Special Report 1

Towards the Realization of Personalized Medicine

Genotype Analysis System with SNP Chips

The ageing population, dwindling birthrate, and spread of obesity and lifestyle-related diseases have drawn increasing attention to the fields of health and medicine in Japan. Globally, the Millennium Development Goals targeted for achievement by 2015 through the combined efforts of international societies include various goals in public health, such as the prevention of the spread of HIV/AIDS, malaria, and other epidemics. Toppan imaginatively uses the technologies it has acquired through printing to develop businesses in support of health, one of the most important foundations for humankind and society.

Personalized Medicine and Toppan

When patients undergo personalized medicine, they receive optimal individualized therapies suitable for their own physical characteristics. A genotype screening of a patient with leading-edge analytical technologies before prescription of medication will enable a doctor to assess whether a drug will have a favorable or adverse effect on the patient and prescribe an appropriate drug at the optimal dose.

If adopted widely, personalized medicine will help to minimize the administration of drug regimens likely to be less efficacious or to have side effects. This, in turn, will help prevent and alleviate pain and physical burdens for patients and limit healthcare expenditures through enhancements in the efficiency of medical care.

Since 2003, researchers running the BioBank Japan Project on the implementation of personalized medicine have been laying the groundwork for the realization of personalized medicine in Japan. This project team has already collected DNAs, blood serum, and clinical data from some 300,000 subjects with 47 types of disease. With these samples and data, the team has been carrying out studies to identify how individual genetic differences correlate with drug efficacy, side effects, and disease.

Since 1999, Toppan has been establishing a set of new research themes with the aim of launching businesses in the life sciences, a field of growing importance for society. Based on the themes, the Company has worked together with RIKEN, Japan and other entities to develop a genotype analysis system with single nucleotide polymorphism (SNP)* chips for medical application. Toppan, RIKEN, and RIKEN Venture Capital Co., Ltd. jointly founded a new company called RIKEN GENESIS CO., LTD. in October 2007. Researchers at RIKEN GENESIS seek to realize the practical use of personalized medicine by providing genotype analysis services on a contract basis and marketing compact genotype analysis systems and chips applicable to patient examinations at hospitals and other healthcare facilities.

Millennium Development Goals
http://www.undp.org/mdg/

BioBank Japan Project on the implementation of personalized medicine
http://www.biobankjp.org/ (in Japanese)

RIKEN Center for Genomic Medicine at the RIKEN Yokohama Institute
http://www.src.riken.jp/english/index.html

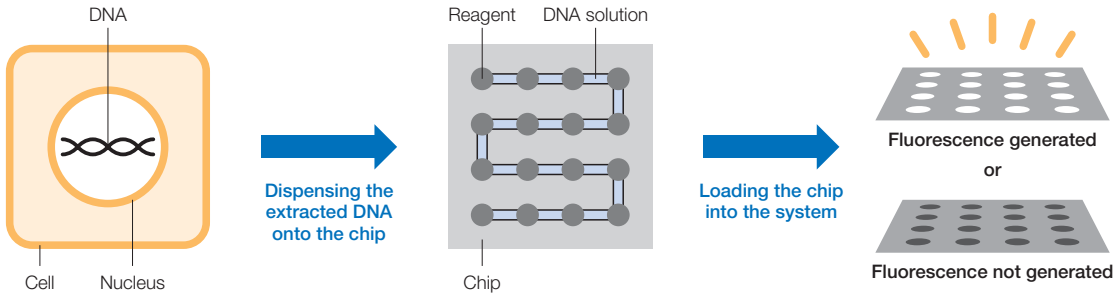
RIKEN GENESIS CO., LTD.
http://www.rikengenesis.jp/en/index.html

Genotype Analysis System with SNP Chips for Medical Application

With the genotype analysis system, a single SNP chip can determine a patient's genotype from a drop of the patient's blood in only an hour.

The procedure works as follows. A blood sample is collected from the patient. DNA is extracted from a blood cell in the sample, and a solution containing the extracted DNA is dispensed onto an SNP chip pre-coated with dots of

Analysis Procedure with an SNP Chip



dried reagent. The reagent on the chip can amplify a tiny strand of DNA on a massive scale and generate fluorescence when particular types of SNPs are applied. Based on the presence or absence of fluorescence activation via reaction with the reagent, the system can accurately predict differences in the patient's response to a particular drug, in terms of efficacy and side effects.

Various Toppan technologies acquired through printing are used to fabricate the chip, including techniques in microfabrication, surface treatment, formation, and coating. With these technologies, Toppan has formed a precision chip on which a tiny amount of DNA correctly reacts to the reagent and onto which the reagent can be coated with extreme accuracy.

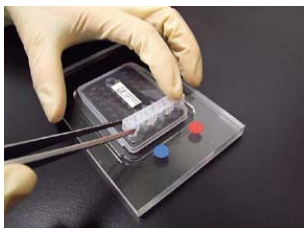
Clinical Studies in Thailand

The estimated number of HIV carriers stood at 33 million worldwide in 2007. An estimated 2.5 million people were newly infected, and 2 million or so died from AIDS. Though the growth of HIV carriers shows signs of slowing, tremendous numbers of people are still being newly infected. HIV/AIDS will remain a devastating social problem until drug makers develop medicines capable of completely curing AIDS after symptoms appear.

The HIV epidemic in Thailand spread relatively early in Asia and reached a serious stage in around 1990. Preventive activities by the Thai government to abort the epidemic have been effective, and the number of newly infected people has been decreasing. Yet even with the progress against the disease, an estimated 580 thousand people in Thailand were HIV carriers in 2005.

Toppan provides genotype analysis systems with SNP chips for studies on dosing strategies for anti-HIV drugs in Thailand. Tests are to be conducted to predict side effects of Nevirapine, a globally prescribed antiretroviral agent effective in postponing the onset of AIDS and preventing mother-to-child transmission of HIV. Nevirapine is relatively moderate in price, but patients treated with the drug can have side effects such as drug rashes. Mahidol University in Thailand and RIKEN in Japan have been conducting a study to determine the risk of drug rash before giving a patient Nevirapine.

Toppan will continuously provide its genotype analysis systems for various other research purposes besides that just mentioned. Applying the study results to practical use, Toppan will strive to upgrade its genotype analysis system in order to achieve broader medical application and more extensive benefits.



SNP chip (left) and genotype analysis system with SNP chips (right)

Laboratory in Ramathibodi Hospital, a facility attached to Mahidol University in Thailand

***SNP:** The individual variations from person to person at birth derive from differences in the estimated 3 billion base pairs in the genome sequence. A single nucleotide polymorphism (SNP) is a site in the genome sequence where a single nucleotide varies from person to person. Differences in SNPs cause individual variations, including variations in drug sensitivity and disease susceptibility. By examining these differences, physicians can tailor drug regimens and therapies to individual patients.

Special Report 2

Energizing the Mind through the Power of Art

Clinical Art

The human mind is sometimes unconsciously exhausted by our busy lives, relationships with others, and gaps between ideals and reality. More and more people of every age are overwhelmed by stress. Some lose confidence and are finding themselves trapped in negative mindsets; others close their hearts. And patients with dementia and their families suffer from heavy burdens. The fostering of creativity and compassion in children today is important for the society of the future. In fiscal 2008, the Toppan Group launched a new endeavor by enlisting a company that uses the power of art to help resolve various issues facing society.

Clinical Art

"Clinical art" is a type of art therapy that seeks to stir the senses and activate the right brain through creative activities such as painting and carving. Its purposes include the prevention of dementia, the cultivation of acute sensitivity, and the refreshing of tired minds. The Institute of the Formative Art Co., Ltd. in the Toppan Group operates a business using clinical art in Japan.

The Institute of the Formative Art began exploring the field of art therapy in the 1990s. Since 1998, it has researched and developed curricula as a member of the art therapy study group at the Kansei Fukushi Research Center at Tohoku Fukushi University. One of its main activities is to train clinical art instructors called "clinical artists" with specialized knowledge and the high-quality skills necessary for working in welfare and education. Some 150 clinical artists are now engaged in clinical art across Japan. As of the end of March 2009, two thousand people had completed training courses for clinical artists in Tokyo and other cities in Japan. Eight local governments and 11 medical corporations and healthcare facilities for the elderly have introduced clinical art therapy to prevent and remedy dementia among the elderly.

In addition to the training courses for clinical artists, the Institute operates original programs for children. Foremost among them are the Da Vinci Class to foster creativity in children (from two to twelve years old) and several programs to leverage the potential of art for the cultivation of aesthetic sensitivity, environmental awareness, and human compassion in daycare centers, kindergartens, and elementary schools.

The Institute has developed more than 400 types of clinical art curricula so far.

About the Curricula

Anyone can paint a picture. But how many people see painting as their forte? Every curriculum developed at the Institute is designed to encourage the participants to concentrate on the creation process and experience a sense of accomplishment and inspiration when they complete their artworks. The motto for clinical artists is "Touch, listen, and praise, but never judge."

The first step of the curriculum is to help participants feel the essence of the subjects of their pictures or formative artworks with their five senses. If the theme is rain, for example, they listen to the sound of falling rain. When the theme is a fruit, they taste the fruit, smell it, and hold it in their hands to feel the texture and weight.

The next steps are to create a representation of what they have just experienced by selecting and combining colors and materials into actual forms. When starting a picture, the participant is asked not to draw an outline, but to paint the background or spread the paint out in patterns that approach his or her mental picture. Through this

nuanced process of creation, anyone can create an excellent work of art with an individual worldview. The process activates the right brain by recruiting the five senses to work actively.

Every finished creation is an outstanding, highly individual artwork. In the last step, clinical artists praise the good elements of each work, without evaluating the skill of execution. When participants receive the praise, positive feelings such as joy, willingness, confidence, and self-affirmation are awakened in their hearts and delightful memories are formed.

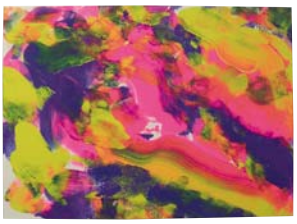
In fiscal 2008, Komatsu Elementary School in Kasukabe City in Saitama, Japan adopted this program for a period of integrated learning. The pupils experienced a clinical art curriculum first, then became supporters of clinical art for the elderly in the local community. The program has been ongoing since fiscal 2006. By cultivating children's individual sensibilities, the program encourages children to praise each other's works as a matter of course. It can also bring lively smiles to the faces of elderly participants. The program has been highly evaluated for its positive effects in both welfare education and the fostering of future generations.

Towards Fiscal 2009

Since November 2008, the Institute has been running a collaborative study with Tokyo University of the Arts. The purpose is to develop curricula with which to refresh the minds of working people and help them discover entirely new viewpoints and ideas. Toppan Group employees have participated in a test program as part of the study. The Institute will fully apply the curricula developed in this collaborative study to operate art salons and art-for-mental-healthcare business as a means of promoting mental health among working people.

With rising awareness of each person's need to make a social contribution, an increasingly wide variety of people are learning and experiencing clinical art. The Institute will continue to use the power of art to contribute to society in the future.

Example of a Curriculum: Bird of Paradise Flower (*Strelitziaceae*)



To stir the senses

With a roller spread out paints with colors imagined to be found in a tropical region. Imagining and choosing colors stimulates and sensitizes the mind.

To activate the right brain

Mark out the shape of the background. Focusing on the shape of the background activates the right brain.

To finish the work

Once the senses are sharpened, watch the *Strelitziaceae* carefully and paint in the details of the flower. The process "further" activates senses and helps the participants create works that give them great joy.