNA from individual PBMC of health donor, RA, SpA and AS patients using PR1 (A), PR2 (B), PR3 (C) and CD40L (D). The relative amount of PCR products were significantly high in AS patients for all primers.

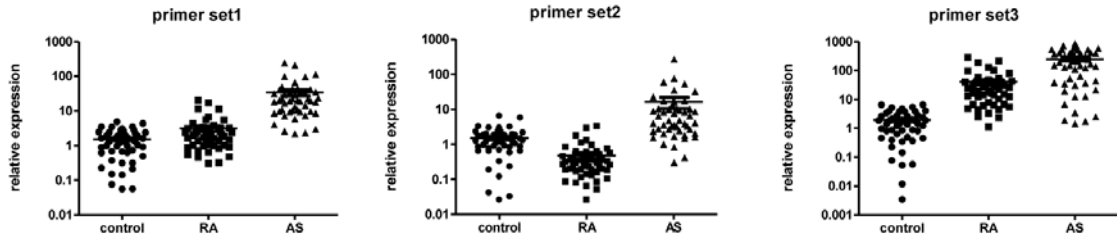

Figure 2: Further Q-PCR was performed with cDNA from 50 healthy donor, 50 RA and 50 AS patients using PR1 (A), PR2 (B) and PR3 (C).The increase of expression levels were exclusively occurred in AS

In our previous study, we observed unique Ig VH gene usages in Korean AS patients. To confirm the research, the expression level of $VH2^{ab}$ genes transcripts from cDNA of 17 AS patients, 20 RA(rheumatoid arthritis) patients, 9 SPA(spondylo-arthropathies, early AS) patients and 23 healthy donors was analyzed by quantitative PCR using three primer sets designed to detect immunoglobulin unique rearrangement in AS patients. CD40L expression level was also analyzed with same samples because our previous data showed the possible relationship between immunoglobulin isotype switching and AS pathogenesis. In comparison of expression level of specific DNA regions which produced by our primer sets were significantly high in AS patient group (Figure1). Elevated CD40L expression was detected in AS patients. The relative amount of CD40L transcripts were 0.30 for healthy donors, 0.62 for RA patients, 1.48 for SpA patients and 2.51 for AS patients. Continuously, PBMC samples from 50 healthy controls and from 50 patients with RA and 50 patients with AS were collected and cDNA was synthesized in and 10 fold higher in RA patients than healthy donor. The relative amounts of PCR product by PR2 were 1.52 for Healthy donor, 0.48 for RA patients, and 16.46 for AS patients. The relative amounts of PCR product by PR3 were 1.93 for Healthy donor, 40.19 for RA patients, and 245.8 for AS patients. Ig $VH2^{ab}$ gene expression from patients with AS significantly increased compared with patients with RA and healthy control with excellent sensitivity and specificity (Figure 2). These results suggest that the amounts of $VH2^{ab}$ gene expression might be employed for AS diagnosis and the potential involvement of CD40L in isotype switching during AS pathogenesis.

Further information: yeonjookim@kist-europe.de, chang@kist-europe.de

Publications

Overexpression and unique rearrangement of VH2 transcripts in immunoglobulin variable heavy chain genes in ankylosing spondylitis patients. Exp Mol Med. 2010 May 31;42(5):319-26.
Kim YJ, Kim NY, Lee MK, Choi HJ, Baek HJ, Nam CH.

Novel immune cell-based drug targeting concepts for cancer therapy

T-cell mediated drug delivery, polymeric drug encapsulations, core-shell nanoparticles

Overall objective of the Cellular Immunotherapy team is to develop novel immune cell-based drug targeting strategies for the treatment of cancer. In 2011, we analyzed whether polyester-encapsulated drugs and core-shell nanoparticles can be utilized for T cell-mediated delivery of anti-cancer therapeutics.

Research focus of our team are innovative cancer treatments which combine the specificity of immune cell-based strategies with the high efficacy of chemotherapies. The new concepts aim at using redirected, ex vivo activated T lymphocytes from cancer patients as targeted delivery system for anti-neoplastic agents. As a component of the adaptive immune system T cells are capable of tracing and infiltrating diseased sites which makes them ideal candidates for the development of targeted cancer therapies. Furthermore, a subclass of T lymphocytes exhibits a natural cytotoxic activity against virally infected and tumor cells that can additionally be exploited to fight malignancies. Challenges include protection of the carrier cells from the toxic effect of the delivered pharmaceutical, preservation of therapeutics against degradation inside the cells as well as target site-specific release and action of the drug.

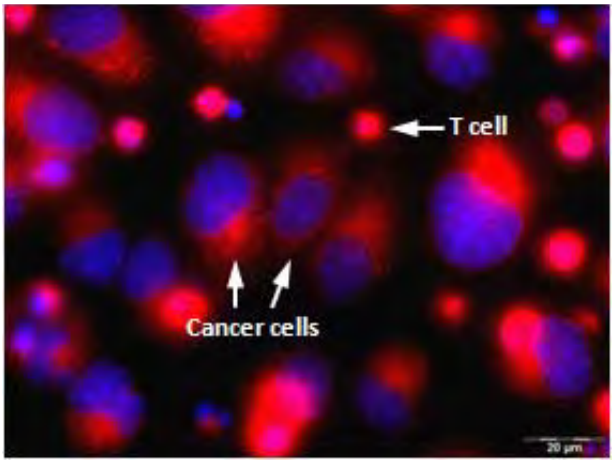

Figure 1: In co-cultures of anti-cancer drug-loaded human T lymphocytes and Skov-3 ovarian carcinoma cells the red fluorescent drug is transferred from the lymphocytes to the cancer cells. Nuclei are stained with Hoechst dye (blue).

To meet these requirements anti-cancer agents were initially enclosed in liposomes and polymeric nanoparticles, before they were introduced in T lymphocytes. Unfortunately, none of the encapsulation materials tested so far has shown a significant protective effect. Therefore, core-shell nanoparticles were developed in order to preserve T cells more efficiently against their toxic payload. In 2011, we performed uptake experiments with metal-coated idarubicin-polyester NPs, prepared by the groups of Prof. Claus-Michael Lehr (HIPS, Saarbruecken, Germany) and Prof. Marc Schneider (Pharmaceutical Nanotechnology, University of Saarland, Germany). First results show that T lymphocytes internalized the metallic NPs, but the viability of the loaded cells decreased. Thus, adding a metal shell to idarubicin-polyester nanoparticles seems to be a promising solution which however needs some improvement with respect to T cell survival.

In addition to the nanoparticle-based strategies we have developed further innovative chemo-immunotherapy concepts. In 2011, a method was established to generate therapeutics expressing T lymphocytes. Furthermore, T cells were loaded with stimuli-sensitive drugs which can lead to long-term survival of the carrier cells and enable specific activation of the drug at the target site. These novel approaches will help to overcome the limitations of the nanoparticle-based strategies and increase the chances of success in the field of immune cell-mediated drug delivery.

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Publications

Stöhr, T.; Blaudszun, A.-R.; Steinfeld, U.; Wenz, G.: Synthesis of glycosylated peptides by NCA polymerization for recognition of human T-cells. Polym. Chem. 2 (2011) 2239-2248.

Positive dielectric barrier discharge treatment of waste wate

carbamazepine, clofibric acid, iopromide, water treatment, landfill leachate

The degradation of carbamazepine, clofibric acid, and iopromide in aqueous and landfill leachate containing solutions by corona discharge over a liquid surface was investigated. Two barrier electrodes, which provided an atmospheric pressure corona, were mounted above a transport roll, which moved a thin water film of test solution from the sample reservoir. Numerous tests were performed on single, mixed, and landfill leachate containing solutions with various combinations of powers, rotational speeds, air gaps, and exhaust restrictions.

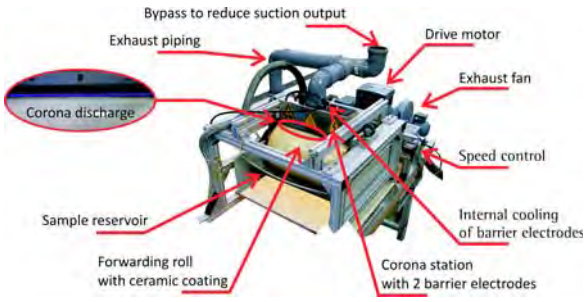

Figure 1: Setup for batch mode experiments in ambient air.

As shown in figure 1, a prototype for batch mode degradation experiments by corona discharge with two barrier electrodes above a rotating drum also functioning as the counter electrode has been developed.

Best results were obtained with the highest rotational speed, a reduced exhaust, and an electrode air gap of 1.5 mm.

Figure 2 shows the comparison of the degradation rates of carbamazepine, clofibric acid, and iopromide (0.1 mM) dissolved in a sample volume of 1 L containing either 40% landfill leachate in in ultra pure water (LL) or only ultra pure water (MIX) using 2 barrier electrodes at 500 W. The treatment time was 90 min, reduced exhaust was used, an air gap between the barrier electrodes and the roll of 1.4 mm, an internal electrode cooling of 1.0 bar, and a rotational speed of 34 rpm (100%). A setup for batch mode in ambient air as shown in Fig. 1 was applied.

In single solution, clofibric acid was removed below the detection limit after a treatment time of 30 min and with a power output of 500 W, carbamazepine to 94%, and iopromide to 98% after 60 min. At the same output power carbamazepine was degraded to 97% in solutions containing landfill leachate after 90 min, clofibric acid to 88%, and iopromide to 19%. Iopromide showed the greatest difference in degradation kinetics dependent on the output power level, while carbamazepine showed the least.

A reduced airflow had a positive influence on the degradation of clofibric acid and iopromide in single solution, presumably because reduction of the airflow leads to a longer loiter time of reactive species.

The influence of the distance between the rotating drum and the barrier electrodes was tested for single, mixed, and landfill leachate containing mixed solutions. The degradation of iopromide and clofibric acid in solutions containing landfill leachate was significantly improved by a reduced air gap. Due to a stronger electric field a reduced gap leads to a higher amount of reactive species, which occur more frequently in solutions with higher compound loads.

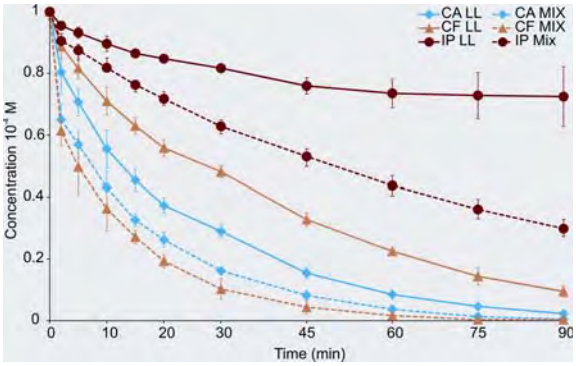

Figure 2: Degradation results.

Due to cost considerations and energy consumption this method would be more suitable for the treatment of concentrated solutions such as hospital or industrial effluents than for more diluted waters. To achieve a degradation of recalcitrant substances in one cycle, a more effective electrode geometry should be found and operating parameters should be optimized. To avoid the mixing of treated with untreated fluids, a scraper for the removal of treated solution could be added to the drum.

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PUBLICATIONS

Krause, H.; Schweiger, B.; Prinz, E.; Kim, J.T.; Steinfeld, U.: "Degradation of persistent pharmaceuticals in aqueous solutions by a positive dielectric barrier discharge treatment", Journal of Electrostatics 69 (2011) 333–338.
Krause; H.; Schuhmacher; J.; Scholl; S.; Schweiger; B.; Steinfeld, U.: "Degradation of the endocrine disrupting chemicals (EDCs) carbamazepine, clofibric acid, and iopromide by corona discharge", Chemospere 75 (2009) 163–168.

Portable Micro Real-time PCR System for Infectious Disease Diagnoses

miniature real-time PCR, micromachining, virtual reaction chamber

Vision 2016 of KIST-Europe is the development of system to diagnose infectious diseases, such as Avian Influenza, Severe Acute Respiratory Syndrome (SARS), Dengue Fever, EHEC and Tuberculoses. One of two identified system was portable miniature polymerase chain reaction system (PCR) capable of detection both, DNA and RNA. Last year we have continued on development of this tool. The system is based on a virtual reaction chamber, where the sample with volume of 1 µl or less is covered with three time larger volume of mineral oil, both placed on a hydrophobic microscope glass cover slip with thickness of 170 µm. There two liquids are together immiscible and due to their surface tensions they form a self aligned system, where the sample (water-based) is symmetrically placed inside the oil droplet. Micromachined silicon chip integrated with 250 nm/5 nm of Au/Cr, respectively, thin film heater and sensor is underneath the glass. It provides sample heating by Joule heat dissipated in the heater and its transfer through the glass as well as sample cooling by dissipating the heat through the silicon to the chip frame. Heating rate is only given by amount of available power, here given by power supply voltage V and heater's resistance.

Figure 1: Micromachined silicon chips each with four integrated heaters and sensors

Increase heating rate is straightforward, either using higher voltage or redesign the resistor to have smaller nominal value of resistance. Compare to that, changing cooling rate is more complicated. It is given by system thermal time constant, which given by system thermal capacitance divided by system is thermal conductance. Increasing cooling rate seems to be simple, "just" increase thermal conductance. The drawback of this approach is shown here that such as system will be increasingly power demanding and thus unsuitable for battery operated applications. The only option for fast system with acceptable power consumption is keeping sample small, i.e. small H. Here we have chosen to work with sample with volume about 0.5 µL, which is a compromise between limit of detection (LOD) and PCR reaction time with moderate power consumption. The first generation of PCR chip made in KIST-Europe had for simplicity of operation all four heater resistors (as well as sensor's) in series resulting total resistance of 600 Ω for heaters and 1.2 kΩ for sensors.

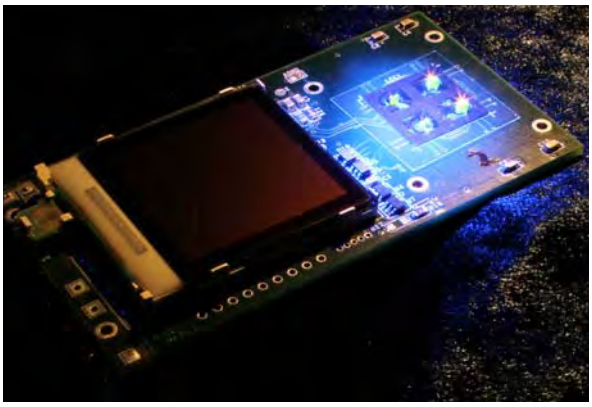

Figure 2: Assembled PCB with LCD display and silicon chips with four virtual reaction chambers

Once the sensor was mounted to printed circuit board (PCB), it was connected to a separated PCB with readout circuit. The sensor PCB was then immersed into a temperature controlled bath filled with Fluorinert FC 70. The system temperature sensitivity was found to be 27 mV/K, which corresponds to temperature coefficient of resistance of 0.3%/K. This value is near to the Au bulk value showing that this sputtered thin film can be used as stable temperature sensor. Nevertheless the resistance value of the heater was far too high for fast PCR processing so we have redesigned the chip and its fabrication is ongoing. Now all resistors are separated from each other giving us an option to connect them (using suitable PCB layout) in series, serial-parallel or parallel as well as to choose individual heater/sensor while avoiding others. We also increased the Au thickness to 400 nm to further lower resistance value of the heater. We have calculated the heater's resistance to be about 100 Ω, making it more suitable for the PCR. The first version of micromachined PCR chips are shown at Fig. 1.

Complete assembled PCB with electronics and VRC is shown in Fig. 2. The microchip controller is currently being programmed. There are new features as subject of patent application submitted by KIST-Europe.

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Ultrafast destruction of biological structures by superheating

microfluidics, superheating, bacterial spores, peptides, proteins

Microfluidical systems are transforming the ways in which traditional bioassays are preformed, and new applications are becoming available. In the absence of nucleation sites, water sample can be superheated, i.e. heated above its boiling temperature at ambient pressure without actually boiling. This condition allows biomolecules to be rapidly destroyed.

In a system designated the virtual reaction chamber, an aqueous sample is covered with oil, both placed on a microscope cover slip with a heater/sensor underneath. As there are no nucleation centers available, the sample can easily be heated up to temperatures of over 200°C (1).

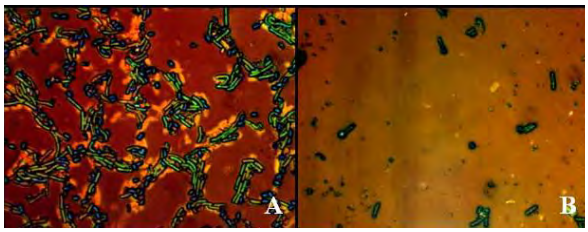

*Figure 1: Results of B. subtilis spore superheating: **A)** and **B)** show microscope images (Zeiss Axiotron) of vegetative cells and spores after contrast staining using malachite-green and safranin O (1500 magnification). The pictures display the same sample before (A) and after (B) superheating at 200 °C for 20 s.*

Here we show that bacterial spores are destroyed within a fraction of a minute by superheating. Thus, the original compounds enclosed by the spore shell are released. The high efficiency of spore disruption was proven by using B. subtilis spores (Fig. 1), a non-pathogenic substitute of B. anthracis. The super- heated treatment of spores eliminates time con- suming spore-germination, growth of vegetative cells for final harvest and DNA extraction.

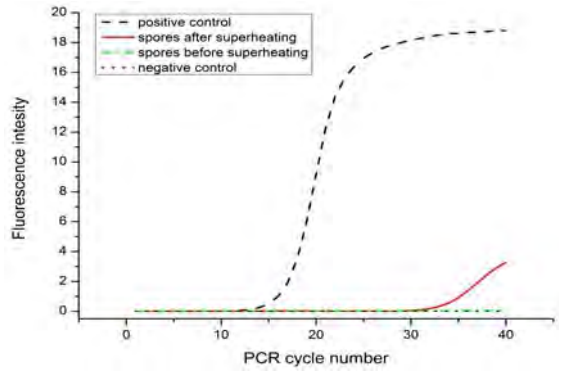

Figure 2: The graph shows the real-time PCR results of sample with purified, superheated spores. Signals from superheated spores (in red) proof access to genomic DNA.

Ongoing experiments will allow us to optimize conditions between spore disruption yield and undestroyed DNA molecules. The number of released DNA molecules can be calculated from real-time PCR (Fig. 2) results by comparison of critical thresholds of PCR curves with known concentrations of DNA molecules from *B. subtilis*.

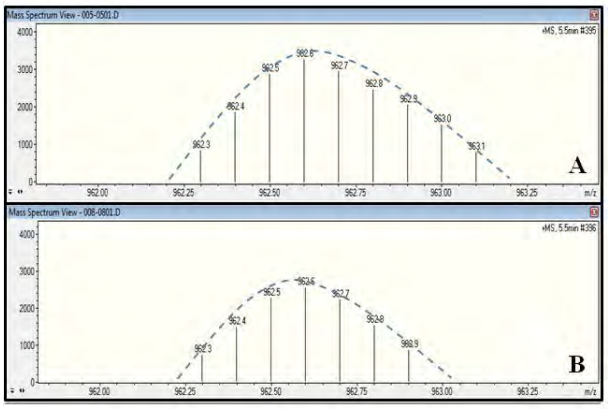

Figure 3: MS2 extracted ion chromatogram of a variable chain of an ovalbumin peptide (av. mass: 962.6m/z) before (A) and after (B) superheating for 10 s at 120 °C. Parent ion peak area has been reduced by 37.3 % by superheating.

Besides the destruction of spores, superheating is used to induce protein- and peptide-fragmentation, similar to the overloading of biomolecules in MS/MS machines for molecular fingerprinting. Such heat-based destruction of molecule can replace the use of proteases, which are expensive and time-consuming. In addition the protein and peptide fragmentations follow known rules, but complete hydrolysis is unspecific. Here, we then concentrate on the optimization for achieving partial hydrolysis, which gives information on protein/peptide structures. HPLC-ESI mass spectrometry was used to demonstrate that the peptide-bound dissociation by superheating happens within a few seconds (Fig. 3).

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Extra-High Voltage Capillary Electrophoresis

Van der Graaff generator, microfluidic sample injection, LIF detection

We are developing a unique capillary electrophoresis (CE) analytical platform, in collaboration with ETH Zurich, that will offer up to 200 times the efficiency and 14 times the resolving power afforded by conventional CE. The setup will feature a microfluidic-based sample injection system and laser-induced fluorescence (LIF) detection, while the critical component is a Van der Graaff generator capable of providing extra-high voltage of up to 6 million Volts, yielding vast increases in the analytical power of the technique.

Capillary electrophoresis (CE) is an analytical technique used to separate and detect analytes via the application of an electric field along a capillary. While an established technique, CE still holds a great deal of untapped potential. The separation efficiency and resolution of CE are dependent on applied voltage, for which commercial products typically have an upper limit of 30 kV, beyond which heating and electrical breakdown start to become problematic. However, this is by no means the limit of CE itself, and here at KIST Europe we intend to push the boundaries of CE further than ever before.

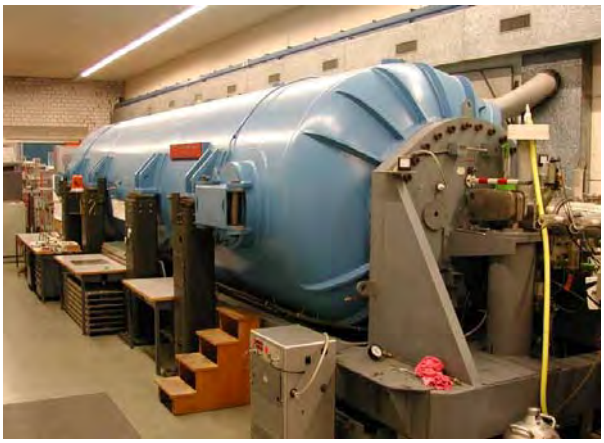

Figure 1: Van der Graaff generator ETH Zurich, capable of producing up to 6 million Volts (photograph from www.ams.ethz.ch).

We are developing a unique analytical platform that employs a Van der Graaff generator capable of producing 6 MV, located at ETH Zurich (Switzerland) (Fig. 1). By adapting this equipment we will produce an "extra-high voltage capillary electrophoresis (EHVCE)" system, capable of increasing separation efficiency and resolution by 200 times and 14 times, respectively, compared to commercial systems. This will yield a powerful analytical tool with unparalled performance in terms of both CE and analytical chemistry in general. Such a platform would be particularly important for the analysis of samples that are conventionally difficult to separate, e.g. glycoproteins, whilst further development could lead to the establishment of an "EHVCE centre". This would be analogous to centres for high field NMR spectroscopy and high resolution TEM, to which researchers take their samples when they find conventional instrumentation lakking.

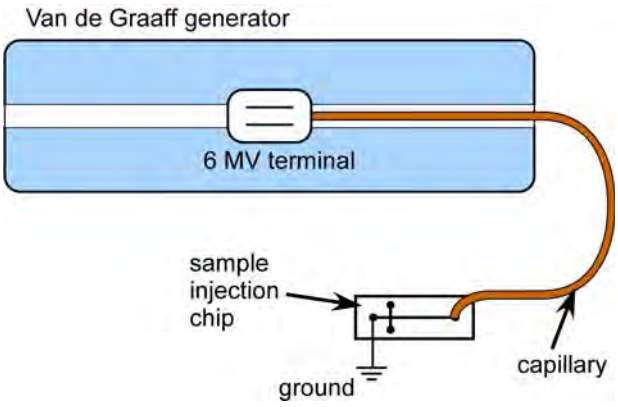

Figure 2: Concept of the extra-high voltage capillary electrophoresis system. A sample is injected via a microfluidic device into the capillary where a separation takes place under a 6 million Volt electric field.

The crux of this work concerns the integration of a separation capillary to the 6 MV terminal inside the Van der Graaff generator (Fig. 2), and the subsequent introduction and separation of a sample. Sample injection will be performed via a novel microfluidic device that, unlike usual examples, will allow injections without disconnection of the voltage supply, an essential feature due to the nature of the generator's operation. First generation devices have been designed and are being fabricated, and they will be tested shortly. A laser-induced fluorescence (LIF) detection system has been designed and manufactured for sensitive detection of labelled species in the capillary. This particular detection setup allows the location of optical components inside the generator, while the electrical remains safely outside. This is currently under assembly, whereupon it will be tested. Integration of the capillary to the 6 MV terminal is being undertaken by our collaborators at ETH Zurich, and the capillary itself has a narrow diameter to suppress Joule heating. Once these individual aspects of the platform have been completed and verified, we will bring them together in Zurich for testing of the final EHVCE system.

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Signals of infections in human breath

Ion mobility spectrometry, exhaled air, volatile metabolites

A rapid detection of infectious agents in human lungs is often crucial, because the choice of the appropriate therapeutic regime depends at first on the identification of the infecting species. Standard methods for detection and identification are either time consuming, of low sensitivity or expensive. We investigated, whether the detection and characterisation of VOCs by Multi-capillary column coupled to IMS in exhaled breath of patients whose airways are either infected or colonized by *Pseudomonas aeruginosa* compared to healthy non-smoker controls is capable of identifying those infectious agents.

It is known that bacteria produce volatile organic compounds (VOCs) that can be detected in exhaled breath by ion mobility spectrometry (IMS). An IMS coupled to a MCC allows the identification and quantification of volatile metabolites present in human breath, down to the ng/L- and pg/L-range of analytes within less than 500 s and without any pre-concentration. For investigations of human breath at a comparatively high level of humidity, a Multi-Capillary Column (MCC) for partly pre-separating of the analytes is used. The IMS investigations are based on different drift times of swarms of ions from metabolites formed directly in air at ambient pressure. About 10 mL of breath is necessary to carry out a full analysis. The MCC/IMS used was a BioScout (B&S Analytik, Dortmund, Germany), consisting of the MCC/IMS and a SpiroScout (Ganshorn Medizin Electronic, Niederlauer, Germany) as sample inlet unit.

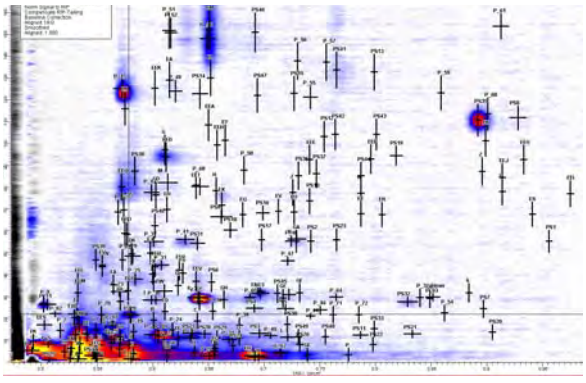

Figure 1: Position of the peaks within the IMS-Chromatogram

All patients were recruited from the Department of Pulmonology, Ruhrlandklinik Essen, Germany. The diagnosis of Pseudomonas was established according to the actual guidelines. Subjects with any other respiratory disease or any concomitant malignant, heart, renal, liver or collagen disease were excluded. All patients were clinically stable. Healthy non-smokers served as control group. The study was approved by the ethic committee of the University of Essen and all subjects provided an informed consent.

To realize a non invasive identification of pathogens the exhaled breath of 53 persons (24 patients suffering chronic or infectious on Pseudomonas and 29 healthy controls) was investigated using the BioScout. In total 224 signals were found as shown in Figure 1.

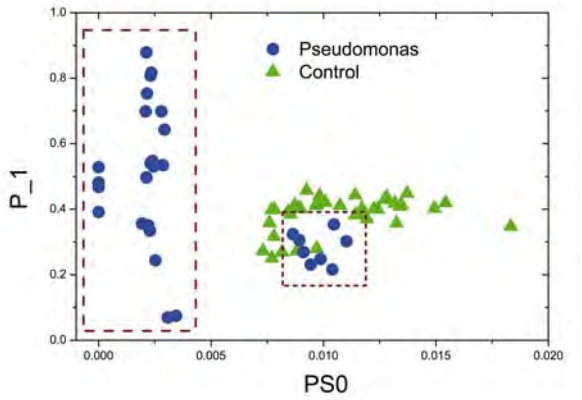

Figure 2: Correlation plot of two different IMS-signals PS0 and P_1 to separate the healthy controls and patients suffering Pseudomonas indicating 2 potential sub-groups of Pseudomonas patients (probably infectious and chronic)

As shown in Figure 2 it seems that within the Pseudomonas group, 2 sub-groups could exist as indicated by rectangles. Starting from more general questions like occurrence of bacteria in the lung and detection of specific metabolites a deeper look into details, e.g. to differentiate patients which are colonized or infected with bacteria such as *Pseudomonas aeruginosa* needs a higher number of investigation and automatic discrimination in the future. In addition, metabolites of bacteria in cultures should be investigated and compared to findings in humans and animals.

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Publications

Rabis, T., Sommerwerck, U., Anhenn, O., Darwiche, K., Freitag, L., Teschler, H., Bödeker, B., Maddula, S. & Baumbach, J. I.: Detection of infectious agents in the airways by ion mobility spectrometry of exhaled breath. *Int. J. Ion Mobility Spectrom.* **11**, 187-195 (2011).

Maddula, S., Rabis, T., Sommerwerck, U., Anhenn, O., Darwiche, K., Freitag, L., Teschler, H. & Baumbach, J. I.: Correlation analysis on data sets to detect infectious agents in the airways by ion mobility spectrometry of exhaled breath. *Int. J. Ion Mobility Spectrom.* **14**, 197-206 (2011).

Database supported decision trees for medical diagnostics

Breath analysis, volatile metabolites, metabolic profiling

The identification of potential biomarkers in metabolic networks with respect to potential application for medical decisions needs reliable analytical methods and unimpeachable data analysis. To establish breath analysis in the medical everyday life the availability of database supported decision trees and receiver operating characteristics are essential.

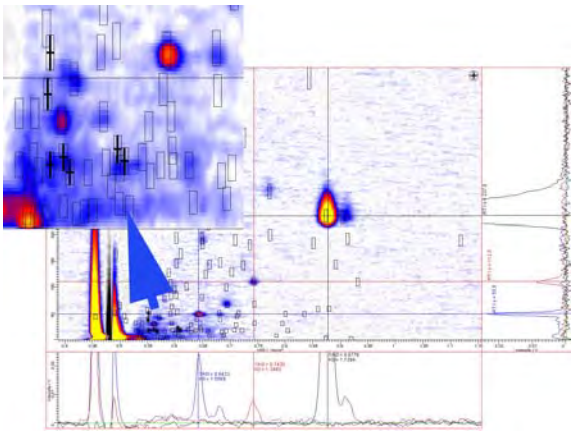

Figure 1: Position of the peaks related to different analytes in the IMS-Chromatogram of exhaled air of an individual marked by black rectangles – inlet: part of the IMS-Chromatogram showing some of the signals marked by a dark black cross representing the signals with the correlation to the lowest (best) rank sum

Human breath analysis is a powerful and especially a non-invasive technique for the monitoring and hopefully also for the diagnosis of respiratory diseases, including chronic obstructive pulmonary disease (COPD). The typical IMS-Chromatogram obtained is shown in Figure 1. Some peaks occur and are marked. How to find out whether the analyte will be a potential biomarker or not?

In clinical situations the main question is, if the VOC-composition of exhaled breath is likely pathological or not. The next step is to decide if a patient has for example COPD or interstitial lung disease. Within these subgroups different phenotypes need further consideratio. If this stepwise clinical approach is transferred to breath analysis by VOCs it seems useful to apply decision trees in choosing relevant VOCs for every single step. As an example, the ROC-curves and a decision trees to distinguish COPD and healthy controls is shown in Figure 2.

Generally, a data based procedure can help to find VOCs which are important in disease metabolism. However, these VOCs need not have high peaks or primarily a high sensitivity when used as single discriminatory VOC. The signals related with the lowest rank sum and the best separation power are not all found in the decision tree. In case, that some peaks in a group are positive correlated and have a high separation power with respect to a decision a consideration of one of them delivers the same power as all together. In such a case, as shown in the comparison of COPD and healthy control signals with lower separation power and higher rank sum could contribute if the other peaks were sorted in an earlier step of the decision. Finally, the peak with the highest separation power followed by signals with lower one will deliver a rather simple 3 step decision tree (see inlet in Figure 2).

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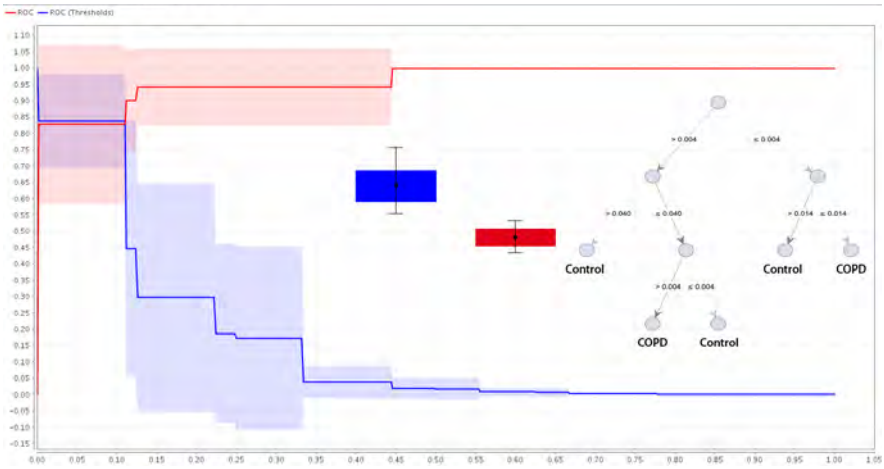

Figure 2: ROC-curve of patients suffering chronic obstructive pulmonary disease – inlet left: box-and whisker plot of patients suffering COPD (blue) and healthy controls (red) – inlet right: decision to differenciate COPD and healthy controls in 2 steps

Publications

Westhoff, M., Litterst, P., Maddula, S., Bödeker, B. & Baumbach, J. I. Statistical and bioinformatical methods to differentiate chronic obstructive pulmonary disease (COPD) including lung cancer from healthy control by breath analysis using ion mobility spectrometr. *Int. J. Ion Mobility Spectrom.* **11**, 139-149
Maddula, S. *et al.* Correlation analysis on data sets to detect infectious agents in the airways by ion mobility spectrometry of exhaled breath. *Int. J. Ion Mobility Spectrom.* **14**, 197-206 (2011).

IMS – GC/MS – Standard format for breath analysis

MCC/IMS, GC/MS, data format, cross-linking

To support the cross-linking of measurement data from multi-capillary column coupled to an ion mobility spectrometer (MCC/IMS) and gas-chromatography coupled to a mass spectrometer (GC/MS) techniques and to reduce the mishaps caused while communicating between scientists from different laboratories, a modification in the header section of the MCC/IMS data file and a specific nomenclature for the file name of the GC/MS measurements are proposed and will be described in detail.

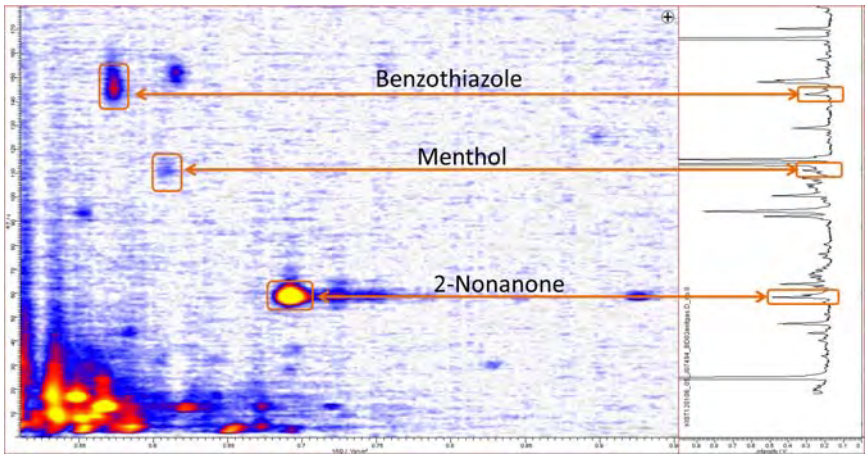

Figure1: Alignment of GC/MS and MCC/IMS data of a room air sample showing the cross-linking or cross annotation of some of the volatile organic compounds such as nonan-2-one, (-)-menthol and benzothiazole.

In the past, a standard format for the data sets from GC/IMS with sensor-controlled sampling, in order to harmonize the data generated by different instruments following the same methodology. This file format incorporates different header sections for different types of information, such as general information, sample information and further information. But it is not able to provide a cross-linkage between the measurements carried out on the same sample using different methodologies, such as both MCC/IMS and GC/MS using thermal desorption sampling or solid phase micro extraction methods. This cross-linking is of great importance for the first hand identification of the unknown volatile organic compounds, producing signals in an MCC/IMS chromatogram by comparing the data from both the MCC/IMS and GC/MS data, because the available standard reference database contains not more than 600 compounds.

Therefore, a modification in the header section of the present data format is proposed as used in the Department Clinical Diagnostics of Korea Institute of Science and Technology Europe. Only the header containing the general information is being proposed for the modification, especially the free line number 10. The data acquired from the GC/MS are stored in a directory and the filenames are restricted to the new format. Thus, important parameter like Instrument unique name, e.g. KIST; measurement year, e.g. “11” for 2011; measurement month, e.g. “11” for November; measurement day, e.g. 26; position number in the GC/MS auto-sampler; TDS tube unique number; Project key word, e.g. Opioids; file name of the corresponding MCC/IMS measurement are stored.

The improvement to the line number 10 of the header to a corresponding GC/MS measurement with a file name of AAAAZZYYXX_ii_BBBBBB_CCCCCCCCC_NNNN_YYMMDDhhmm_ims is as follows:

General information:

Line		Name	Type or value	comment
9	#	file	NNNN_YYMMDDhhmm_ims.csv	file name
10	#	GCMS	AAAAZZYYXX_ii_BBBBBB_CCCCCCCCC	GC/MS file name without the IMS file name part

With this cross-linkage between the MCC/IMS and the GC/MS data, the identification of the signals from unknown analytes in the MCC/IMS could be achieved by comparing with the signals that are identified in the GC/MS measurement of the same sample in parallel.

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Database-Driven Rapid Metabolic Profiling

Applied bioinformatics, data mining, medical data, MCC/IMS, GC/MS

In collaboration with various lung clinics and university hospitals, KIST Europe is involved in research into the discovery of volatile metabolites for noninvasive medical diagnostics. Multi-capillary column coupled to an ion mobility spectrometric (MCC/IMS) and gas chromatography – mass spectrometric (GC/MS) measurements of human breath taken at different stages of a clinical trial must be analyzed in order to find characteristic peak patterns corresponding to various metabolite profiles. Driven by the demand for rapid data analysis and biomarker discovery, there is a need for the establishment of a centralized data repository to facilitate identification of analytes and data mining for studies such as clinical trials. The basic structure of such a system being developed at KIST Europe is described.

It has been demonstrated that volatile metabolite profiles consisting of MCC/IMS peak intensities show significant differences between disease and control groups.

In cooperation with the Computational Systems Biology Group, Max Planck Institute for Informatics, Cluster of Excellence for Multimodal Computing and Interaction, Saarland University, a central ontology-driven data repository providing a generalized data structure for clinical trials is being developed. Before storing any new data in the database, there is a preprocessing phase in which, for example, peaks are to be found and aligned to make them comparable to measurements from different instruments. The grand challenge is to allow the flexible management of analytical data (MCC/IMS, GC/MS) combined with medical data (diseases, medication, age, gender, etc.) provided by physicians. Flexibility is ensured by a generalized data structure which enables the system to store any information without changes to the database schema. A database system including metabolite profiles and corresponding patient data will allow the extraction of interesting patterns, for example chronic obstructive pulmonary disease (COPD) patients with and without pseudomonas. Statistical analysis can be used to find significant differences in the metabolite profiles to separate both groups, which can lead to biomarker discovery. Additionally, applying machine learning methods to the data can also provide disease prediction models for unknown metabolite profiles or clustering data according to similar metabolite profiles. Considering a double-blinded large scale patient study, the system could pave the way towards noninvasive clinical diagnostics.

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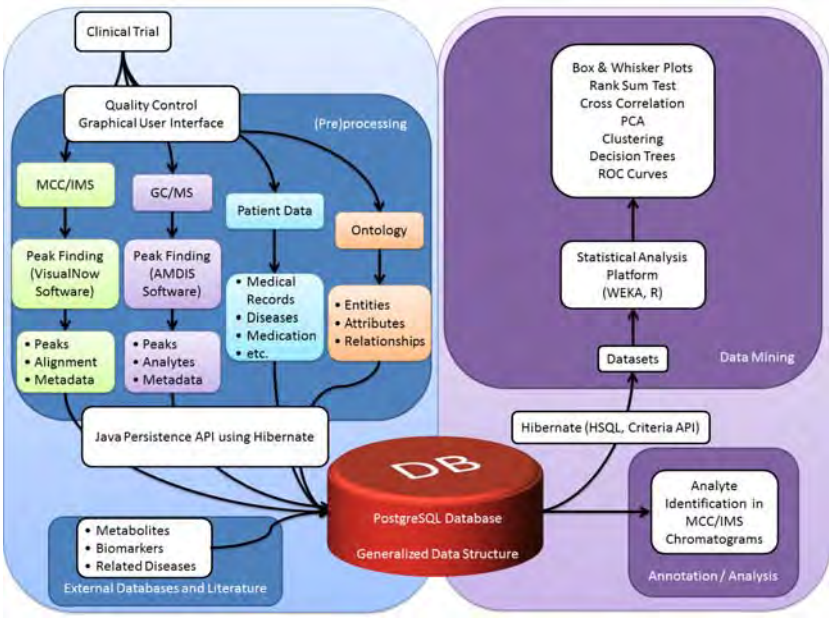

Figure 1: Semi-automated pipeline through different parts of the system. A clinical trial is the input data source where MCC/IMS, GC/MS and patient data is provided in specific file formats. After a quality control step the whole project or its (individual) parts are processed and uploaded to the database via a graphical user interface. The processing step includes peak finding and assignment of coupled GC/MS and MCC/IMS measurements. The relational information of the database system is represented by object-relational mapping via the use of Hibernate, which implements the Java Persistence API. In the data mining part, datasets are retrieved by queries, whereupon machine learning tools are applied for classification, and so forth. The database is also able to manage MCC/IMS and GC/MS reference measurements for the identification of unknown analytes.

Good breath – Bad breath – a preliminary study

exhaled breath, disturbances

Detecting volatile organic compounds (VOCs) with ion mobility spectrometry (IMS) coupled to a multi capillary column (MCC) in exhaled breath is a fast and non-invasive method. Unfortunately the data acquired in the course of the measurements does not only show substances related to diseases but also disturbances. It is important that one is able to identify those unwanted substances. One major disturbance is the toothpaste used by patients. At KIST Europe, the Clinical diagnostic group demonstrated that in exhaled breath some of the VOCs are related to the toothpaste rather than to the appropriate disease under investigation.

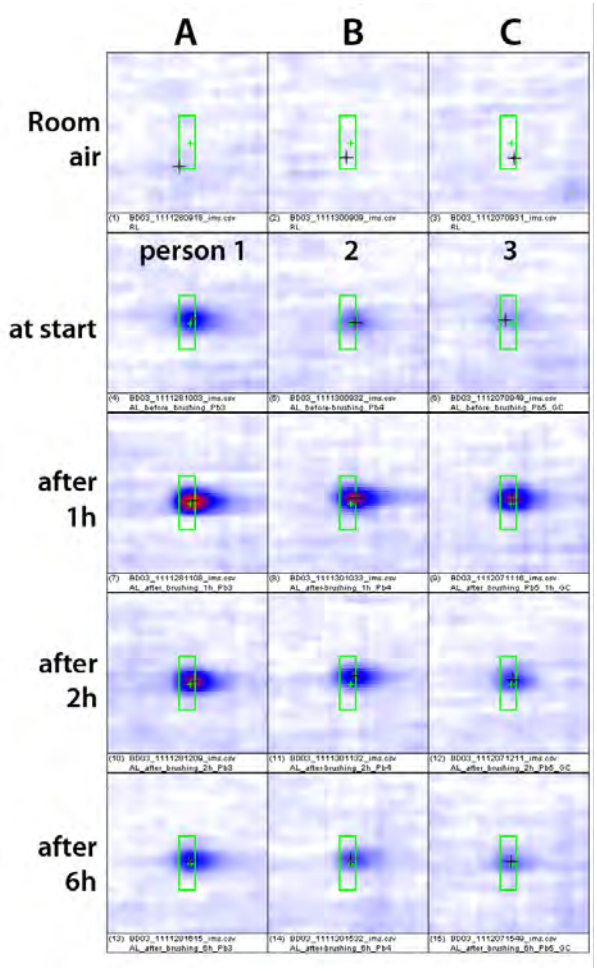

Figure 1: Toothpaste signals during the day compared to room air (3 persons different duration)

In IMS measurements most of the time there are many peaks not related to the exhaled breath itself. They might be from the room air or plastic devices used to collect the sample etc. It is important to distinguish between the peaks arising from the human breath, where we hope to identify analytes related to certain diseases, and analytes which are disturbances that can distort or hide the peaks relevant to the study.

Therefore a toothpaste study was conducted, where breath samples were taken before brushing and 1,2 and 6 hours after brushing. 10 mL of breath were used for each sample.

The temperature in the MCC as well as in the drift tube IMS was held at 40°C. The peaks were characterized using the software VisualNow.

Different brand of toothpaste with different ingredients were tested. One exemplary breath measurement is shown in figure 1. All measured brand of toothpaste showed a similar pattern. All test persons already showed a peak before brushing. This might be some residual substances from brushing the evening before the measurement was conducted. These initially present peaks increase after brushing and then decrease again over the day. After 6 hours, at the end of the measuring cycle they are still present.

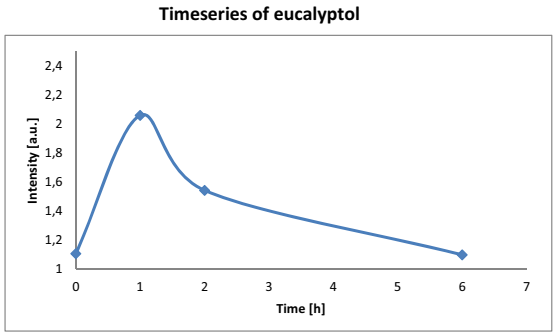

Figure 2: Timeseries of eucalyptol

In summary, it is virtually impossible to eliminate all toothpaste related peaks from any given breath sample, if the test subject has an average oral hygiene. Similarly, many VOCs show significant day-to-day variation in the signal intensities, which are related to various nutrients consumed by the individual under study for breath analysis. Finally, it can inferred that, systematic and environmental variabilities must be taken into consideration in order to relate the outcomes to medical questions.

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Development of QSAR-based TSP model for Predicting Mixture Toxicity

mixture toxicity, QSAR, two-Stage prediction, integrated addition model

The two-Stage Prediction (TSP) model has been developed as an integrated addition model to carry out the Concentration Addition (CA) and Independent Action (IA) calculations stage by stage. However, the use of the conventional TSP is limited if knowledge on the modes of toxic action (MoAs) on mixture components is not readily available. The objective of this study is to develop and evaluate a quantitative structure activity relationship (QSAR)-based TSP model for estimating mixture toxicity in the absence of knowledge on the MoAs.

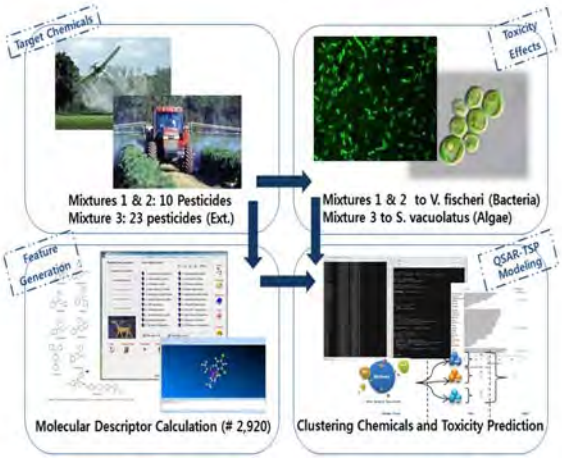

Figure 1: Overview of materials and methods in this study.

Conventionally, concentration addition (CA) and independent action (IA) models based on the concept of additive toxicity are often used to estimate the mixture toxicity of similarly and dissimilarly acting chemicals, respectively. However, organisms and their environments are simultaneously exposed to both types of chemicals. Therefore, an integrated model to predict mixture toxicity from various chemicals needs to be developed. The two-Stage Prediction (TSP) model has been developed as an integrated addition model to carry out the CA and IA calculations stage by stage. However, the use of the conventional TSP is limited if knowledge on the modes of toxic action (MoAs) on every mixture component is not readily available.

The objective of this study is to develop and evaluate a quantitative structure activity relationship (QSAR)-based TSP model for estimating mixture toxicity in the absence of knowledge on the MoAs. For this purpose, the different clustering methods of mixture constituents using computerized analysis based on the structural similarity between chemicals are applied as part of the prediction of mixture toxicity. The relative importance molecular descriptors for clustering chemicals are additionally analyzed by the Random Forest analysis.

The QSAR-TSP model was validated by three complex mixtures of pesticides with similar- and dissimilar-acting components: EC10 and EC50 ratio mixtures of 10 pesticides on Vibrio fischeri, and a mixture of 23 pesticides on Scenedesmus vacuolatus strain 211-15. For the three mixtures used in this study, the QSAR-TSP model based on the structural information on each compound, as an IAM combining the CA and IA concepts, successfully estimated mixture toxicity in the

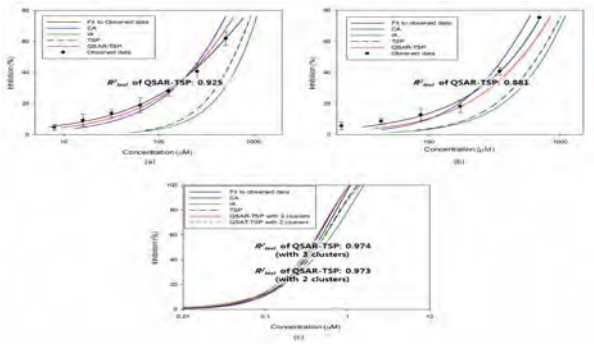

Figure 2: Comparison of the CA, IA, TSP, and QSAR-TSP predictions against observed toxicity for validation datasets: Mixture 1, EC50 ratio mixture from 10 pesticides (a); Mixture 2, EC10 ratio mixture from 10 pesticides (b); and Mixture 3, a realistic pesticide mixture including 23 compounds (c).

absence of knowledge on MoAs of mixture components (Fig. 2). This advantage of the QSAR-TSP model reflects a potential to overcome the critical limitation of not only the conventional TSP model requiring knowledge on the MoAs of all chemicals, but also that of the CA and IA models which can be theoretically available to either similarly or dissimilarly acting chemicals. In addition, the relative important descriptors in calculations of structural information for clustering chemicals in the three target mixtures were found by the RF analysis in this study. Further studies for the validation of the QSAR-TS model need to be conducted with toxicity data based on different types of mixtures and test organisms.

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Acknowledgment

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EUSES - An Exposure Estimation Tool for Environmental Risk Assessment

Risk assessment, EUSES, K-REACH

With the introduction of EU REACH regulation, the aspect of global chemical management has been reorganized with the concept of risk assessment of chemical substances. Risk assessment is to determine the probability of harmful effect to human or the environment and consist of 4 stages; hazard identification, exposure assessment, dose-response assessment, and risk characterization. Under REACH regulation, it is the obligation of manufacturer and formulator to produce and distribute the exposure scenarios used in exposure assessment to downstream user. For compliance the requirement of REACH, European Union system for the evaluation of substances (EUSES) is popular as exposure assessment tool.

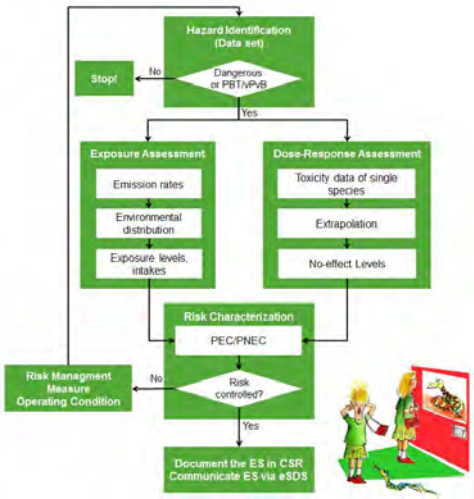

Figure 1: A follow diagram of risk assessment applied in REACH regulation.

To trace back to the origin of risk assessment in Europe, we normally recollect the old chemical regulation that is established in 1967 (Council Directive 67/548/EEC), the first modernized regulation to control the hazards of dangerous chemicals. Main concepts of the Directive are the classification, packaging, and labeling of dangerous substances. However, risk assessment was not an issue by the publication of Commission Directive 93/67/EEC. With the introduction of the directive, Commission Regulation 1488/94/EEC and Commission Directive 98/8/EEC appeared for risk assessment of pre-existing chemicals and biocidal products.

Risk assessment is a step-wise action to determine a quantitative and qualitative value related to a situation in threatens. Risk consists of hazard and exposure. Hazard is a characteristic of chemicals that cause harm (a potential). Exposure is a quantitative and qualitative measurement of extent to which a given hazard is present. Therefore, risk is summarized as a chance or probability that cause harm by exposure to a certain chemicals.

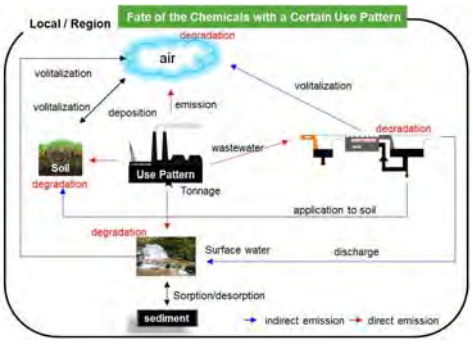

Figure 2: Environmental fate of chemical substances applied to EUSES model.

The basic risk assessment technology is given in Technical Guidance Document and published in 1996 for new and existing chemicals and 2003 for biocidal products. However there was continuing concern on the existing chemical regulation that it may fails sufficient protection of human health and environment, which triggered the development of new chemical regulation named REACH (Registration, Evaluation, Authorization, and Registration of Chemicals).

EUSES is a risk assessment tool for human, environment, and consumer and first developed by European Union in 1996 and continuously updated thereafter. It is a decision-supporting instrument which enables government authorities, research institutes and chemical companies to carry out effective of risks posed by chemicals to human and environment. Model focuses on the initial and refined risk assessment rather than comprehensive assessment and specialized for environment. The model describes environmental fate of chemicals according to various discharge event. The operation of EUSES model is base on the following parameters; 1) physico-chemical properties, 2) octanol-water partition coefficient, 3) total tonnage, 4) use pattern, and 5) release fractions.

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Acknowledgment:
This project is funded by the Korean Ministry of Knowledge Economy & the Korea Institute of Science and Technology.

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FP7 International Cooperation: KORRIDOR & KESTCAP

Korea-EU science and technology cooperation, FP7 capacities programme

Promotion of science and technology cooperation and the technology transfer between Korea and the European Union (EU) is one of the main functions of KIST Europe. Pursuing this objective, KIST Europe has conducted R&D collaboration improvement projects between Korea and the EU under the 7th Framework Programme of European Commission: KORRIDOR and KESTCAP. KIST Europe contributed to the enhancement and development of S&T partnership by supporting S&T competitiveness.

KORRIDOR is the FP7 International Cooperation project with the purpose of stimulating and facilitating the participation of European researchers in Korean R&D programs, coordinated by KIST-Europe having consortium parties of DLR, CNRS, National Research Foundation of Korea and Korea Institute of Advancement of Technology for 28 months (from Dec. 2009 to Mar. 2012)

Figure 1: Information day in Barcelona, Spain

In spite of the fact that Korea is one of the most important RTD partners of the EU with well-established legal frameworks for cooperation, the level of European researcher's awareness of cooperative opportunities in Korean RTD programs has been significantly low for many reasons. In 2011, as the second year of the project, the KORRIDOR project has developed and organized diverse activities to promote cooperation between Korea and the EU. The Korean RTD workshops, titled Information day, were held at three different countries, Germany, France and Spain to inform European researchers about Korean RTD opportunities. Final conference was held in Brussels to discuss lessons and results learned by the KORRIDOR project with policymakers, NCPs, research funding agencies and European researchers. Other than these organized workshops, diverse disseminating activities of KORRIDOR have occurred at several European venues. Numbers of deliverable reports were completed and will be published: Policy paper, Participation guideline, FAQ, Liaison building analytical report, Monitoring report, Training report and Dissemination report. Especially, Policy paper analyzes Korean RTD programs and existing hindrances for European researcher's attendance and finally suggests recommendations for both European and Korean sides.

Helpdesk has been established at common webportal for the eleven ACCESS4EU projects (http://www.access4.eu/southkorea). Every information and presentation materials have been uploaded instantly and advising service has been provided through helpdesk.

Figure 2: Final Conference in Brussels, Belgium

KESTCAP, Korea EU Science and Technology Cooperation Advancement Programme, is a three and a half year project (from Jul. 2008 to Jan. 2012) based on the Science and Technology Agreement signed between Korea and the EU in Nov. 2006, having consortium parties of KIST Europe, the Ministry of Education and Science and Technology and NRF. KESTCAP project organized several top-down forums and events and provided a platform to strengthen the S&T Agreement between Korea and the EU.

The accumulated knowledge and acquired experience through KORRIDOR and KESTCAP projects are valued properties of KIST Europe and will be utilized actively for initiating new Korea-EU Bilateral Cooperation project and further more developing innovative collaboration model.

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Publications

Policy paper "Access opportunities for European researchers in Korean RTD programmes: status and recommendations" (Nov. 2011)
Participation guidelines, target audience: research communities in Europe and Korea (Nov. 2011)

The development of the Energy Efficiency Management System

Energy saving system, sensor network, smart meter, artificial intelligence, user behavior

The energy efficiency management system aims to help users to aware their energy consumption and provide them with information on energy saving in home and building. To achieve those objectives, a prototype of energy efficient management system based on multi home environment has been proposed and developed. Unlike ordinary energy management system used in smart home, our system is designed to provide elaborate intelligent services using additional data gathered from neighborhood as well as monitoring and controlling service.

Recently, the unexpected increase in energy consumption becomes an important issue related to the current global problems such as environmental problem, fossil fuel crisis, economic crisis, and so on. To cope with those problems, various kinds of techniques are under developing. As one of possible solutions, energy management system for the home and building is proposed and some results are available in the market. However, they are confined to a single home environment. Hence, users have limitation on getting enhanced information for energy saving due to the absence of the comparable data from the usage of others. To provide enhanced information for energy saving, our system is developed to consider multi home environment, which make it possible to flourish data and intelligent service.

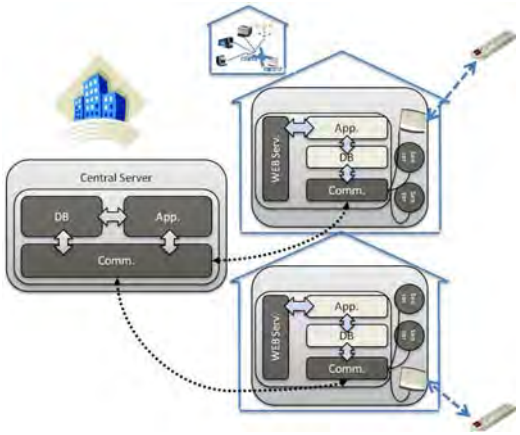

Figure 1: Schematic description of the energy efficiency management system

To do this, the developed energy efficient management system consists of two main components; the central server (CS) and the home gateway (HG). The aim of the CS is to retrieve and store data that is collected and transferred from the HGs located at each home. The HG is responsible for monitoring and storing energy consumption of home appliances. The wireless energy monitoring sensor attached to the home appliances transfers real time energy consumption data to the HG. The developed system architecture for multi home environment is illustrated in Figure 1.

Figure 2: Demonstration of the energy efficiency management system

The stored data is used to generate and provide intelligent service for energy saving. The developed intelligent services in our system are described in Figure 2:

- Statistics: The historical monitoring data of energy consumption during the requested period
- Energy Consumption per one House Inhabitant: The comparison of energy consumption per person comparing with others. This information helps users to know how much energy is efficiently consumed compared to others.
- Energy Consumption Distribution: The ranked comparison of energy consumption among home appliances during the requested period. The user can recognize the most energy consuming home appliances.
- Energy Efficiency: The comparison of energy efficiency with similar equipment of neighborhoods

Using multi home environment, the additional data becomes available and the enhanced information is generated. Hence, it becomes possible for users to understand the behavior of energy usage and find the way to save energy. In addition, our system can help to achieve the overall reduction of energy consumption in society through the connection with smart grid.

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Publications

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Woong Hee Kim, Sunyoung Lee, Jongwoon Hwang: Real-time Energy Monitoring and Controlling System based on ZigBee Sensor Networks, Procedia CS 5: 794-797 (2011)

Sustainable Waste Management for Green Printing Industry

Sustainable development, green technology, recycling process

A new green technology, as recycling process for waste ink management is employed for sustainable waste management, which its concept is basically on the infrastructures to establish closed loops employing distillation process instead of incineration. This technology is expected to result in less environmental impact and enhance the use of recycled products as raw materials, thus greatly reduce production and waste treatment costs. For a suitable adaptation at industrial and social level, the systemic implementation strategy has to be established. A new green business model for the relevant industry by employing the new recycling technology will be developed depending on the systemic implementation strategy resulting from the integrated evaluation through Environmental Impact Assessment (EIA) and Life Cycle Assessment (LCA).

Figure 1: Olax 22 Process for Recycling of waste

TThe flexographic/gravure printing industry is responsible for the significant part of waste generation within European countries (mainly Germany, France and Italy). The EU generates more than 61,000 tonnes of ink-paste waste and each plant has tasked to process 1,200 tonnes annually and 50 plants would be needed to cover the amount of waste generated in Europe. Ink-waste recycling by the printing industry is believed to have great potential in the area of waste reduction and long-term cost benefit. However, the industry has yet to produce a recycled product of good quality because most of the conventional technology for recycling is based on incineration. Ink wastes by the printing industry are high in solvent, resin, and pigment. Incineration of these components generates CO2, nitrogen oxides, and contaminants like PAHs (polycyclic aromatic hydrocarbons). EU member-states should be obliged to draw up specific waste management strategy and plans in light of the '2005 Thematic Strategy on the Prevention and Recycling of Waste' by the EU.

Therefore, EU member-states are required to establish sustainable waste management plan not only to develop their own program on environmental sustainability but also so they could strictly comply with the directive that should be observed until the end of 2013. For the purpose, the printing industry has to seek for a strategy on sustainable waste management, which demands a new business model employing advanced technology for waste recycling. Both environmental and economic impacts of the technology for adoption by concerned industries should be evaluated using optimal methodologies of EIA and LCA.

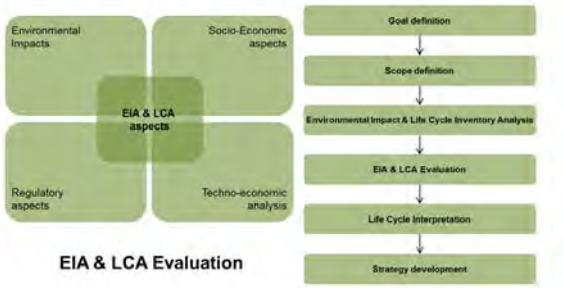

Figure 2: Main Aspects and Procedure of EIA and LCA

A new advanced technology for recycling of ink wastes, called Olax 22 process, is employed. Figure 1 shows a detailed description of the new green technology. EIA evaluates environmental factors to be given due weight, along with economic or social factors, when planning applications are being considered and the relevant environmental analysis may indicate ways in which the project can be modified to avoid possible adverse effects through considering more environmentally friendly alternatives. The targeted Olax 22 technology will be assessed using the LCA since it provides an innovative life cycle change for the end of life stage from disposal to recycle. The main aspects and procedure of the life cycle analysis are shown in Figure 2.

Consequently, it will address three dimensions of sustainability related to environmental impact reduction and sustainable growth in economic and social welfare by the application of the new green technology. For the purpose, scientific collaboration between three EU countries, Kist Europe (Germany) for new business model development and EIA evaluation, EPFL (Switzerland) for LCA evaluation and Alicante Univ. (Spain) for green technology development is reached.

Furthermore, mutual collaboration between Alicante Univ. (Spain) and Kist Europe has been promoted for scientific research and green technologies transfer to Korean market to strengthen sustainable development in Korea.

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J Breath Res	2009	Baumbach, J.I. et al.	10

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Journal	Year	First Author*	Impact-Factor
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REACH impact on Chemical Industry after 2010

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Ion mobility spectrometers in point of care, intensive care and systems biology

Workshop Future Cooperation Saarland - Wonju; Wonju Medical Industry Techno Valley, Wonju, Korea; 29.11.2011

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REACH compliance

Korea Industrial Technology Association, Seoul, Korea; 22.11.2011

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Recent Regulation Trends

Korea Industrial Technology Association, Seoul, Korea; 22.11.2011

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Chung-Ju, Korea; 19.11.2011

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Neuzil, P.:

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Bubble Tech to Bio App, 2nd Korea – EU Workshop on Microfluidic Technology for Chemical, Biological & Medical Applications, Saarbrücken, Germany; 17.10.2011 - 18.10.2011

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Lab on Chip - for Biochemical or Biological Applications

DFKZ - 21st Annual Conference of the German Society for Cytometry, Bonn, Germany; 12.10.2011 - 14.10.2011

Baumbach, J.I.:

Ion mobility spectrometers in point of care, intensive care and systems biology

Breath Analysis Summit 2011, Parma, Italy; 11.09.2011 - 14.09.2011

Jeon, H.:

The compliance strategy to global chemical regulations

Invited lecture in Chemistry Department Hanyang University, Seoul Korea; 08.09.2011

Kim, Young Jun:

Tissue engineering and bacteriophage

Tritiny college, CRANN 2011, Dublin, Irland; 07.09.2011

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Microfluidics & miniaturization - the teenage years are over...

CSIR, the presidents lecture, Pretoria, South Africa, 07.09.2011-10.09.2011

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Miniaturized diagnostic instrumentation for breath analysis / infectious diseases

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M13 phage as a material of nanotechnology

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The compliance strategy to global chemical regulations

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Filamentous phage based new type scaffolds for tissue regeneration

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Kim, S.:

Strategic preparation of 2013 registration for REACH

REACH Compliance Seminar (KITECH), Seoul, Korea; 02.09.2011

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Preparation and use of Exposure Scenario for Industry

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Best practice; Exposure assessment for workers using ECETOC TRA v2.0

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Detection of volatile organic Compounds in Exhaled Breath using Ion mobility Spectrometers

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Ion mobility spectrometers in point of care, intensive care and systems biology

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Microfluidic modules for pre-concentration and removal of [18F]fluoride in PET radiotracer synthesis

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Miniaturization for clinical diagnostics instruments

Enabling Technologies for Quantitative Bioscience, Manchester, UK, 14.06.2011

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Hand-held Lab-on-a-Chip System

Thing-Hua University, Beijing, China; 09.06.2011

Philippi, A.:

Development of pharmaceutical-containing nanoparticles for a novel immune cell-based cancer therapy approach.

4th WCU International Symposium on Nanobio Materials and Electronics, Münster, Germany; 04.05.2011 - 07.05.2011

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Detection of Infectious Diseases by Metabolomics or DNA

26th International Symposium on MicroScale Bioseparations (msb2011), San Diego, USA; 01.05.2011 - 05.05.2011

Ra, J.-S.:

Global Regulatory Compliance

Korea Industrial Technology Association, Seoul, Korea; 19.04.2011

Ra, J.-S.:

Compliance Strategy for Authorization and Notification in Articles

Korea Industrial Technology Association, Seoul, Korea; 19.04.2011

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Post Management Strategy after 2010 REACH Registration

Korea Industrial Technology Association, Seoul, Korea; 19.04.2011

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Early Regitstration Strategy of Target Registration Substances for 2013 and 2018

Korea Industrial Technology Association, Seoul, Korea; 19.04.2011

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Microfluidics & Miniaturization - the Teenage Years are Over…

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Gefahrstoffdetektion (Bakterien, Atemluft, Raumluft) mittels µIMS

TechnologieZentrumDortmund,Germany; 17.03.2011

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µIMS - Schnelltest für pathogene Erreger in der Medizin

Zenit GmbH, Mülheim, Germany; 11.03.2011

Neuzil, P.:

Gecko Mimicking Tape & Miniaturized LOC system

Italian Institute of Technology, Genoa, Italy; 24.02.2011

Baumbach, J.I.:

Breath Analysis using Ion Mobility Spectrometry

Fresenius Kabi - Bad Homburg, Germany; 26.01.2011

Baumbach, J.I.:

A Puff of Breath - Are volatile metabolites in human breath relatable to bacteria, diseases, infections, inflammation, lung cancer, medication, ...?

Samsung - Gyeonggi, Korea; 18.01.2011

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A Puff of Breath - Are volatile metabolites in human breath relatable to bacteria, diseases, infections, inflammation, lung cancer, medication, ...?

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Harada - Osaka, Japan; 11.01.2011

CONTRIBUTED LECTURES

Kim, J.:

A QSAR-based Two-Stage Prediction for Estimating Mixture Toxicity

32nd SETAC North America Annual Meeting, Boston, United States, 13-17.11.2011.

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4th Symposium Metabolites in Breath, Saarbrücken. Germany; 26.10.2011

Westhoff, M.; Litterst, P.; **Maddula, S.; Baumbach, J.I.:**

Differentiation of COPD including lung cancer from healthy control group by breath analysis using ion mobility spectrometry

4th Symposium Metabolites in Breath, Saarbrücken, Germany; 26.10.2011

Neuzil, P.; Wanxin, S.; Chung, W. C.:

Nanoliter-sized Superheated Bioreactor

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Kurth, J.I.; Darwiche, K.; Theegarten, D.; **Baumbach, J.I.**; Purkhart, R.; Freitag, L.:

A step towards easier diagnosis of lung cancer: Detection of volatile organic compounds in air releasing tumour samples with ion- and differential mobility spectrometry

ERS Annual Congress, Amsterdam, Netherland; 24.09.2011 - 28.09.2011

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M13 phage as a material for nanotechnology

International conference and exhibition on virology. Baltimore, USA; 03.09.2011

De Leonardis, F.; **Tarn, M.D.**; Pascali, G.; Salvadori, P.A.; Pamme, N.:

Microfluidic modules for the pre-concentration of [18F]fluoride for PET radiotracer synthesis, and its subsequent removal during product purification

19th International Symposium on Radiopharmaceutical Sciences, Amsterdam, Netherlands; 28.08.2011 - 02.09.2011

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World Korean Chemists conference, Dae-Jeon, Korea; 19.08.2011

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Smart 11, Saarbruecken, Germany; 06.06.2011 - 08.06.2011

Anhenn, O.; Sommerwerck, U.; Rabis, T.; **Baumbach, J.I.;** Bödeker, B.; Darwiche, K.; Freitag, L.; Teschler, H.:

Nicht-invasive Identifikation verschiedener Erreger in der Atemluft durch Ionen-Mobilitäts-Spektrometrie

52. Kongress der Deutschen Gesellschaft für Pneumologie und Beatmungsmedizin e.V., Dresden, Germany; 07.04.2011 - 10.04.2011

Sommerwerck, U.; Anhenn, O.; Rabis, T.; Darwiche, K.; Freitag, L.; Kamler, M.; Jakob, H.; **Baumbach, J.I.**; Bödeker, B.; Teschler, H.:

Ionenmobilitätsspektrometrie- ist eine nichtinvasive Diagnose des Bronchiolitis-obliterans-Syndroms möglich?

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Ionenmobilitätsspektrometrie vor und nach Lungentransplantation

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Signifikant unterschiedliche volatile Biomarker in der beidseitigen bronchoskopischen Ionenmobilitätsspektrometrie bei Patienten mit Bronchialkarzinom

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COPD: Differentation by exhaled breath analysis using ion mobility spectrometry

ANAKON 2011, Zürich, Switzerland; 22.03.2011 - 25.03.2011

Baumbach, J.I.:

IMS für flüchtige Stoffwechselprodukte

3rd Symposium Metabolites in Breath, Essen, Germany; 16.02.2011

POSTERS

Kim, J.; Kim, S.; Schaumann, G.E.:

Multi-linear Regression Methods to Develop an Integrated Addition Model for Predicting Mixture Toxicity

32nd SETAC North America Annual Meeting, Boston, United States, 13-17.11.2011.

Park, J.; Müller, M.; Kim, J.; Kim, D.-P.; Seidel, H.:

Single Cell Array of Microwells coated with Dopaminergic Organic-inorganic Hybrid Resin

The 5th IEEE Int. Conf. on Nano/Molecular Medicine and Engineering (IEEE-NANOMED 2011), International Convention Center (ICC), Jeju, Korea; 10.11.2011 - 12.11.2011

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Microfluidic modules for the purification of [18F]FDG in PET radiotracer synthesis

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Trietscha, S.J.; Rauwéa, W.; Urban, G.A.; **Manz, A.**; Hankemeier, T.; van der Linden, H.J.; Vultoa, P.:

The phaseguide paradigm: priming and emptying of monolithic polymer chips

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Simone, G.; Malara, N.; **Neuzil, P.**; Di Fabrizio, E.; **Manz, A.**:

Carbohydrate-Protein complex for specifically isolating metastatic circulating cancer cells

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A simple in situ microfluidic procedure ot create multivalent biofuntionalized surfaces

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Vojtíšek, M.; **Tarn, M.D.**; Hirota, N.; Pamme, N.:

Lab-on-a-chip in superconducting magnets - A tool for particle separations and bubble manipulation via diamagnetic repulsion

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Trapping and focusing of particles and cells based on magnetic attraction and diamagnetic repulsion

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Detection of pseudomonas aeruginosa (Pa) specific peaks by ion mobility spectrometry (IMS) in exhaled breath of bronchiectasis patients

ERS Annual Congress, Amsterdam, Netherland; 24.09.2011 - 28.09.2011

Besa, V.; Darwiche, K.; Teschler, H.; Sommerwerck, U.; Kurth, I.; Rabis, T.; **Baumbach, J.I.;** Freitag, L.:

Volatile organic compounds (VOCs) in COPD patients with exacerbation

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Anhenn, O.; Rabis, T.; Sommerwerck, U.; Weinreich, G.; **Baumbach, J.I.;** Kurth, I.; Darwiche, K.; Freitag, L.; Teschler, H.; Costabel, U.:

Detection of differences in volatile organic compounds (VOCs) by ion mobility spectrometry (IMS) of exhaled breath in patients with interstitial lung diseases (ILDs) compared to healthy controls (HC)

ERS Annual Congress, Amsterdam, Netherland; 24.09.2011 - 28.09.2011

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Volatile organic compounds in lung cancer patients before and after tumour resection

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A new possibility of process monitoring in lung cancer: Volatile organic compounds detected with ion mobility spectrometry to follow the success of the therapeutic process

ERS Annual Congress, Amsterdam, Netherland; 24.09.2011 - 28.09.2011

Kim, Y.J.; Arora, A.; Nam, C.-H.:

Construction of phage based new type scaffolds using genetic and chemical modification

24th European conference on biomaterials, Dublin; 04.09.2011 - 09.09.2011

Wong, C.-C.; Chen, Y.; Reboud, J.; **Neuzil, P.**; Soon, J.; Liao, K.;

Silicon Nanowires for Cellular Mechanosensing

DSR-2011: Defence Science Research Conference and Expo, Singapore; 03.08.2011 - 06.08.2011

Darwiche, K.; **Baumbach, J.I.**; Sommerwerck, U.; Teschler, H.; Freitag, L.:

Volatile Organic Compounds (VOC) sampled during bronchoscopy in lung cancer patients

20th Annual conference on Ion Mobility Spectrometry, Edinburgh, Scotland; 24.07.2011 - 29.07.2011

Kreuder, A.-E.; Buchinger, H.; Kreuer, S.; Volk, Th.; **Rupp, K.; Maddula, S.; Baumbach, J.I.:**

Characterization of Opiates in human breath of patients within intensive care units

20th Annual conference on Ion Mobility Spectrometry, Edinburgh, Scotland; 24.07.2011 - 29.07.2011

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Large Scale Scanning of Metabolites in IMS-Chromatograms

20th Annual conference on Ion Mobility Spectrometry, Edinburgh, Scotland; 24.07.2011 - 29.07.2011

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Volatile Organic Compounds in Chronic Obstructive Pulmonary Disease

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Westhoff, M.; Litterst P.; **Maddula, S.; Baumbach J.I.:**

Drug delivery related to metabolites in human breath – first results of long term clinical studies using MCC/IMS

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Influence of room air and operational background emissions on breath analysis using MCC/IMS

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Kim, Y.J.; Nam, C.-H.:

Design of Phage network as functional scaffold using chemically modified phage for tissue regenerating biomaterials

EKC 2011, 2011 Paris, France; 21.07.2011 - 23.07.2011

Kim, J.; Kim, S.; Schaumann, G.E.:

An Application of Different Multi-linear Regression Methods to Develop an Integrated Addition Model for Predicting Mixture Toxicity

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Ryu, B.; Kim, J.; Kim, S.:

Development of Rational Exposure Assessment Strategy under K-REACH for Risk Assessment for Workers by ECETOC TRA

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Feasibility of Application of EUSES to Chemical Risk Assessment in K-REACH

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Scientific challenges for compliance to global chemical regulations

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Ion mobility spectrometry for real time metabolomics in clinical diagnostics

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Drug delivery related to metabolites in human breath – first results of long term clinical studies using MCC/IMS

1st international HIPS Symposium on Pharmaceutical Sciences devoted to Infection Research, Saarbrücken, Germany; 16.06.2011

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Identification of human pathogenic bacteria using microbial volatile organic compounds

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Infections, drug delivery and metabolites detectable in human exhaled

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Neuzil, P.; Soon, B.-W.; Fang,C.; Reboud, J.; Wong, C.-C.; Kao, L. T.-H.:

Monolithic Silicon-based Microfludic Device Made by Single Step Lithography

Transducers 2011, Beijing, China; 05.06.2011 - 09.06.2011

Neuzil, P.; Woon, J. S.-B.; Novak, L.; Wong, C.-C.; Wee, Y.-J.:

Simple Read-out System for Multiplexed 64 Nanowire-based Biosensors

Microtechnologies in Medicine and Biology, Luzerne, Switzerland; 04.05.2011 - 06.05.2011

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Simple read-out system for multiplexed 64 nanowire-based

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Palm-sized detection read-out system for array of ultra sensitive nanowire nanosensors

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Westhoff, M.; Litterst, P.; Bödeker, B.; **Baumbach, J.I.:**

Ausatemluftanalyse mittels Ionenmobilitätsspektrometrie (IMS) zur Differenzierung von COPD und interstitiellen Lungenerkrankungen

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Anti-neoplastic drug targeting to EpCAM-expresing tumors by redirected, ex vivo activated T lymphocytes

6th International Symposium on the Clinical use of Cellular Products, Erlangen, Germany; 24.03.2011 - 25.03.2011

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Volatile Biomarker bei Lungenkarzinom über MCC/IMS

DGMS Jahrestagung, Dortmund; 27.02.2011 - 03.03.2011

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MCC/IMS zur Detektion von COPD-Markern in der Ausatemluft

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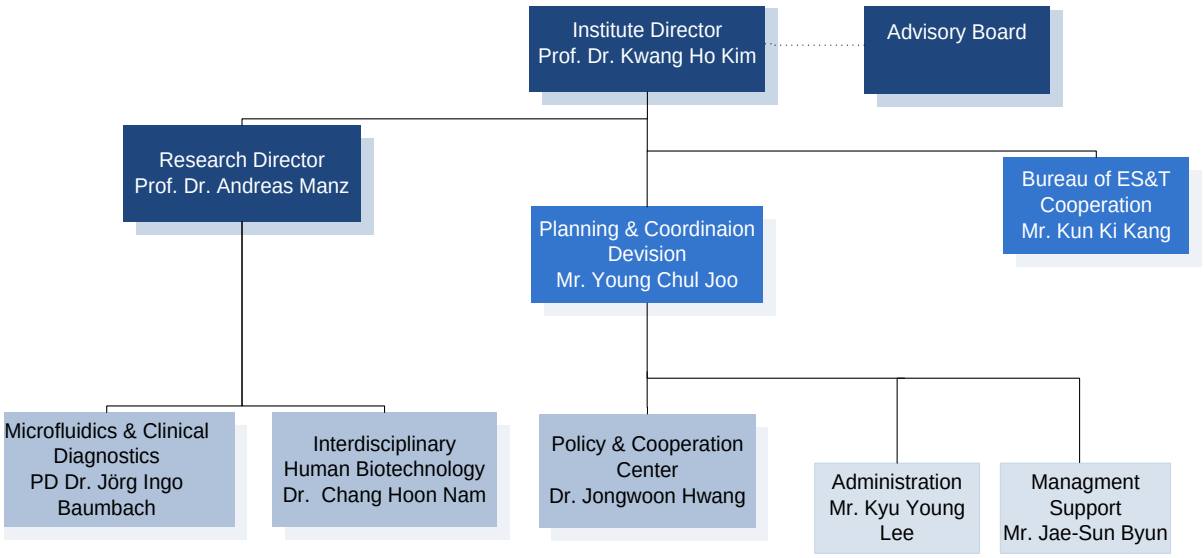
KIST Europe Organisation



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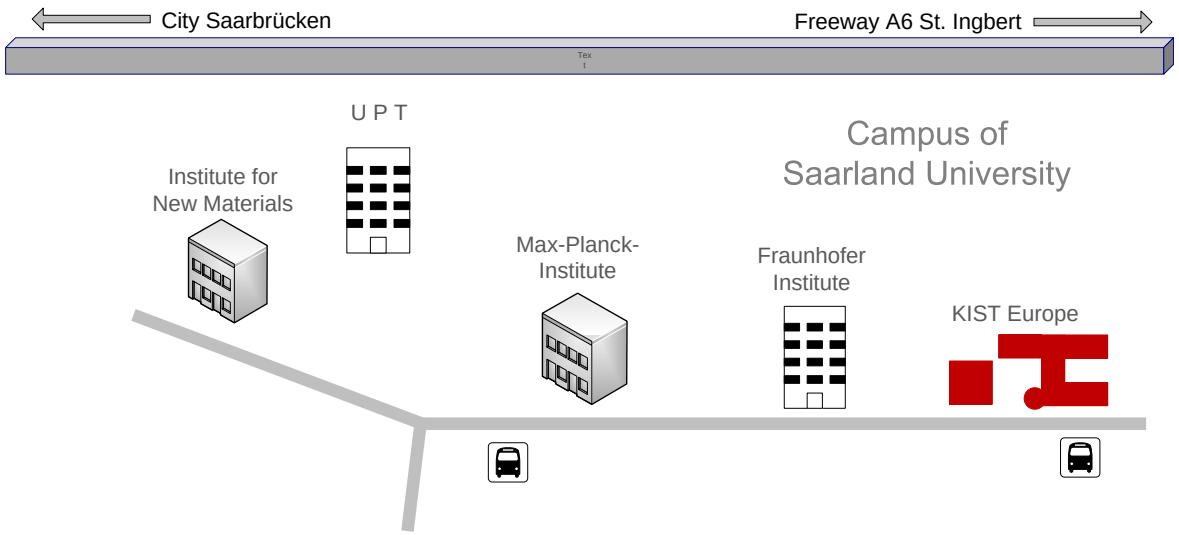
Head of Division Asia and Oceania, German Federal Ministry of Education and Research, Germany

How to reach KIST Europe



By Airplane (Airport Saarbruecken)

Flughafen Saarbrueken (Saarbruecken airport) is approached directly by following cities: Hamburg, Berlin TXL, Munic and Luxembourg.

By Car

Information for the navigation system:

66123 Saarbruecken, Stuhlsatzenhausweg 97

From east (Mannheim/Karlsruhe) to University: Freeway „A6 Mannheim-Paris“ up to the exit „St. Ingbert west“. From there, follow up to the sign of „Universität Ost“. Then finally you can find the main entrance of the university.

From north (Koblenz/Trier) to University: Freeway „A1“ to the interchange „Saarbruecken“, from there on „A8“ (direction to Karlsruhe) up to the freeway interchange „Neunkirchen“, from there on „A6“ (direction to Saarbruecken). That is the way to city center. In the city, you can find the sign "Universität Ost" easily.

From France to University: Freeway „Paris-Mannheim“ up to the exit „St. Ingbert West“, from there follow the sign-posting „Universität Ost“ up to the main entrance of the university.

From Luxemburg to University: Follow the freeway „A620“ to the sign-posting „Saarbruecken“ and from there follow the sign „Universität Ost“ up to the main entrance of the University.

By Train (Main Station of Saarbruecken)

If you start from the north over Koblenz/Trier, you can use RE (Regional Express) or IR (Inter Regio) in every hour. From the east over Mannheim or Karlsruhe, you can take IR or IC (Inter City). From the west over Metz (in France) and from the south over Strassbourg (in France), look at the information of Deutsche Bahn (German Railroad AG).

By Bus

Take city bus # 101, 102, 138 or 150 with directions to „Dudweiler Dudoplatz“ or „University Campus“ from the main station Saarbruecken to KIST Europe and get off the bus at the stop „Stuhlsatzenhausweg“. You can get more detail information from Saarbruecker Busfahrplan (Saarbruecker bus timetable) or Online-Fahrplanauskunft (Online timetable information) of the VGS (traffic network company Saar Ltd.).

KIST Europe

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