Cure for Ebola virus disease

The fast-tracking of ZMapp for human use in the current Ebola outbreak is notable. Professor Shima Gyoh looks into the background of this intriguing development

It is becoming clearer to me that I do not belong to this era. The landing on the moon was too remote from me to properly wonder, but many miracles do involve me, personally. I flew from Paris to San Francisco in what seemed to me like a flying village. Yes, much more than a flying house, for I know of many villages in my local government with no more than five families, but I have never heard of a house in which 500 people lived. That was the content of the Airbus 380 that took me to San Francisco, and I sat upstairs! It is bad enough for me to sit in a craft carrying 20 people and still be able to take off, but this huge beautiful monster, weighing 560 tons that can reach its cruising height of 39 000 feet in less than 15 minutes, simply leaves me breathless with wonder.

In the medical field, development of the drug against Ebola virus astounds me. ZMapp, the antiserum for Ebola that has been catapulted to fame too early in its scientific history has a most intriguing origin. The sting of the Ebola virus is a glycoprotein that enables it to attach itself to human cells. The company Mapps set out to find a way of neutralising this glycoprotein.

First, mice were infected with Ebola virus. The antibodies they produced against the glycoprotein were extracted, tested and found to be active. Then the cell responsible for its production in the mouse was isolated and fused with a cancer cell to enable it to replicate rapidly and produce the antibodies.

However, the resultant antiserum was mouse protein and would stimulate severe rejection in the human; so it needed to be humanised. Sections of its molecules were spliced and replaced with human protein, care being taken to avoid removing the parts that were relevant to neutralising the Ebola glycoprotein.

The next stage was to produce the now humanised antibody in large quantities, so the gene was then injected into the genome of Nicotiana, a tobacco plant. This was done through two plant viruses via the Agrobacterium (known for its ability to transfer DNA between itself and plants) as an intermediate step. The plant now produced the antiserum which was harvested and purified, QED!

John Trimmer who explained the process said[1] 'If the process described above - with infinite antibodies, cloning, mixing genes from different species, and mass production in plant cells - sounds like science fiction, it shouldn't. Every single one of those procedures is well established and has probably been used by a hundred biotech startups by now. Biotech doesn't tend to get the same attention as the work done by the people who make our processors and batteries, but it's some of the most amazing technology on the planet.'

I totally agree.

Trial in monkeys has shown that the drug is effective even for prophylaxis, but it had not yet to undergone human trials when two American health workers lay dying of Ebola in Liberia. They were given it as a desperate measure when the symptoms that precede death were noticed. Dr. Kent Brantly developed dyspnoea and Mrs Nancy Writebol was extremely prostrate and weak. The situation was hopeless, and, as Mrs Writelbol's husband said on CNN, the family was preparing for her funeral. Administration of ZMapp was a desperate last minute risk.

Fortunately, Dr. Brantly showed dramatic improvement, but scientifically, it would be reckless to jump to the conclusion that the drug did it. Science insists we must not regard 'post hoc, propter hoc' as deduction that is always true. Brantly had previously had a blood transfusion from a 24-year old boy that survived Ebola. The dramatic improvement might have already been in the works and drug injection an entirely fortuitous coincidence. ZMapp would have to produce consistently positive results in many different patients before the medical world would accept it as truly efficacious.

Its effect on the lady has been, well, good but less dramatic, justifying treading with caution. On the other hand, the Spanish priest who died despite the injection does not necessarily invalidate its claim to efficacy. Still, the question of tolerance, the correct dose, and the timing of administration are all crucial requirements usually determined at clinical trials and serve to guide doctors using the drug.

Suppose the drug was first tried on Africans? I can best quote[2] the Director of Caprisa, an AIDS research centre in South Africa:

'It would have been on the front page with screaming headline: Africans used as guinea pigs for American drug company's medicine.' Heads I loose, tails you win!

The World Health Organization approval for use of ZMapp would also serve for clinical trials, but it amounts to putting the cart before the horse as approval at this level is usually done only after clinical trials.

Prof Shima Gyoh has held many posts ranging from village doctor to DG of Nigeria's Federal Ministry of Health and Chair of the Medical and Dental Council of Nigeria.

Reference

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