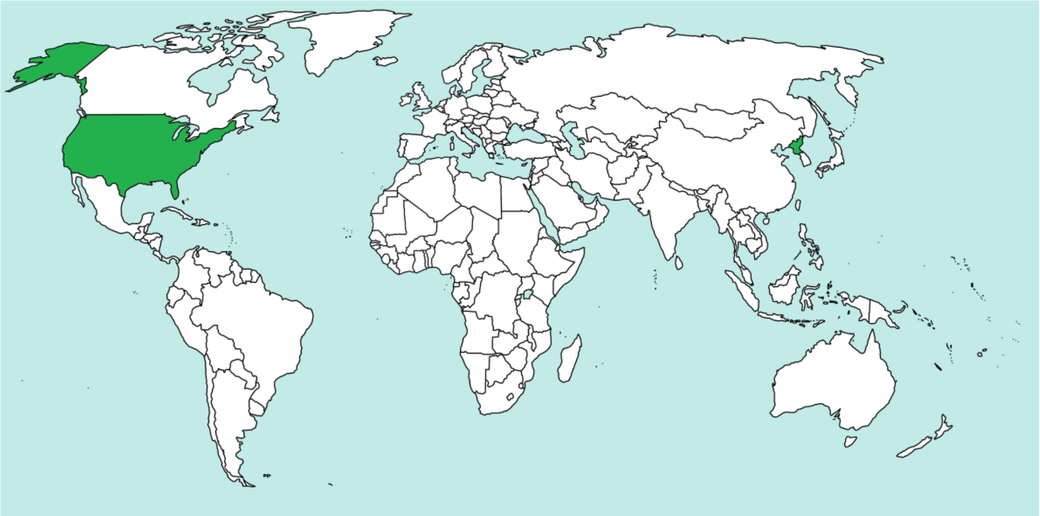

## Hyangsan County, NORTH KOREA

# North Korea Hunkers Down For Harsh Winter

North Koreans are hunkering down for a harsh winter that some fear could be made worse by a poor harvest following summer floods. In rural areas like Hyangsan County, in North Pyongan Province, about 130 kilometers (80 miles) from Pyongyang, people are out each day on snow-covered roads pulling cartloads of firewood and cabbage and stockpiling whatever else they can for the months ahead. Most have just finished preparing their kimchi - the pickled and spiced cabbage that is a staple of the Korean diet. To get through the winter, many rural North Koreans will be using charcoal braziers or burning wood or corn husks for heat, which can lead to asphyxiation if homes shut tight against the sub-zero temperatures are not ventilated properly. They will also be stretching out their supply of kimchi, government rations and whatever they can grow from their own "kitchen gardens" - small plots of land that families are allowed to maintain to grow food for their own needs. If they are lucky enough to have a chicken, they may have an egg or two. In some regions they might have access to a very small amount of meat and fish. The combination of the limited variety of foods that are available and the stresses on the body from enduring the frigid weather is a major hardship for most North Koreans. But while it has the added burden of being bitterly cold, winter is generally not the toughest time of year as far as the food supply goes. North Korea's "lean season" is actually from March to August, when leftover supplies are depleted and the next harvest is still growing. Conditions have also improved dramatically since the widespread famine in the 1990s, when a combination of bad weather, a dysfunctional distribution system and the fall of the Soviet Union and other Eastern bloc benefactors led to a massive calamity euphemistically referred to here as the "Arduous March." North Korea is now closer to food self-sufficiency than it has been in decades. Even so, with a limited and often unreliable power grid, rural homes, hospitals, schools and other public places often have little or no functioning electrical heating. And if the main crops of rice, potatoes and corn are thin and the winter crop, mainly wheat, is poor, that could make the coming lean season even leaner in a country where it is estimated that roughly 80 percent of the population still do not have an adequately varied and nutritious diet. According to the World Food Program, North Koreans consume 25 percent less protein and 30 percent less fat than the amount required for a healthy life. Darlene Tymo, the WFP's country director in North Korea, said that although official statistics from the North Korean government are not out yet, the main harvest of the year is believed to have been worse than last year and that could mean especially remote and impoverished areas - particularly the mountainous provinces of Chagang and Ryanggang along the border with China - could be looking at a harsher than usual winter ahead. "All indications are that it will be down from last year and the question is what percentage down," Tymo told The Associated Press in an interview at the WFP's office in Pyongyang. "The big problem that remains, and I think it's particularly difficult in the winter, is the lack of diversity in the diet. Outside of the capital it is a population that very seriously lacks in proteins and fats, and certainly in vitamins and minerals," Tymo said. By Eric Talmadge. Originally from AP.

## Singapore, SINGAPORE

# New Paradigm in Genetics for Cell Survival

Agency for Science, Technology and Research (A*STAR)'s Institute of Medical Biology (IMB) and Singapore Immunology Network (SIgN) have identified a new paradigm for the identification and evaluation of genes for cell survival. By challenging long-held notions on gene essentiality and drug development, the study holds great potential to predict future drug resistance, thereby saving lives and

optimising the use of resources. Traditionally, basic and applied genetics have relied on the core concept of gene essentiality, which states that certain genes are essential for a cell's survival. When the cells in question are cancer cells or pathogenic microbes, drugs can be developed to block these essential genes, so as to eradicate these harmful cells. Yet, drug resistance, in which cells mutate and render the drug ineffective, is on the rise. According to a recent World Health Organization (WHO) report, "antibiotic resistance is happening right now, across the world." Other examples include chemotherapy resistance, which is a leading cause of cancer treatment failure, or the recent spread of antifungal drug-resistant fungi. The rising trend of drug resistance suggests that cells can in fact adapt to the inactivation of some of these seemingly essential genes. Drug discovery is a long-drawn process that takes many years from development stage to first-in-man clinical trials. Currently, there is no way to predict future drug resistance at the early stages of drug development. Very often, companies spend billions on developing a single drug candidate, only to discover several years later during clinical trials or even after approval, that that resistance can occur. In fact, the success rate of clinical trials globally is estimated to be as low as 25 per cent, partially due to the high number of drug candidates found to be resistible only during trial stage. This represents the loss of time and resources which could otherwise have been used to develop more effective drugs and therapies. Now, A*STAR scientists have redefined the underlying concept of gene essentiality by putting forth a new genetic paradigm. Previously, genes were divided into non-essential ones that are dispensable for cell viability, and essential genes that are required for cell survival. The new study found that essential genes can be further split into two kinds - one being the kind that cells need for survival, known as 'non-evolvable' essential genes, and the other being those that cells can find ways to survive without, by an evolutionary process of mutation and selection. Genes belonging to this latter class were termed 'evolvable' essential genes. Cells knocked-out of one of these 'evolvable' essential genes need to adapt very quickly so as to survive. Through examining approximately 1,000 essential genes in yeast, the team found that cells were able to adapt so quickly because they mutate to change their number of chromosomes. In so doing, they change the relative balance of genes in their genome and use alternative pathways to perform the original function carried out by the missing gene. This also explains why the presence of extra chromosomes has been reported commonly in chemotherapy-resistant cancer cells and drug-resistant fungi and parasites.

This study holds great potential to improve the current drug discovery and development process, with applications for illnesses varying from cancer to infectious diseases. Drug candidates can be tested to see if they are in fact targeting 'non-evolvable' essential genes. This would then suggest a lower possibility of drug resistance since cells would not be able to adapt to the loss of these genes. With this new paradigm, drug resistance can be predicted at the discovery stage and resources can be optimised to develop more effective drugs that can save lives. Dr Giulia Rancati, Principal Investigator at IMB and corresponding author of the paper, said, "We are thrilled to challenge a longstanding paradigm in genetics, especially one with such clinical implications. The next step will be to translate these findings in pathogenic fungi and human cells, and to find non-evolvable essential genes as novel antifungal and chemotherapy targets, respectively." Professor Rong Li, Bloomberg Distinguished Professor of Cell Biology and Chemical & Biomolecular Engineering at Johns Hopkins University (JHU), and a world renowned expert in cellular asymmetry, division and evolution commented, "This is a fantastic study that takes a systematic approach to re-define the essentiality of gene function, taking into account the cell's adaptive potential. The findings demonstrate high-level plasticity across the genome-wide molecular network toward a range of genetic perturbations."

Both corresponding authors of the study, Dr Giulia Rancati and Dr Norman Pavelka, Principal Investigator at SIgN, are recipients of the A*STAR Investigatorship, a prestigious research award designed to


attract the most promising young researchers around the world to do independent research at A*STAR. This breakthrough therefore attests to the world-class quality of R&D by researchers under the programme, and the strength of the award in nurturing leading scientific innovators.

## Chicago, USA

## Neuroscientists Now Can Read the Mind of a Fly

Northwestern University neuroscientists now can read the mind of a fly. They have developed a clever new tool that lights up active conversations between neurons during a behavior or sensory experience, such as smelling a banana. Mapping the pattern of individual neural connections could provide insights into the computational processes that underlie the workings of the human brain. In a study focused on three of the fruit fly's sensory systems, the researchers used fluorescent molecules of different colors to tag neurons in the brain to see which connections were active during a sensory experience that happened hours earlier. Synapses are points of communication where neurons exchange information. The fluorescent labeling technique is the first to allow scientists to identify individual synapses that are active during a complex behavior, such as avoiding heat. Better yet, the fluorescent signal persists for hours after the communication event, allowing researchers to study the brain's activity after the fact, under a microscope. "Much of the brain's computation happens at the level of synapses, where neurons are talking to each other," said Marco Gallio, who led the study. "Our technique gives us a window of opportunity to see which synapses were engaged in communication during a particular behavior or sensory experience. It is a unique retrospective label." Gallio is an assistant professor of neurobiology in Northwestern's Weinberg College of Arts and Sciences. By reading the fluorescent signals, the researchers could tell if a fly had been in either heat or cold for 10 minutes an entire hour after the sensory event had happened, for example. They also could see that exposure to the scent of a banana activated neural connections in the olfactory system that were different from those activated when the fly smelled jasmine. Northwestern University neuroscientists have developed a new tool that lights up active conversations between neurons during a behavior or sensory experience, such as smelling a banana. Gallio and his team wanted to study the brain activity of a fruit fly while it performed a complex behavior, but this is not easily achieved under a microscope. The scientists figured out a different approach using genetic engineering. Starting with the gene for a green fluorescent protein found in jellyfish, the authors derived three different colored markers that light up at the point of contact between neurons that are active and talking to each other (the synapse). The fluorescent signals can be read one to three hours after the action is over. "Different synapses are active during different behaviors, and we can see that in the same animal with our three distinct labels," said Gallio, the paper's corresponding author. The fluorescent green, yellow and blue signals enabled the researchers to label different synapses activated by the sensory experience in different colors in the same animal. The fluorescent signals persisted and could later be viewed under a relatively simple microscope. The researchers studied the fruit fly Drosophila melanogaster, a model animal for learning about the brain and its communication channels. They tested their newly engineered fluorescent molecules by applying them to the neural connections of the most prominent sensory systems in the fly: its sense of smell, sophisticated visual system and highly tuned thermosensory system. They exposed the animals to different sensory experiences, such as heat or light exposure and smelling bananas or jasmine, to see what was happening in the brain during the experience. To create the labels, the scientists split a fluorescent molecule in half, one half for the talking neuron and one half for the listening neuron. If those neurons talked to each other when a fly was exposed to the banana smell or heat, the two halves came together and lit up. This only happened at the site of active synaptic transmission. "Our results show we can detect a specific pattern of activity between neurons in the brain, recording instantaneous exchanges between them as persistent signals that can later be visualized under a microscope," Gallio said. This is the kind of new technology scientists discuss in the context of President Obama's BRAIN (Brain Research Through Advancing Innovative Neurotechnologies) Initiative, Gallio said. Such a tool will help researchers better understand how brain circuits process information, and this knowledge then can be applied to humans.■

BASE BASE