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Bioinformatics, Nanotechnology & SARS1

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In the wake of all the hoopla about SARS (severe acute respiratory syndrome), there were more than enough news, books and merchandize to overwhelm the average individual, blurring the lines that separate facts from rumors, science from myth, and reality from hype.

Drowned in all the information and misinformation overflow, most people, if not all, fail to relate the role information technology (IT), and in particular bioinformatics (BITS), plays in the identification of SARS virus and the various mutants, and a potential cure for SARS. Even fewer people managed to look beyond the narrow scope to see the ramifications of the recent SARS outbreak.

Race to Sequence SARS Genome

Patient Zero of the recent SARS rampage is a point of contention. There have been more than enough rumors out there to confuse the average people: some claim SARS to be a bioweapon intentionally released to cause havoc; some claim SARS to be a bioweapon accidentally released from a weapon laboratory; some claim the first SARS patients were in the U.S.…

Nevertheless, the SARS rampage was at one point a public health issue threatening most of the Asian Pacific Rim countries: China, Hong Kong, Vietnam, Singapore, and Taiwan included. Aided by globalization and the ease of air travel today, the disease was reported in many other countries, such as Canada, the U.S. and some parts of Europe, with a large number of infections and a significant number of deaths. By May 2003, SARS had spread to 28 countries, infecting more than 7,000 people, and killing more than 500. Of these, China, Hong Kong and Taiwan account for 92.0% of all SARS cases, and 89% of the deaths.

On March 12, 2003, the World Health Organization (WHO) issued a global alert on the outbreak of the epidemic – a new form of pneumonia-like disease with symptoms that are similar to those of the common flu. This illness is potentially fatal and highly contagious, and had spread quickly to many parts of the world in a matter of a few weeks.

In a *tour de force* of genomics, government research centers in Canada and the U.S. decoded the genome of the coronavirus - which was proven to be the cause of SARS. The British Columbia Cancer Agency (BCCA) in Vancouver was the first to sequence the SARS genome in the early hours of Sunday, April 13, 2003,3 followed closely by the Center for Disease Control and Prevention (CDC) of the US on April 14, 2003.

The sequence information itself does not provide a cure, but rather the test and diagnostics for this particular virus. The sequencing success was a combination of several events, serendipity being one of the most significant.

The challenge was producing a DNA copy of the virus's RNA genome to work with. After several days of effort, scientists managed to produce one millionth of a gram of the genetic material on April 6, 2003. To sequence the SARS genome, the genome was broken in manageable fragments. Within a week, all the fragments had been sequenced. Once started, the sequencing itself was "fairly routine." The sequenced genome fragments were then assembled into the complete genome in mere 12

Figure 2. *The figure shows how photocatalysis works, in this particular case, as a disinfectant. When the surface of the TiO2 transparent thin film is exposed to UV light (~400nm), negatively charged electrons are released, in much the same way as electrons are released when sunlight hits the surface of the silicon solar power cells. Simultaneously, positively charged holes are formed on the surface of the thin film.*

Under UV light, electron-hole pairs are created. The negative electrons and positive holes create very strong oxidizers, called hydroxide radical, even stronger than chlorine used as a sterilizer. When harmful substances stick to the positive holes, they are completely broken down into the carbon dioxide and other harmless compounds. As a disinfectant, the hydroxide radical also can inhibit the growth of bacteria and mold.

Bacteria can be found all over the place and they multiply quickly. Within an hour after conventional disinfection using bleach for example, the disinfected body will have returned to 80% of pre-disinfection state; and in further 23 hours, it will have returned to the original state. The idea is to have a disinfectant agent, such as TiO2 that will kill bacteria faster than they multiply to sustain cleanliness.

For TiO2 to be effective as a disinfectant, the size has to be in the nanometer (10-9 m) range. In this size range, it has been shown that the effectiveness of TiO2 as a disinfectant can go as high as 70%-99.9%. The problem that we have is that the cost to grind the substance increases with diminishing size. Many industries now use micrometer (10-6 m) range TiO2. Though much cheaper, the effect is drastically reduced.

On May 23, 2003 and during the SARS epidemic, the WHO recommended that the cabin or quarters occupied by a SARS patient be disinfected with sodium hypochlorite bleach and formatin 1 or chloro-meta-xylenol. There have been technologies developed along this line to deliver one of these ingredients at an extremely low concentration to create a powerful hospital grade disinfectant that is non-hazardous and environmentally safe. One particular product line, employing unique nano-emulsive technology, is reported to be able to reduce the spread of a broad range of diseases, including E. coli, salmonella, listeria, staph, strep, pseudomonas, MRSA, VRE, Norwalk-like virus, Influenza A, Hepatitis B and C, vaccin.

Another product has been developed using proprietary technology to create a nano-emulsion. The nano-emulsion can be sprayed, smeared on clothing, vehicles, people or anything that has been exposed to a slew of deadly substances. It can also be rubbed on the skin, eaten or put into beverages like orange juice, and used in the water of a hot tub. The working principle is that the nano-bubbles contain energy that is stored as surface tension. The energy is released when bubbles coalesce, thus zapping the contaminant. The hurdle is that a huge amount of energy is needed to make the nano-emulsion, with bubbles of sizes smaller than bacteria and viruses.

For those products which have been scientifically proven feasible, for them to get into the market, the cost for producing them will have to come down drastically so that they are affordable.

The major concern is that opportunists might seize the opportunity arising from the fears of to market cheap prevention kits, disinfectant substances, sterilizing systems that are of dubious effectiveness. The risk is that the public may lower their guard under the false impression that they are fully protected.

Malaysia is also active in these areas. Current ongoing efforts include the nano-biotechnology effort, headed by Professor Datin Khatijah Yusoff at Universiti Putra Malaysia, and NanoBiotech Sdn. Bhd. at UPM-MTDC Technology Centre. The main focus is to use nanotechnology as a means for detecting infectious agents, or to develop diagnostic platforms. Professor Nor Muhammad Mahadi and Professor Rahmah Mohamed of the National Institute for Genomics and Molecular Biology, one of the three institutes of BioValley, are leading an effort to sequence the SARS genome.

Note that all the products, if they are effective, are good only for preventing, disinfecting or detecting infectious agents; they do not offer a cure, yet.

The SARS Lesson

SARS still has no known cure at present. It may be spread directly by inhaling the microscopic, airborne droplets left in the air by a SARS patient. Alternatively, the virus can survive up to several hours outside the body and touching an object that has become contaminated when coughed on, sneezed on, or touched by a SARS patient may spread infection.

The fact is that each year during the flu season, 95 million Americans are affected, resulting in some 20,000 deaths annually. The leading scourge, but a preventable man-made plague - smoking - kills about 3 million worldwide each year, from smoking-related illnesses.13 Of these 10,000 are Malaysians. By comparison, SARS infected less than 10,000 people, killed less than 1,000 victims, and yet the public response seemed to be much more immense. The response to the outbreak of SARS in Asia is a typical example of mass hysteria. Knowing that there is still no cure for SARS, the public responded with an epidemic of vulnerability, an outbreak of mass psychogenic or sociogenic illness.

The good news is that the rampage of SARS has ebbed for now. The bad news is SARS will likely return in the future, and just like SARS, other emerging diseases unbeknown for now, will surface in the future.

SARS and emerging diseases have become a global issue for which every responsible citizen has a duty to help his or her government to contain. There is no doubt that our genetics plays a huge role – certain people are more susceptible to disease attacks, while others are not, technology and public awareness can only play a significant ancillary role.