Genetic Engineering of Smallpox Virus for Drug Development?

In a bold, unprecedented request, an expert committee that advises the World Health Organization (WHO) has recommended that researchers in the United States and Russia be allowed — along with numerous provisos and conditions — to genetically engineer variola virus, which results in smallpox, in order to accelerate drug development.

It was proposed that a green fluorescence marker be inserted in the variola genome to help speed up and automate drug screening. Use of the marker would accelerate screening by factors of 10 or 100, and it would also reduce the amount of time that lab workers would need to be in biosecurity level 4 labs handling live variola virus.

Geoffrey Smith, from Imperial College London, who chaired that meeting, said that smallpox drug development needs to be accelerated because of fear of bioterrorism. That view was echoed by a WHO spokesman, who added: “It’s all been given new impetus over the last 3 to 4 years, since 9/11, and the deliberate use of anthrax in the US.”

The spokesman emphasized that the advisory group’s role is only to make recommendations to the World Health Assembly. In practice, he said, the proposal will first be seen by the WHO executive board and director general before it is considered by the World Health Assembly in May next year.

The committee’s first proviso for its recommendation is that the research must only be done in the two laboratories currently handling live variola: the Centers for Disease Control and Prevention (CDC) in the US, and Novosibirsk in Russia. The second is that the proposal must also be put to the relevant institutional and national safety committees and submitted to the scientific subcommittee of the Advisory Committee on Variola Virus Research.

WHO has requested further detailed research proposals and a full safety assessment. There is some concern about the stability of the large virus and a small risk of increasing virulence.

Smallpox

Smallpox (variola) represents both the zenith and nadir of human medical achievement. It is the only disease eradicated through a concerted and extensive effort that transcended political and ideologic boundaries — the last known case of naturally occurring smallpox was in 1977, in Somalia, and smallpox was officially declared eradicated by WHO in 1980. It also represents one of the most devastating potential biological weapons ever conceived. After the September 11 attack in 2001, the Bush administration decided that smallpox is a bioterror threat and that vaccination is prudent.

The variola virus now only exists within a few laboratories around the world. The official virus repositories are at the Centers for Disease Control and Prevention (CDC) in Atlanta, GA, and the Institute of Viral Preparations in Moscow, Russia. Viral stocks also exist at the Russian State Research Center of Virology and Biotechnology in Koltsovo. Multiple dates for destruction of the remaining viral stocks have been proposed by the WHO Committee on Orthopoxvirus Infections, only to be pushed back under pressure from various factions, including the US government.
In October 2004, member nations of the United Nations were involved in a heated debate over the merits of human cloning, specifically the respective merits of two opposing proposals on how to regulate cloning technology that could well determine the fortunes of future stem cell research.

And as vigorous as the latest ongoing discussions on a long-drawn debate — in fact, a three-year battle fought between two sides over the issue — might be, there is no resolution in sight. After all, the agenda pursued by both side adds nothing new or refreshing to the diplomatic wrangling of an already complicated issue, this time again centered on whether cloning technology should be even allowed or not for medical research and therapeutic purposes.

And again, not surprisingly, the two opposing sides have struggled to reach a compromise.

The United States, backed by 60 other countries, lobbied hard for an outright ban on all forms of human cloning, citing the fears and objections that may arise from the prospects of the technology being misused to push for a bill to ban all “unethical cloning.” The position of the 60 countries, including the US, is that all scientific research using cells extracted from cloned embryos should be banned immediately, supporting Costa Rica’s proposal to ban both reproductive and research cloning.

On the other side of the fence, a contingent of European and Asian nations led by Belgium was quick to refute the American-led position on the issue, supporting the continuance of human cloning for important research purposes. These nations are supporting a proposal by Belgium that would ban reproductive cloning but allow research cloning based on individual nation’s discretion.

The Belgian-led proposal calls for regulations that would ban the cloning of humans but allow countries a fair amount of leverage to decide for themselves whether or not they want to impose laws that would ban or permit specific forms of therapeutic cloning for research.
This latest debate on human cloning comes hot on the heels of recent news regarding the development of embryonic stem cells — news that the researchers who created Dolly the infamous sheep have applied for a license to obtain stem cells from the cloning of human embryos. The team of researchers at Edinburgh’s Roslin Institute, led by Prof. Ian Wilmut, hopes to develop a cure for motor neurone disease through experiments using the cloned embryos.

If their appeal for a license is approved, it will mark only the second time the license is granted since a team of researchers were granted a license in August — believed to be the first time such a license had been granted in Europe — to clone human embryos to develop new treatments for diabetes and degenerative diseases such as Alzheimer’s and Parkinson’s.

According to reports, scientists from Harvard University are also attempting to gain access to clone human embryos, with two separate teams of researchers wanting to use cloning to produce embryonic stem cells that match the genetic material of patients with juvenile diabetes, Parkinson’s disease and other illnesses. While cloning is legal in the United States, the scientists still needed to receive approval through an institutional review process.

Elsewhere, in Asia, the Singapore government has passed a law that bans human cloning for reproduction but allows scientists to clone human embryos and keep them alive for 14 days to produce stem cells. Japan’s supreme science council has also voted in favor of policy recommendations that would permit human embryos to be cloned for scientific research.

One of the concerns is that the cloning technology would be misused for reproductive cloning if the technological means was to fall into the wrong hands. The United States’ vehement support for such a comprehensive action to ban human cloning research on all levels is pretty much an attempt to prevent manipulators from exploiting the therapeutic purposes of technology to advance the possibility of successfully cloning humans.

Even the track record of stem cell researchers has been called into question here, with anti-cloning activists criticizing the meager number of treatment breakthroughs achieved relative to the huge amount of investments poured into developing stem cells for therapeutic research. Religious leaderships including the Vatican have also spoken out on the danger of hindering the promising benefits of stem cell research by diverting too much attention into the cloning of human being as a source of embryonic stem cells.

Still, many observers have pointed out though that an outright ban on cloning is far from realistic. Controversial or not, cloning research cloning have become an integral component of the modern development of science and medicine, a valuable asset of understanding and treating diseases. However, the inherent danger is that it’s a fine ethical line for lawmakers to tread when deciding the merits of stem cell research and ambiguity over the legislative process may also result.

Indeed, with stem cell research and development progressing at an astonishing pace, life sciences ethicists are having a field day trying to balance between stem cell research for therapeutic purposes only and the potentially far-reaching possibilities of harvesting embryonic stem cells for other vilified intentions.
With the ratification by Russia on 18 November 2004, the Kyoto Protocol will become legally binding on 16 February 2005. Russia’s accession gives Kyoto support from countries that emit at least 55% of the world’s greenhouse gases. The formal ratification of the protocol ended years of uncertainty over the future of the agreement; Russia’s vote swung it over the critical threshold, taking the percentage of emissions covered from 44.2% to 61.6%.

The Protocol

The Kyoto Protocol, first agreed in Kyoto, Japan, 1997, is a legally binding international agreement to reduce the greenhouse gas emissions causing climate change.

The agreement would commit 55 industrialized countries to reduce emissions of six greenhouse gases (excluding O3 and water vapor) to 5.2% below the 1990 level by 2012. Rather than placing a specific target on each of the gases, the overall emissions targets for all six would be combined individual gas reductions would be translated into “CO2 equivalents” used to produce a single figure.

Developing countries are not legally bound to emissions reduction targets as yet because these countries have historically been responsible for only a small portion of the global greenhouse gas emissions.

Ratification

The treaty becomes effective 90 days after ratification. The ratification procedure requires the signatures of at least 55 Parties to the Convention, and must include enough Parties (industrialized nations) to account for at least 55% of total CO2 emissions from industrialized countries in 1990. As of April 15, 2004, 122 countries had ratified or acceded to the Kyoto Protocol — but those countries represent only 44.2% of the total CO2 emissions from industrialized countries in 1990. After the US withdrew in 2001, the only way that the Protocol could enter into force is if Russia ratifies the agreement. Russia is responsible for 17.4% of emissions.
US Withdrawal

The US, the world’s largest emitter of greenhouse gases, withdrew from the protocol in 2001. The Bush administration said that it would gravely damage the US economy, and that there was not enough sound science surrounding the climate change issue. The Administration also criticized the protocol for not forcing developing nations, including India and China, to cut emissions immediately.

The US — with just under 5% of the world’s population — is responsible for over 20 to 25% of the world’s CO₂ emissions.

China’s Efforts

According to a study in Science, levels of greenhouse gases in China have fallen. Chinese energy sector reforms have helped reduce the country’s emissions, and the economic slowdown following the 1997–98 Asian financial crisis also may have played a role.

China’s overall CO₂ emissions fell by 7.3% between 1996 and 2000, and its methane emissions declined by 2.2% between 1997 and 2000. If one looked at CO₂ emissions produced from the combustion of fossil fuels, the decline was 8.8% from 1996 to 2000 — an even greater reduction than the 7.3% drop for emissions from all sources.

US President Bush has said the treaty lacks binding commitments for developing countries to reduce their greenhouse emissions and thus ensures that China, with its “huge population and endless coal reserves”, would surpass the United States as the world’s largest source of gases blamed for global warming.

In actuality, China’s emissions have dropped over the past five years, while those of the United States and other industrialized countries have increased. Western Europe’s CO₂ emissions from fossil fuel combustion have by 4.5% from 1995 to 1999, and the US, by 6.3%.

The researchers, comprising of scientists from China and the US, cited Chinese emission reductions as a result from the closure of small and inefficient industrial plants, improved efficiency of energy use, improved coal quality, the switching of many residential fuel users from coal to gas, technological progress in energy-intensive sectors, and the opening up of coal and electricity markets. China’s reversal of past forest clearing activities and recent promotion of reforestation also have increased the net absorption of CO₂ by the country’s forests over the past decade.

However, a slow increase in Chinese fossil fuel use is still predicted. Much will depend on the performance of the Chinese economy in the coming years.

Global Warming

Actually, experts think that Kyoto will not even come close to solving the problem of climate change — some have claimed that a drastic cut of around 60% is needed to avoid the worst effects of global warming.

Every year, almost 7 billion tonnes of carbon are released into the atmosphere — carbon that had lain buried for millennia. The released carbon will remain in the atmosphere for around a century.
Before the industrial age, the CO₂ level was steady at around 280 ppm. When the Kyoto protocol was drawn up in 1997, the CO₂ level had reached 368 ppm. In 2004, it hit 379 ppm.

Most dire predictions of soaring temperatures, floods, droughts, storms and rising sea levels are based on a CO₂ concentration of 550 ppm. Extrapolating from current trends, this figure is likely to be reached in the second half of this century. Even if levels rose no higher, this would just be the start. Time lags in natural systems such as ice caps and ocean circulation mean that changes will continue for millennia after the CO₂ level stabilizes.

Only drastic cuts in global emissions of CO₂ can be considered truly effective. The more quickly the world can make such cuts, the lower the level at which concentrations will eventually stabilize. The Kyoto protocol, however, involves only very modest reductions of less than 5% and it expires in 2012.

**CO₂ Cap**

One option under discussion is a global plan to cap concentrations of critical greenhouse gases, especially CO₂. This would set a firm and scientifically coherent benchmark to measure the success of future negotiations. Most climate scientists would like to see CO₂ concentrations in the atmosphere kept below 450 ppm, but many admit that 550 ppm is more realistic. This would still lead to substantial climate change: temperatures could rise by 2–5°C, and the sea level by 0.3m to 0.8m by 2100, and by 7m to 13m over the next millennium.

Agreeing on a CO₂ ceiling would be the easy part. The sensitive part will be deciding who is entitled to make those emissions. Developing countries insist they can only accept quotas based on population and suggest extending the Kyoto plans for emissions trading to smooth the transition. Industrialized countries such as the US, which emits 8 times as much CO₂ per head of population as China and 18 times as much as India, reject such suggestions, but are having difficulty finding a fair alternative.

**The Clock's Ticking**

The rate at which CO₂ levels are rising is alarming. It took 150 years for CO₂ concentrations to rise from 280 ppm to 330 ppm; and only 30 years to get from 330 ppm to 380 ppm. Last year, concentrations rose by a record 3 ppm. Extrapolating, we would hit 450 ppm by 2030, and 550 ppm by 2060.

Despite the modest goals of the Kyoto Protocol, the treaty remains a very important initial step that hopefully paves the way for future regulations. Already, the protocol's signatories are meeting this December in Buenos Aires to decide on what to do next.

The Bush administration insists that research into better technologies is more important than premature, expensive measures to cut emissions. But, do we have the time? And, is it more expensive to cut emissions now, or to pay for it later?  

---