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Korea Institute of Science and Technology (KIST) Europe Forschungsgesellschaft mbH

Director: Dr. Kwang Ho Kim

Research Director: Prof. Dr. Andreas Manz

Address: Universität des Saarlandes

Campus E 7.1

66123 Saarbrücken

Germany

Phone: +49 (0) 681 9382 - 0

Fax: +49 (0) 681 9382 -109

Internet: http://www.kist-europe.de

E-Mail: info@kist-europe.de

Preface - Greetings of the Director

Dear readers,

I am very pleased to present the first annual report of KIST Europe research institute. It covers the most notable events in 2009, along with a number of scientific highlights, an overview of our research outputs and the publications in international scientific journals.

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

KIST Europe has made a lot of progresses in the research fields including Nanomedicine, Bio-MEMS, Medtronics, Mechatronic sensors and actuators. In addition, KIST Europe has performed many activities to build a cooperation network between Korea and EU. For this purpose we have so far managed many seminars and joint workshops on R&D issues.

I took charge of KIST Europe as a new director since last September. Meanwhile I have recognized that our all members have made a great work and contribution to build up this current KIST Europe, under sometimes difficult circumstances. I would like to extend my appreciation to previous directors and all the ex- and current members of KIST Europe 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. Last year we have called Prof. Dr. Andreas Manz as the research director to enhance our research activities. Together with him KIST Europe will achieve a breakthrough in our research areas in near future.

This time, KIST Europe can have opportunity to publish our activities thanks to our researchers' efforts. The major goal of publishing 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.



Dr. Kwang Ho Kim Director kwhkim@kist-europe.de



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KIST Europe - a summary

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

blems 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.

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

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.

with R&D capability in its own right.

Its partners are research institutes and industrial companies in Europe and Korea. Together with its partners, the KIST Europe solves pro-

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, including Germany.

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



Facts & News

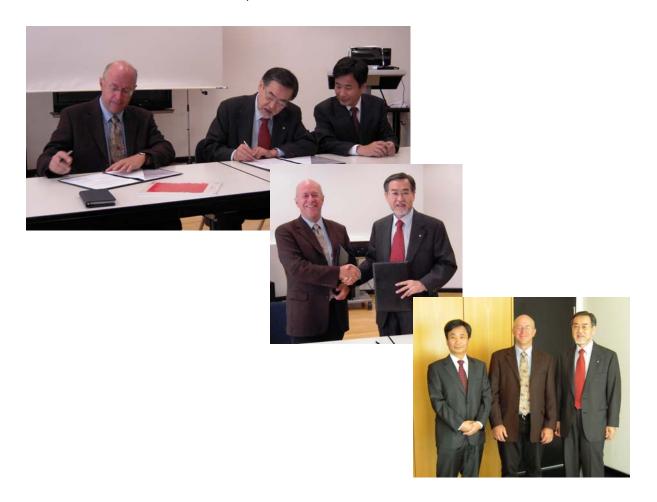
August 31st, 2009: adoption of the director of the institute Prof. Dr. Chang Ho Kim and inauguration of the new director Dr. Kwang Ho Kim.



Since August 2009, Young Jong Kim is the new leader of the administration.

We were represented together with our mother institute at the Hannover fair from April 20th until April 24th, 2009.

Prof. Dr. Andreas Manz took over the position of the Head of Research.



The roofing ceremony of the second building took place on September 30th, 2009.



Technology for the treatment of harmful trace pollutants in water

A concentration and follow-up degradation technology has been developed for the specific treatment of harmful trace pollutants in water. For the specific adsorption of these pollutant molecules, molecularly imprinted polymers with the respective "tailormade" cavities were synthesized. After their concentration, the pollutants are degraded by a novel developed non-equilibrium plasma based reactor operating at the boundary between the liquid and gas phases for the effective decomposition of refractory pollutants.

Sustainable water resources development and management needs reliable new strategies. Special attention should be drawn to the removal and degradation of toxic trace pollutants, which can easily pass through sewerage treatment plants due to interfering substances present at higher concentration. Thus, contaminants like pharmaceuticals and endocrine disrupting compounds are consistently infused and detected in surface waters, ground water, and drinking water.

In this project, we develop innovative technologies for the selective concentration and the subsequent degradation of persistent pharmaceuticals such as Carbamazepine (CBZ), Clofibric acid (CF), and iopromide (IP) from waters.

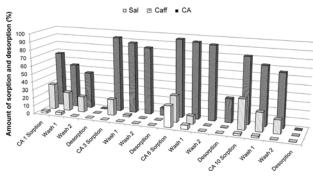


Fig. 1: Adsorption of carbamarzepine (CA) from a complex landfill leachate solution containing caffeine (Caff) and salicylic acid (Sal) by selective sorbents and desorption of the pre-concentrated carbamazepine

Polymer adsorbents

The antiepileptic drug CBZ has low biodegradation in waste water treatment plants. In order to selectively remove CBZs from the aqueous medium, we synthesized a series of CBZ-imprinted polymers as specific filter material by varying the composition parameters. Tests about the efficiency to which they selectively remove the contaminant CBZ from polluted water showed that most of the developed materials had an excellent uptake of the target pollutant CBZ of more than 90% in water and 80% in landfill leachate mixtu-

res (Fig. 1), along with an effective separation from selected easily degradable accompanying substances. Almost 100% of the adsorbed pollutant could be released for further treatment and for reuse of the filter. The results of the CBZ uptake and release prove that the usage of CBZs is superior to that of the adsorbent activated carbon (AC), as the latter only unselectively binds both biodegradable and persistent compounds and is expensive to recycle.

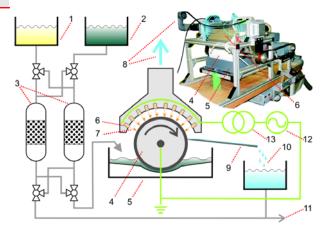


Fig. 2: Set-up of the combined system of selective adsorbents and the forward-rolling plasmareactor protoype

Plasma reactor

The degradation of the pre-concentrated CBZ, CF, and IP solution by corona discharge (Fig.2) was investigated. Two barrier electrodes, which provided an atmospheric pressure corona, were mounted above a transport roll that moved a thin water film of test solution. The rotating drum also served as the counter electrode. Numerous tests with various combinations of powers, rotational speeds, air gaps etc. were performed on single, mixed, and landfill leachate containing solutions. Effective removal of CBZ, CF, and IP occurred at a power output of 500 W. The combination of the highest rotational speed, with a reduced exhaust, and an electrode air gap of 1.5 mm achieved the best results.

steinfeld@kist-europe.de

Publications

Krause, H.; Schweiger, B.; Schuhmacher, J.; Scholl, S.; Steinfeld, U.: Degradation of the endocrine disrupting chemicals (EDCs) carbamazepine, clofibric acid, and iopromide by corona discharge over water, Chemosphere 75(2):163-8 (2009)

Schweiger, B.; Bahnweg, L.; Palm, B.; Steinfeld, U.: Development of Molecular Imprinted Polymers (MIPs) for the Selective Removal of Carbamazepine from Aqueous Solution. World Academy of Science, Engineering and Technology Vol. 54: 2009

Multistage Hybrid-Immuno-Chemotherapy for Cancer treatment

For the treatment of cancer, we developed a new multistage hybrid-immuno-chemo-therapy. The overall strategy was to exploit the capability of the patient's own immune cells to not only act as natural killers, but also as a living drug targeting system. So, high specificity of the cellular immunotherapy and high effectiveness of chemotherapy were combined.

While the main benefit of cellular immunotherapy lies in the high specificity of cancer cell targeting, the treatment by chemotherapy is characterised by high effectiveness.

Our present strategy combines the advantages of both of the therapies.

The recruitment of cytotoxic T lymphocytes (CTL) to the tumor site and the activation of CTL effectors' functions are part of the natural immune response. Tumor cells, however, are able to induce an antigenspecific tolerance or anergy and thus escape the immune surveillance.

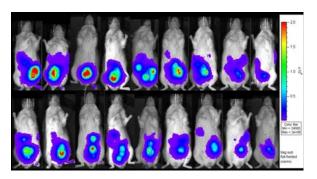


Fig. 1: Tumor growth 43 days
Upper panel: Immunotherapy treated mice
Lower panel: Multistage Hybrid-Immuno-Chemotherapy

To overcome tolerance and to additionally enhance the cellular-mediated cytotoxic effect, we produced artificial tumor-specific CTL. Therefore, we retargeted polyclonal activated CTL with a BiAb and additionally loaded them with cytotoxic cancer drugs.

For this purpose, we selected the BiAb EpCAMxCD3 (HEA125XOKT3)*, which includes an anti-CD3 x anti-tumor—associated antigen (TAA) unit. So, the conventional major histocompatibility complex restriction is circumvented, and the CTL mediate perforin/granzy-me cytotoxicity. This is how the usage of polyclonal CTLs for the therapy is made possible.

Additionally, these BiAb redirected tumor targeting CTLs were loaded with an anticancer drug to use them as a living drug targeting system. Target specific deli-

very and release of the drug can enhance the CTL mediated perforin/granzyme cytotoxicity on carcinoma cells.

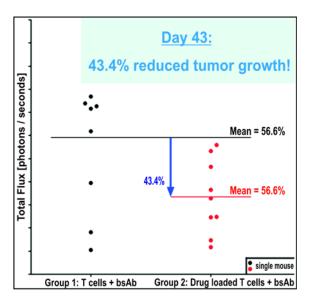


Fig. 2: Tumor growth in mice (43 days) following different treatments: Group 1: Immunotherapy treated mice Group 2: Multistage Hybrid-Immuno-Chemotherapy treated mice

Up-to-date results of *in vivo* studies with NOD SCID mice underline the feasibility and potential of this new cancer treatment strategy:

CTL, loaded with Idarubicin and retargeted by BiAb EpCAMxCD3, recognize and kill carcinoma cells. The cancer cell killing rate was increased by approximately 43%, when in addition to the effect of the intrinsic perforin/granzyme cytotoxicity, Idarubicin was released from the retargeted carrier cells. Amazingly, the drug amount loaded here was less than 5% of the drug amount applied in a conventional chemotherapy.

*kindly provided by Dr. G. Moldenhauer, DKFZ

steinfeld@kist-europe.de hee@kist-europe.de

Bio Cell Processor for Drug Discovery

μTAS, Lab On A Chip, Cell-based Assay

Aim of this project is the development of a versatile, micro-sized bio cell processor feasible for long-time and multi-parameter monitoring of viable cells in vitro. Functionality of the chip includes transport of cells and reagents, cell-sorting and —cultivation as well as bio-chemical analysis systems. An array of those functional compartments with several in- and outputs for reagents and media allow for a highly reproducible, multiplexed analysis of target cells over a long period of time.

LMM* and KIST-Europe develop a LOC device for cell-based, high-throughput screening of defined numbers of viable cells providing automation from sorting to analysis of cells and media. Modular design with convertible parts allows versatile operation with different cell lines and a range of detection methods.

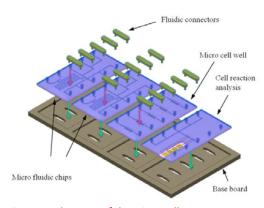


Fig. 1: Total system of the micro cell processor

Currently the development focus of KIST-Europe lies on design and make-up of the μ -structures for cell attachment for the cell culture unit. Materials were investigated for their suitability for fast and reliable immobilization of cells. Choongnam Universities` superhydrophilic resin (SHR), Fibronectin and Collagen IV (ubiquitous proteins of the ECM), glass and PDMS were used as substrate. SHR is based on sulfonated SiO_2 - TiO_2 and is synthesized by binary sol-gel reaction of TEOS- $TiCI_4$ and subsequent sulfonation (contact angle 7°). It has excellent coating processibility on various substrates (roughness <1nm, thickness 20nm—2 μ m) and a controllable wetting range.

Glass and PDMS substrates were spin-coated with SHR (D3.5, D4, D4-dopamine) and cured by plasma oxidation at 50°C/5h and 100°C/2h. Fibronectin and Collagen IV coated slides were commercially available.

For a survey of the substrates adhesive properties, the well-established cancer cell lines, MCF-7 (human breast carcinoma, epithelial-like monolayer) and Jur-

kat (human T cell leukemia, suspension cells) as well as naive T cells were incubated at 37°C/5% CO₂ for varying periods of time. Subsequent exposure to a uniform strain force removed false positive cells only residing on the surface rather than having contact to the substrate.

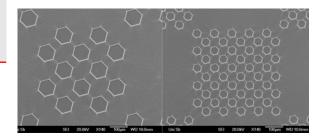


Fig. 2: Fast cell adhesion patches for micro cell chamber

The amount of cells left in the wells was measured with CASY counter (Schärfe Systems, Germany) and cells immobilized on substrate were counted by using microscope. All of the cell lines showed considerable adhesion levels to the substrate (except PDMS and bare glass) in various timeframes. No substrate showed elevated levels of cell adhesion less than 1h. However, T cells generally exhibit only weak tendency to form tissue or complexes with other cells or the ECM besides specific interaction like rolling along blood vessel walls or conversion into the lymphatic system at high endothelial venules. Using rare or unusual cell types, a different strategy for the construction of the adhesion patches needs to be devised.

2D SHR patch arrays were produced using $\mu\text{-CP}$ with a PDMS stamp. Micro molding pattern was fabricated with negative photoresist (SU-8 10, 12 μ m) which was cured by soft baking at 65°C/2min and 95°C/5min, UV exposure for 7 seconds and post expose baking at 65°C/2min and 95°C/3min. Dimensions from 5 to 100 μ m and either square or hexagonal shape were realized.

hee@kist-europe.de seidel@lmm.uni-saarland.de

* LMM: Lehrstuhl für Mikromechnik, Mikrofluidik / Mikroaktorik, Unversity of Saarland

Publications

"Micro Cell Adhesive Patch array with Super Hydrophilic Resins for drug discovery", Jihwang Park, Sungjune Park, Michael Müller, Jungtae Kim, Lan-Young Hong, Sang-Hee Jung, Dong-Pyo Kim, Hyeck-Hee Lee and Helmut Seidel, The 13th International Conference on Miniaturized Systems for Chemistry and Life Sciences (2009)

"Hydrophilic adjuvant", KIM, Dong-Pyo et al., World Intellectual Property Organization, WO 2007/069867 A1 (2007)

μ-CIMACS(Micro Continuous Immune-Magnetophoretic Cell Sorter)

Micro Cell Sorter, MACS, Fast Cell Capturing, Uniform Magnetic Mobility

A new micro continuous immune-magnetophoretic cell sorter (micro CMACS) has been developed to isolate T lymphocytes from biological suspensions such as whole blood. By using two permanent magnets, the micro cell sorter is designed to isolate target cells continuously and automatically without a preliminary labeling process which is often acting as a bottleneck in automated micro cell sorters. The fast capturing method of the target cells was achieved in the straight or curved microfluidic channel within 20 seconds of flow time.

Micro continuous immune-magnetophoretic cell sorter which utilizes unique 2 magnets system and the fast target cell capturing method has been developed. Several advantages over conventional micro cell sorters have been achieved as follows.

- · Continuous / full automatic operation
- Fast capturing of target cells within 10-20 seconds.
- Integration of labeling process with magnetic particle).
- No or minimum dilution of the sample(blood.)
- No mixing between sample and particle solution.
- · No other reagent or buffer.
- · Less non-specific binding.
- · Minimum use of Antibody: cost effective.
- · Very specific targeting (immune-affinity).
- · Cost effective with simple devices and chip.

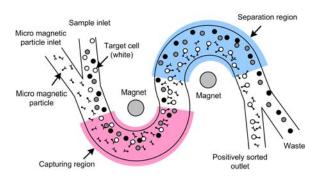


Fig. 1: Conceptual diagram of micro CIMACS

A PMMA micro chip has been fabricated with 50 μm deep and 300 μm wide microchannels, by using hot embossing and thermal bonding process. T lymphocytes for the target cell and anti-human CD3 magnetic particles (Chemicell SiMAG, 1 μm diameter paramagnetic particles) have been used for cell sor-

ting experiments. The cell suspension has been prepared having human erythrocytes and T lymphocytes mixture (1x10⁶ cell/ml each). With a 3 mm/s of flow speed for each inlet, the cell suspension and the particle solution (1x10⁸ particles/ml) were introduced to the chip. The samples of outlets were collected and measured by FACS flow cytometer after target cell isolation. As a control, a conventional batch-wise sorting experiment with equal quantities of cells and particles was performed. The protocols of the respected particle providers were used to carry out the experiment.

Results shows higher recover rate and capture rate of the μ -CIMACS cell sorter with curved channels and competitive purity rate which is relatively 87% of the manual work which were performed by standard procedures in laboratory.

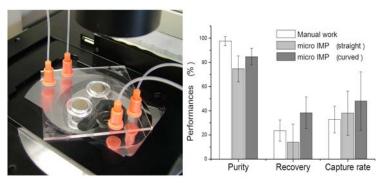


Fig. 2: The experimental setup and T lymphocyte sorting results

The iso-motive magnetic field gradient in the curved channel prevented magnetic particles from subsequent bunching and immobilization to each other and to the channel walls. As the further study, magnetic force optimizing will be performed by using electromagnets which can provide more controllability of the magnetic field and target cell sorting directly from whole blood as well as buffy coat will be tested also.

tais@kist-europe.de

Publications

Kim, J.; Lee, H.-H.; Steinfeld, U.; Seidel, H.: Fast capturing on micro magnetic cell sorter, *IEEE Sensors Journal*, Vol. 9 (8) (2009) 908-913

Kim, J.; Park, J.; Müller, M.; Lee, H.-H.; Seidel, H.: Curved channels of immune-magnetophoretic micro cell sorter for uniform magnetic mobility, *The 13th International Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS)*, Jae-Ju, Nov. 2009

Search for peptide inhibitors against P450 using phage display Cytochromes, ELISA test, inhibitor, Phage display

Overexpression or deficiency of P450 results in disorganization of signal transduction and gene-expression and can produce cardiovascular-diseases and cancer. The common inhibitors of steroid biosynthesis in clinical use e.g. mitotane, have little selectivity and extra-adrenal effects are likely. In this project we started an innovative approach using phage display to screen for the first time for peptides which selectively and specifically inhibit cytochromes P450. This will open a new class of potential inhibitors of CYPs with less side effects on the endocrine system.

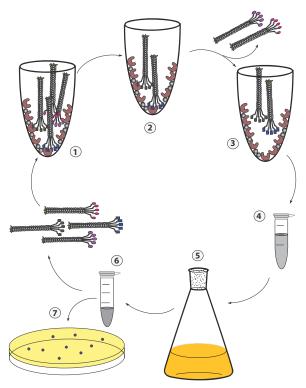


Fig. 1: Affinity selection procedure. Phage library displaying different peptides at the N-terminus of minor capsid protein plll. The phage particles are added to an immunotube already coated with the target of interest and blocked with e.g. BSA solution (1), after incubation, non-binding phages are washed off from the tube (2), the bound phages are eluted from the target by pH denaturation with 0.2 M Glycin-HCl pH 2.2 (3), neutralized with 1M Tris-HCl pH 9.1(4) and amplified by infection in E.coli (5). The purified phages are plated out (7) for the estimation of the titer. The steps 1-6 are then repeated for more times starting with purified phages from the previous round.

Cytochromes (CYPs) are involved in conversion and breakdown of molecules like drugs and xenobiotics and in the biosynthesis of a variety of very important endogenous compounds. When CYPs are over-expressed or deficient, pathological effects like cardiovascular diseases and cancer can occur. There are already some drugs in clinical use that inhibit steroid

biosynthesis, but they have a little selectivity thus extra-adrenal effects are likely. Non-steroidal inhibitors could lower the side effects on the endocrine system that's why we want to find peptides that specifically selectively inhibit cytochromes. For this purpose we use the phage display technology [Fig.1]. Combinatorial peptides are fused to one of the capsid protein of the phages therefore creating a phage library. They can be expressed to the N-terminus of the major coat protein pVIII (ca. 2700 copies) or to the minor coat protein pIII (ca. 5 copies) of M13 filamentous phages. Such phage libraries are able for molecular interactions with targets of interest that are bound to a surface of plastic by nonspecific hydrophobic or electrostatic interaction or to special magnetic particles by corresponding binding. After blocking and washing steps phage libraries are passed over the bound target. Then the non bound phages are washed away and the bound phages are eluted from the target by a pH denaturation step. Once the pH is neutralized the phages are infectious and thus can be further amplified and used for additional screening called affinity selection or panning. Several panning rounds later, this differs between 3-4 rounds, one gets an enriched pool of binders.

To establish this method for Cytochromes we used the enzyme CYP 106 A2 from *Bacillus megaterium ATCC 13368* as our starting target. We decided for this prokaryotic cytochrome due to its advantages. Bacterial cytochromes are more stable and their solubility is characteristic for them. So one can purify them and handle very easy. Aside from this they are much better available due to higher expression levels. Thus our first target CYP 106A2 serves as a model for mammalian steroid hydroxylases and was produced in the Lab of Prof. Dr. Bernhardt's group.

We conducted three rounds of affinity selection and picked randomly 40 phage clones from a titering plate and then amplified them. The specificity of the selected phage clones to the target CYP106A2 was confirmed by an Enzyme-linked Immunosorbent Assay (ELISA). In this experiment the optical density (OD) signals from phages bound to the target were compared to the signals generated by the same phages bound to the uncoated, milk blocked wells. As an additional negative control unmodified M13 phages were used. Our ELISA test [Fig.2] showed high ratio signals, so 30 candidates with the best CYP/Milk binding ratio were chosen for sequencing. We could find 6 different peptide sequences.

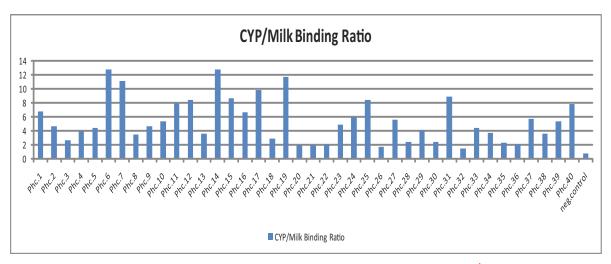


Fig. 2: ELISA results. The binding specificity of 40 randomly picked phage clones after the 3rd biopanning round was tested by ELISA. The ratios of OD signals from phages bound to the target and the signals from the same phages bound to the uncoated, blocked wells are shown. As negative control unmodified M13 phages were used.

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Schuster, I.; Bernhardt, R.: Inhibition of cytochromes p450: existing and new promising therapeutic targets, Drug Metabolism Reviews 39, no. 2-3 (2007) 481-499

Appert, A., Nam, C.H., Lobato, N., Priego, E., Miguel, R.N., Blundell, T., Drynan, L., Sewell, H., Tanaka, T., Rabbitts, T.: Targeting LMO2 with a peptide aptamer establishes a necessary function in overt T-cell neoplasia. Cancer Res. 69 (2009) 4784-4790

Development of diagnostics for Ankylosing Spondylitis Bacteriophage, Biomarker, Biosensor

To identify Ig VH gene usages in Korean ankylosing spondylitis (AS) patients, expression level of VH2 genes from peripheral blood mononuclear cells of 8 AS patients and 9 healthy donors was analysed by Q-PCR. Q-PCR results demonstrated VH2 genes were overexpressed in AS patients. The sequence analysis revealed the majority of them contained CDC42 binding protein kinase beta (CDC42 BPB) genes. Our study revealed VH2 overexpression and unique rearrangement in Ig VH genes from peripheral blood of AS patients.

Ankylosing spondylitis (AS), a prototype of spondyloarthritis (SpA), is a chronic inflammatory arthritis that mainly affects the sarcroiliac joints and the spine. It is characterized by peripheral arthritis, enthesitis, and extraskeletal features such as uveitis and inflammatory bowel disease.

Analyses of immunoglobulin (Ig) variable region (V) gene usages have revealed differences in the basic Ig V repertoire of patients with B cell- and/or T cell-mediated autoimmune diseases, including systemic lupus erythematosus, myasthenia gravis, rheumatoid arthritis, and Sjögren syndrome, compared to healthy controls. Such differences could be derived from intrinsic abnormalities in the generation of Ig V genes or B cell development and functions. Thus, the analysis of Ig V gene usages can offer new insights into possible pathogenic role of B cells in diseases.

We investigated VH germline gene usages of patients with AS compared to healthy donors using Q-PCR with additional primer sets (Fig1A). Q-PCR results show that there was significant difference in the level of expression of VH2* genes between healthy donors and AS patients (relative amount of mRNA of VH2* genes to human acidic ribosomal protein (HuPo), 0.68(mean) / 0.55(SD) and 7.13(mean) / 7.77(SD), respectively; p=0.024, Fig1B)

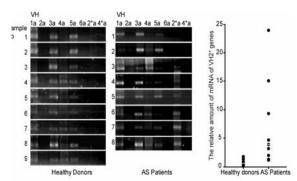


Fig. 1: (A) Comparison of VH gene usages in PBMCs from healthy donors and AS patients. (B) Comparison of the relative amount of mRNA of VH2* genes to HuPo in AS patients and Healthy donors

Strikingly the sequence analysis and homology search of overexpressed VH2* PCR products revealed unexpected features of VH gene structure. In the sequences of VH2* PCR products, a short stretch of CDC42 BPB intron gene was found (Fig. 2). It is worth noting that this intron segment is located in chromosome 14q where human Ig VH gene locus is present. Ig gene rearrangement requires recombination signal sequences (RSS) that consist of a heptamer, 23 nucleotides (nts), and a nonamer in this order. A short stretch of intron sequences of CDC42 BPB was found between VH and DH genes. The 5' end of this fragment includes homologous region (15 nts) to that of the VH2 germline gene (Fig 2).

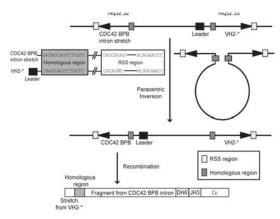


Fig. 2: Proposed gene structure of rearranged VH2* genes in AS patients.

Interestingly, further analysis of CDC42 BPB genomic sequences identified a nonamer of RSS, which is located following an insertion site of this fragment by 18 nts, exists in CDC42 BPB genes. In addition, a heptamer-like sequence (CAGCAGAG), which has one G base added feature to generally known heptamer of RSS (CACAGAG), also appears in the end of the inserted CDC42 BPB intron genes, as seen in Fig 2. This gene structure implies that unusual gene rearrangement or recombination may occur during construction of VH gene segments during B cell development in some of the AS patients. Paracentric inversion following recombination activating gene (RAG)-based recombination might be suggested to explain unique rearranged VH2* gene structure (Fig 2).

yeonjookim@kist-europe.de chang@kist-europe.de

Publications

Kim, Y.J.; Kim, N.: Lee, M.K.; Choi, H.J.; Baek, H.J.: Nam, C.-H.: VH2 overexpression and unique rearrangement in immunoglobulin variable heavy chain genes from peripheral blood of ankylosing spondylitis patients. Experimental Molecular Medicine. 2009, submitted.

Kim, Y.J.; Baek, H.J.: Nam, C.H.: The primer sets for As diagnostics. 10-2010-0001904 (2010) Patent

Isolation of peptide regulators of focal adhesion kinase Phage display library, biopanning, focal adhesion kinase

Isolation of allosteric regulators of the signal transducing focal adhesion kinase (FAK) can be useful in the development of anti-cancer drugs, because this enzyme is overexpressed in invasive tumors and probably plays an important role in the development of metastasis. In order to identify the potential inhibitors and/or enhancers of the FAK activity, screening of the phage display peptide library was performed. Several FAK binding peptide were identified after biopanning experiments and their binding ability was confirmed by ELISA.

Focal adhesions are integrin-mediated points of contact between the cell surface and the extracellular matrix. Focal adhesion kinase (FAK) integrates signals from integrin and growth factor receptors to regulate cellular responses including cell adhesion, migration and survival. FAK is autoinhibited by domain interaction and activated by phosphorylation.

Since this enzyme is overexpressed in invasive tumors and most likely plays an important role in the development of metastasis, isolation of allosteric regulators of the FAK can be useful in the development of anticancer drugs. Short peptides are very promising in development of treatment of several diseases and might represent a group of such regulators.

Phage display peptide library

Immobilized target

Binding

Stringent wash

Phage elutions

Fig. 1: Biopanning with the peptide phage display library

Screening of the random peptide libraries - either yeast or phage display - has emerged as a great tool for the investigation of protein function or regulation (e.g. inhibition, activation or modification). Peptide inhibitor (or regulator) screening strategy has several advantages: easy library construction, high selectivity

and specificity because of the large size of the library, efficient and low cost screening procedure (Fig. 1).

As a target for the phage display peptide library screening the purified FAK is used. The protein is bound to the microtiterplate and incubated with the phage library. The phages containing peptides capable to bind to the target protein are eluted after the washing out of the unbound phages. Then the phages with potentially binding peptides are amplified and the selection is repeated. After 3 or 4 rounds of the phage amplification and selection the enrichment of the binding sequences occurs.

These biopanning experiments require optimization of several steps for the specific target protein and therefore different condition were tested for FAK protein including optimization of target concentration, wash stringency, elution conditions.

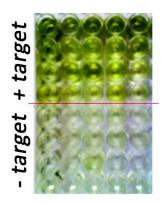


Fig. 2: ELISA - microtiter plate
wells either coated with
FAK (+target) or without
protein coating (-target)
after detection reaction
indicating binding of the
eluted phages (yellow
color).

further analyzed for
their ability to affect
the function of FAK.
Identification of these
peptides enables
further investigation of

After different pannig experiments several random phage clones were selected after elution and amplified. These clones were further analyzed through ELISA (Fig. 2). So, the screening lead to the isolation of the pool of the binding sequences which can be their ability to affect Identification of these peptides enables further investigation of FAK regulatory

mechanisms as well as development of FAK inhibitors for drug development.

o.perlova@kist-europe.de chang@kist-europe.de

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Computational methods in chemical risk assessment under new chemical regulations QSAR, PNEC, Risk Assessment, REACH

Recently, several new chemical regulations reforms were introduced worldwide. In Europe, the new regulation Registration, Evaluation, Authorisation and Restriction of Chemical Substances (REACH) was adopted. Companies attempting to fulfil REACH requirements were challenged with the limited available testing facilities and the increasing opposition to animal testing approaches. To overcome these challenges, non-testing (computational) approaches provide great assistance. In this area, we focus mainly on QSAR applications and mixture toxicity prediction.

Non-testing approaches using Quantitative Structure-Activity Relationship (QSAR) models were strongly encouraged to predict substances' physico-chemical, environmental and toxicological properties in the context of the new European chemical regulation REACH. The extensive use of these methods to produce data for the purpose of fulfilling REACH registration requirements raises the question about the accuracy and reliability of the obtained results. To highlight this issue, an evaluation attempt of some non-testing models was conducted in one of our projects.

In this project, several physico-chemical, environmental and toxicological properties of a group of similar substances (DBP and similar substances) were determined using different non-testing models. Direct comparison of the obtained data with the available tested data was used to verify the applicability of these models in data gap filling under REACH registration.

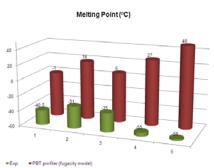


Fig. 1: Comparison of experimental and estimated melting point values of 5 DBP-like substances

value- and trend agreement. In the light of this study the possibility of pro-

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ducing results largely deviated from the right values was confirmed. It was recommended to apply non-testing methods with great care to avoid drawing chemical and environmental risk assessment conclusions on the basis of wrong inputs.

Chemical risk assessment for human health and the environment frequently focuses on single substances in conducting the risk characterization of chemical products and mixture. Nevertheless, living organisms including human beings are normally exposed to chemical mixtures rather than individual substances.

Conducting toxicological tests for a whole chemical mixture as a single entity might be regarded as unrealistic expectation because the number of combinations of every substance found in the environment or used in chemical products is almost infinite. Appropriate and reliable mixture toxicity prediction models are hence needed.

To over-come such difficulties, new concepts and techniques in computational toxicology are being attempted



to predict the mixture toxicity. Advances in

predict Fig. 2: Using computational approaches the PNEC of a mixture may be predicted for the PNEC values of its individual components

molecular biology and chemistry are combined with modelling and computational science to strengthen the predictive ability in this area of toxicology.

This approach enables us to:

- effectively assess the hazards posed by the many chemicals present in our environment;
- determine the risk of chemical exposure at low levels of exposures;
- better predict the effects of chemicals across species; and
- reduce research costs.

jwkim@kist-europe.de samer.aburous@kist-europe.de shkim@kist-europe.de

Publications

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Effective Use of Exposure Assessment tools for Exposure Estimation

REACH, risk assessment, exposure estimation, exposure assessment tools

Under REACH regulation, the exposure assessment is required and aims to evaluate the potential exposures to humans and the environment from all life cycle stages of a chemical substance. In the case of absence of measured exposure information, computer models are often used to estimate various exposure scenarios from product use, ranging from worst case to most likely. The main study is on the process of exposure estimation and the related estimation tools, especially on the practical applications of available tools.

According to the new EU chemical regulation - REACH, if a substance meets the criteria for classification as dangerous or is considered to be a Persistent Bioaccumulative and Toxic Substances / very Persistent, very Bio-accumulative (PBT/vPvB). Substance, an exposure assessment is required. The goal of the assessment is not to establish whether or not there is risk, but to identify and describe the conditions under which the risks are controlled.

Conducting of exposure assessment includes the development of exposure scenarios and exposure estimation. An exposure scenario can be derived using a tiered approach to exposure estimatimation. Initially a first tier exposure estimate can be used to derive a 'reasonable worst-case' exposure, which has the most potential that the risk may not be controlled. Subsequent higher tiered estimates can be used to further characterise the exposure.

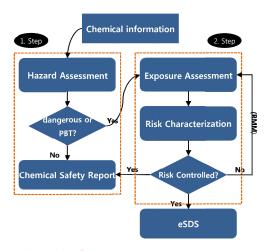


Fig. 1: Chemical Safety Assessment process

To estimate exposure, ideally, the estimating process would be based on actual measured exposure data. However it will not always be possible. If there is no measured data available or the measured data is not sufficient for the exposure estimation, the modeled

estimates should be considered. In many cases, a combination of measured data and modeling approaches may lead to the most appropriate assessment.

There is a wide range of exposure estimation models that could be used to estimate exposures for the specific purpose of developing an Exposure Scenario. The different models vary in their complexity and purpose. Some models have been developed and used as initial screening (Tier 1) models e.g. the ECETOC TRA and COSHH-BAuA-Tool. Some other models have been designed for one specific purpose, such as RIS-KOFDERM model for dermal exposure estimation. These models often provide more accurate estimates of actual exposures. But because they demand expert knowledge to operate them, they are generally only used if a Tier 1 approach indicates a potential for concern.

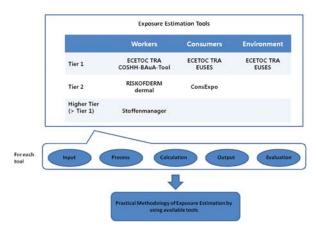


Fig. 2: Study on the use of exposure estimation tools

Although many models are available, there is less guidance on how to choose a proper model for the exposure estimation. The choices vary because of different pathways of exposures. This study summaries the strength and limitations of a number of existing tools in the context of REACH and also contains the comparison of different exposure estimation tools. Some practical questions, like which kind of model can be used as the preferred tool for estimation of a specific exposure route (e.g. for inhalation, dermal, oral) and at which tier level, are discussed. Finally according to the practical situation of Manufacture/ importer or downstream user, based on the information on uses and conditions, an appropriate estimation tool can be selected. Furthermore a case study is described in detail.

> zhang@kist-europe.de shkim@kist-europe.de

Development of energy efficiency management system

Energy saving system, smart meter, sensor network

In this project, we have developed an efficient energy monitoring and management concept and design based on internet and communication technologies for households and buildings to realize energy saving system. As shown in Fig. 1, households and building have a significant energy saving potential compared with other sectors. For efficient energy management saving, measurement, monitoring management of energy consumption information are required. In the developed concept and design, wireless sensor was installed to measure the energy consumption like a smart meter and home gateway was integrated to monitor and manage the energy consumption.

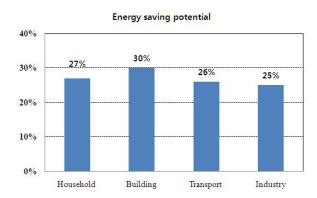


Fig. 1: Energy saving potential

Wireless sensors are attached additionally in the conventional power taps, which means they are independent from electronic products. They have ZigBee or IEEE 802.15.4 network interface for communication. Because wireless sensor network is used in our system, the mobility of the nodes is higher than wired communication network. Also, this concept and design could be installed without additional communication infrastructure. It has several services such as analyzing energy consumption, identification of inefficient appliances, and remote power control.

Wireless sensor has a ZigBee network interface for communication. It measures AC current and voltage information. It receives remote power control signal from an energy portal or an intelligent home gateway. Because it is attached in general power taps, it could be used with all of the house appliances.

Intelligent home gateway is a monitoring and management component of the proposed concept and design, which is based on OSGi(Open Services Gateway initiative). It has various network interfaces like a conventional home gateway. Additionally, it has ZigBee network interface for energy consumption

monitoring and management. All of the services are implemented in it.

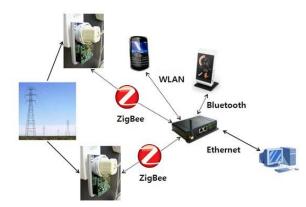


Fig. 2: Conceptual diagram of energy management system.png

Fig. 2 shows a conceptual block diagram of the proposed concept and design. Wireless sensors in power taps are connected to an intelligent home gateway with ZigBee network interface. Home gateway as an energy portal provides a transparent interfaces to end-user. Easy and convenient user interfaces for different network devices will be provided. For example, cellular phones, MP3 players with network interface like Wi-Fi, and PC with Ethernet interface will be supported.

Smart grid is a critical infrastructure of the future power system. For efficient electricity management, bidirectional information exchange is required between power companies and subscribers. Our proposed system could be extended to a smart grid system. We expect that the proposed system is not only an energy saving system but also basic unit for smart grid integration in the future.

hwang@kist-europe.de jhseo@kist-europe.de whkim@kist-europe.de

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EU Projects on S&T cooperation enhancement between EU and Korea

KESTCAP, KORRIDOR, Korea EU Science and Technology Agreement, International Cooperation, Korean R&D and Innovation Programs, ACCESS4EU

KESTCAP, Korea EU Science and Technology Cooperation Advancement Programme, is based on the joint Korea-EU interest and aims of mutual benefit by strengthening the S&T agreement between Korea and the EU. The major objectives are to develop sustainable S&T cooperation strategies, to disseminate information and promote cooperation, and to organize and support cooperative events between Korea and the EU.

KORRIDOR (Stimulating and facilitating the participation of European researchers in Korean R&D programs) project aims to widen and strengthen the RTD cooperation between Korea and the EU in common research areas of interest by opening the opportunities for European researchers in Korean research and innovation programs, facilitating joint research initiatives supported by the Korean side, and improving the cooperative climate between Europe and Korea.



Fig. 1: KESTCAP Top down Forum 2009

KESTCAP, Korea EU Science and Technology Cooperation Advancement Programme, is based on the Science and Technology agreement signed between Korea and EU, Nov. 2006. The basic principle of this agreement includes mutual and equitable contributions and benefits; mutual access of the research and technological development programme, projects and facilities of each party by visiting each other; timely exchange of information which may concern cooperative activities; promotion of a knowledge-based society for the benefit of an economic and social development of the parties; and protection of intellectual property rights. The specific objectives are to develop sustainable cooperation strategies; disseminate information and promote cooperation; and organize and support cooperative events between Korea and the EU.



Fig. 2: KESTCAP logo

The programme seeks to provide a platform to strengthen the S&T agreement between Korean and the EU; improve the cooperation by identifying S&T fields of common interests of Korea and the EU; set up a website and information help desks to respond to specific inquiries on existing opportunities and available funding instruments; and contribute to the Korea-EU policy dialogue on science, technology, and innovation. The project plan is described in five work packages, one for management and the other four for supporting the activities. The individual tasks of the work packages cover a broad range of activities such as creating and maintaining a web portal with an extensive database of partners and also providing the information on S&T issues, published calls, and preparing of reports and supporting the Korea-EU S&T fora.



Fig. 3: KORRIDOR as a part of ACCESS4EU program

KORRIDOR project aims to open all existing thematic and organizational options to European participation and study the participation regime and existing problems to develop recommendations. The Korean RTD programs Helpdesk service set up in Europe will provide fast and free consulting and advising services about the access opportunities, legal, organizational, financial and cultural issues and available supporting mechanisms. This Helpdesk will monitor the participation of European researchers in Korean RTD programs and distribute this information to all stakeholders. The aim is to equip existing multipliers (European

INCO NCPs, all Korean FP7 NCPs) with the project findings and facilitate partner search and consortia building and provide consulting and advice both in Europe and Korea.



Fig. 4: KORRIDOR logo

The project delivers the impacts as following: In a short-term, identification of most suitable funding opportunities, provision of clear and transparent

guidelines for their uptake, building a system of facilitation services (Helpdesk, NCP network), dissemination and promotion. In a long-term, identification of existing obstacles and pitfalls (legal, organizational, etc.) and direct dialogue with the major agenda-setting entities of EU-Korea S&T Cooperation will initiate necessary improvements in the frameworks for European participation in Korean RTD programs. The improvement of the frameworks shall lead to the increase of effective collaborations of European research organizations in Korean programs, as well as the less-readily measurable improvement of mutual understanding of the respective research systems in Europe and Korea.

kicheol.kim@kist-europe.de (KESTCAP) helenkim@kist-europe.de (KORRIDOR) kangmj@kist-europe.de

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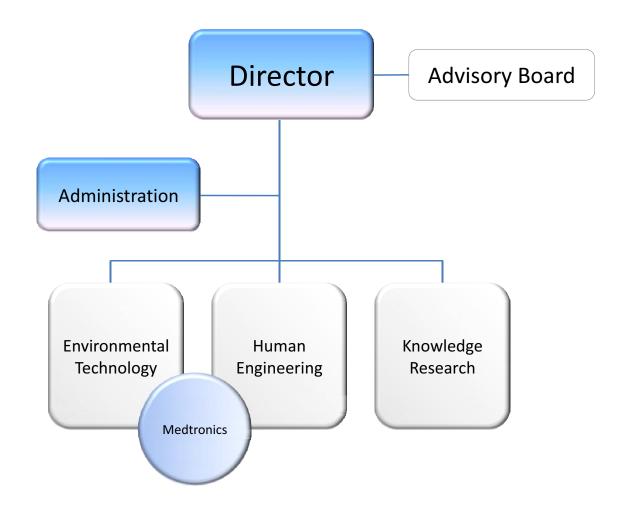
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Nano Letter	2008	Salieb-Beugelaar, G.B. et al	10.4
Cancer Res	2009	Nam, CH. et al	7.5
Lab Chip	2009	Salieb-Beugelaar, G.B. et al	6.5
Lab Chip	2008	Cai, Y. et al	6.5
Lab Chip	2008	West, J. et al	6.5
Oncogene	2008	Nam, CH. et al	6.4
Anal Chem	2009	West, J. et al	5.7
Biosens Bioelectron	2009	Jose, J. et al	5.1
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Electrophoresis	2008	Ohno, K. et al	3.6

KIST Europe Organisation



Dr. Kwang Ho Kim

Director

phone +49 (0) 681 9382-100 e-mail kwhkim@kist-europe.de

Prof. Dr. Andreas Manz

Head of Research

phone +49 (0) 681 9382-210 e-mail manz@kist-europe.de

Young Jong Kim

Head of Administration phone +49 (0) 681 9382-200 e-mail yojokim@kist-europe.de

Dr. Ute Steinfeld

Group Leader Environmental Technology

phone +49 (0) 681 9382-220 e-mail steinfeld@kist-europe.de

Dr. Hyeck-Hee Lee

Group Leader Human Engineering phone +49 (0) 681 9382-250 e-mail hee@kist-europe.de

Dr. Jongwoon Hwang

Group Leader Knowledge Research phone +49 (0) 681 9382-325 e-mail hwang@kist-europe.de

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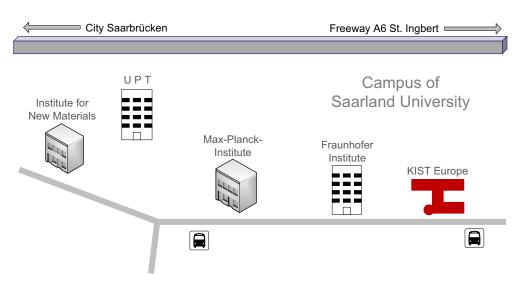
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<u>From east</u> (Mannheim/Karlsruhe) to University: Freeway "A6 Mannheim-Paris" up to the exit "St. Ingbert west". From there, follow up to the sign of "Universität Ost". Then finally you can find the main entrance of the university.

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Korea Institute of Science and Technology (KIST) Europe Forschungsgesellschaft mbH Universität des Saarlandes, Geb. E7 1 Campus E 7.1 66123 Saarbrücken

phone +49 (0) 681 9382-0 fax +49 (0) 681 9382-109 www.kist-europe.de

