Korea

Korean Kimchi — A Possible Cure for Avian Influenza?

A team of researchers, led by Professor Kang Sa-ouk, of the School of Biological Sciences, Seoul National University, have found a lactic ferment extract from kimchi to be effective against the avian influenza (bird flu) virus and other viral diseases affecting poultry. The experiment was conducted on three groups of 13 chickens infected with the bird flu virus. The first group was given only water, while the other two groups were given either a concentrated or diluted culture fluid of *Leuconostoc kimchii*, a lactic acid bacteria extracted from kimchi. A week later, all the chickens in the first group died, but 11 chickens in each of the second and third groups survived and showed signs of recovery. In addition, the chickens in the second group fed with the concentrated culture fluid not only recovered fully but also showed a robust gain in weight from 750,800 grams to 1.5 kilograms, and diarrhea symptoms also ceased. "We found that the chickens recovered from bird flu, Newcastle disease and bronchitis. The birds' death rate fell, they were livelier and their stools became normal," said Prof. Kang. Prof. Kang's previous research had already proven the anti-bacterial power of *Leuconostoc kimchii* but recent research has found it to be effective in curing viral diseases in poultry.

Kimchi originated during ancient times when vegetables were preserved in salt for the purpose of lasting long, cold winters. Today there are more than 100 types of kimchi, depending on the materials used and length of fermentation unique to different regions in Korea. Typical fermentation process takes about 23 weeks at 27°C and pH of 4.3. The process also produces lactic acid bacteria and acetic acid which are known to protect against cancer as well as germs by suppressing the growth of other types of bacteria. Kimchi contains more lactic acid bacteria than yoghurt which promotes healthy intestinal micro flora. "Kimchi is already known to have anti-bacterial powers. But this is the first time kimchi's effectiveness in curing viral diseases has been proven," said one researcher. The research team has plans to distribute the kimchi culture fluid to poultry farms across the nation with permission from the National Veterinary Research and Quarantine Service after conducting more extensive research. The results though far from being scientifically concrete, promises a possible cure for the bird flu epidemic that has spread throughout Asia since late 2003.

Bird flu is an infection caused by avian influenza viruses which are found occurring naturally in wild birds. However when spread to domesticated birds such as chickens, ducks and turkeys, bird flu viruses are exceptionally contagious and lethal. Bird flu viruses do not usually infect humans but during an outbreak amongst poultry, there is a possibility of it infecting the human handlers or anyone coming into close contact with the excretion of the birds. The H5N1 virus is an influenza A virus subtype that occurs mainly in birds. It does not usually infect humans. However, in 1997 the first case of bird to human infection occurred during an outbreak of bird flu in poultry Hong Kong. Since then, cases of H5N1 infection in humans have been reported in Thailand and Vietnam during outbreaks of H5N1 bird flu in poultry. There are up to 46 confirmed H5N1 human deaths in Cambodia, Thailand and Vietnam alone since 28 January 2004 according to a report by the World Health Organization (WHO).

The latest person to contract the bird flu virus is a five-year-old boy from central Vietnam. His 13-year-old sister died on 9 March 2005 upon exhibiting similar symptoms after eating a chicken given to them by a neighbor after the bird died three weeks ago. However she was not tested for the virus. The boy from Quang Binh province showed typical bird flu symptoms like high fever, coughing and lung infection but remains in a stable condition. Other symptoms of bird flu include sore throat, muscle aches, eye infections, pneumonia and severe respiratory diseases. The H5N1 virus currently infecting birds and humans in Asia is resistant to amantadine and rimantadine, two antiviral drugs commonly used for influenza. Two other antiviral drugs, oseltamavir and zanamavir would probably work to treat the disease but studies are still underway. Fears of the virus developing resistance to antiviral drugs are driving research in the area of developing vaccines to protect humans against the H5N1 virus. Prof. Kang's novel research into the use of a kimchi extract could prove to be useful in curing the disease as well as in the prevention of a global epidemic.

Singapore

The **Contact Lens** That **Heals**

Most people use eye drops to relieve discomfort or treat various eye diseases. However, 95% of eye drop medication can be ineffective, as the eye drops mix with tears and drain into the nasal canal. This can then cause negative side effects. Researchers at the Institute of Bioengineering and Nanotechnology (IBN) have solved this problem by developing polymeric contact lens material that can be loaded with eye medication.

Using an *in situ* micro-emulsion polymerization process, Dr. Edwin Chow and Dr. Yang Yi-Yan were able to incorporate drugs within a nanostructured polymer matrix. To do this, they used a bi-continuous micro-emulsion as a medium to prepare the drug-loaded contact lens material. This material is ideal for biological and biomedical applications, as it is compatible with human skin cells and corneal epithelial cells, and is also permeable to gases, water and components of the tear fluid.

"This process involves combining oil-based monomers, water and a polymerizable surfactant," said Dr. Chow, lead scientist for this research project. "The surfactant binds the monomers and water to create a clear mixture. A specific dose of drugs is added and the combined mixture is then poured into a lens mold. When this mixture is hard, the resulting lens is full of tiny nanometre-sized channels. This cross-polymerization of organic components in a bicontinuous micro-emulsion can be initiated readily using either heat or UV light. Using this simple process, one can easily fabricate transparent and mechanically strong contact lens material in the form of sheets or ophthalmic molds."

Dr. Chow and Dr. Yang's lenses are made in a novel one-step process, allowing the polymer network to be fabricated easily and cost-effectively. Another advantage of using these contact lenses over other ophthalmic drug delivery systems is that the drug delivery rate can be controlled and remains effective over longer periods of time.

"The drugs 'sit' in the structure of the material and are released into tiny channels, from which they leak onto the eye surface. We can control the flow of the drugs by varying the width of the channels. This can be done by changing the constitution of the mixture that makes up the lens material," said Dr. Chow.

IBN is currently looking for partners to commercialize the lens materials and they have already received enquiries from several contact lens companies. The technology could be used to deliver medication for a range of eye diseases, including glaucoma, which is currently difficult to treat.

"Our technology allows different types of eye medication to be incorporated into the lens' mixture," said Dr. Chow. "We are able to increase the drug-loading capacity without affecting the properties and clarity of the lens. In addition to glaucoma medication, we can load antibiotic or anti-inflammatory drugs. This material could also be modified to produce self-lubricating contact lenses to relieve the discomfort of contact lens wearers suffering from dry eyes. Other potential applications include loading wound-healing drugs in the lenses to treat corneal wounds, or to fabricate the lens material for use in vision correction."

Moving ahead, the researchers are now conducting *in vivo* animal studies, in order to understand the detailed pharmacokinetics of drug release with their lenses.

Unraveling the X Chromosome Code

An international consortium of scientists, headed by the Wellcome Trust Sanger Institute in Britain, has cracked the genetic code of the female X chromosome, as reported in the science journal *Nature*.[1]

The female X chromosome encodes for about 1,100 genes or approximately 5% of the human genome, and is linked to more than 300 human diseases ranging from autism, blindness, and hemophilia to obesity and leukemia. The information gleaned can then be used to improve the diagnoses of these illnesses.

The research has shown that females are indeed genetically more complicated than their male counterparts than previously thought.

According to Dr. Mark Ross from the institute "The X-chromosome is definitely the most extraordinary in the human genome in terms of its inheritance pattern, its unique biology… and its association with human disease."

The X chromosome contains the largest gene in the human genome — the Duchenne Muscular Dystrophy (DMD) gene. Mutations within this gene cause disabling and fatal diseases in men. In addition, the chromosome is home to many other genes linked to mental retardation.

The institute's Dr. David Bentley said, "There are a disproportionate number of known diseases mapped to the X chromosome … In seeing what goes wrong, we can begin to understand the biological processes of the normal body much better."

Every cell's nucleus has DNA which contains the genetic information of an individual. The study found that the X chromosome is bigger than the Y chromosome, which is an eroded version of the former encoding fewer genes.

Females have two X chromosomes wherein one X chromosome is largely switched off or inactivated. This inactivation differs extensively among females.

Males, on the other hand, have one X and one Y chromosome, which bestows them their male attributes.

Autism, color blindness, and hemophilia are X-linked genetic mutations that tend to affect men because men do not have another X to compensate for the defective one.

Dr. Laura Carrel from Penn State College of Medicine, Pennsylvania, USA who also reported her findings in *Nature*[2] found that not all the genes on the silenced X chromosome are inactive and this might clarify some of the differences between males and females.

In a statement she says, " The effects of these genes from the inactive X chromosome could explain some of the differences between men and women that aren't attributable to sex hormones."

[1] *Nature* **434** : 325–337, 17 March 2005.
[2] *Nature* **434** : 400–404, 17 March 2005.

Tracking Diabetic Sugar

Researchers at the Center for Fluorescence Spectroscopy at the University of Maryland, US, headed by Chris Geddes, have come up with a new monitoring system to help diabetic patients track blood glucose levels.[1]

Diabetes, classified as Type 1 or Type 2, is a chronic disease that affects the body's ability to produce or respond to insulin. This causes wide fluctuations in blood sugar levels, from extremely high to extremely low. In Type 1, the body stops producing insulin or produces too little insulin to regulate blood glucose level. These patients generally need insulin on a daily basis to sustain life. In Type 2, the pancreas secretes insulin, but the body is partially or completely unable to use the insulin. Type 2 diabetes is usually controlled with diet, exercise, oral medications and weight loss. More than 50% of patients with the condition need insulin to control their blood sugar levels at some point.

Both forms ultimately lead to high blood sugar levels, a condition called hyperglycemia, which over time damages the eye retina. It is common for diabetic patients to use glasses or contact lens to aid them in their vision.

Focusing on this attribute of diabetics, the team adapts fluorescence as the mode of detection. Boronic acid is added to disposable contact lens, and moisture from the tear ducts contain glucose that binds to boronic acid. This reaction triggers fluorescence. A hand-held device is then used to flash blue light into the eye. The device measures this intensity, which corresponds to the level of glucose in the patient's blood.

Concerns

There are three concerns however. Firstly, they found that boronic acid molecules prefer a slightly alkaline environment, whereas the inside of a contact lens is acidic. Geddes remarked that "We had to go back to the drawing board and design molecules that used boronic yet survived in mildly acidic environment." Moreover, the new molecules also had to be sensitive to ultra-low concentrations of glucose."

Secondly, glucose levels in tears lag about 30 minutes behind the levels in the blood. But this is not a problem, since most patients have gaps of hours between their skin-prick tests.

Lastly is the presence of another sugar — fructose — in the tear ducts. But because it exists in much lower levels, Geddes believes it would not interfere with the glucose readings.

Future work

Instead of having the entire contact lens to glow, tiny sensor spots could be placed to mointor levels of cholesterol, potassium and sodium in addition to glucose detection.

The group is looking into lens that could imitate a traffic light, and change color from green to yellow to red — enabling the patient or an observer to gauge a wide range of blood sugar levels. The new contact lens are not on the market yet. Geddes and team are currently interested in search of commercial partners.

[1]*Curr Opin Biotech* **16**(1): 101–107, 2005.

Note: The above system is not the first non-invasive glucose monitoring method developed. In 2001, FDA, approved GlucoWatch Biographer, made by Cygnus Inc, Of Redwood City, California. Worn on the wrist, the device applies a small electric current to drawing the fluid between cells through the skin for glucose testing. But its makers recommended the occasional glucose monitoring through skin prick tests.