EU gets ready to combat a flu pandemic

Commentary
A visit to the GP. This patient's symptoms are obvious. She is suffering from winter flu. Every year, according to the World Health Organisation, 5 to 15% of the population suffers from infections caused by the flu virus. Vaccination is the main method of flu prevention. The vaccine stimulates the organism's natural defences which can combat a viral attack by producing antibodies. These react against the proteins which are found on the surface of the virus.

To get a better understanding, let us look at a model of the flu virus. On its surface you can see two different proteins. Hemaglutinin (H) in orange and Neuraminidase (N) in blue. They define the virus and the immune response of the infected organism.

ITV John Oxford - Institute of Cell and Molecular Science – Retroscreen Queen Mary, University of London
The current vaccines are composed of these two spikes, the hemagglutinin toblerone and the neuraminidase mushroom. Just those two spikes make up the current vaccine. And of course the vaccine has to be reformulated each time they changed.

Comment
Indeed, the genetic composition of flu viruses allow frequent mutations of these two proteins and therefore of the virus itself. The result is that every year, the vaccine has to be modified to combat the new form of the virus. Faced with this problem, European research is exploring new avenues, notably that of a universal vaccine which will offer a protection for 5 to 10 years.

Europe has decided to co-finance the "Universal Vaccine" project to arm itself against flu in a different way. This is Ghent, in Belgium. One of six laboratories who are partners in the European programme.

ITV Walter Fiers - Dept. for Molecular Biomedical Research - University of Ghent
What the vaccine that we have developed sees is a protein which is absolutely conserved in all human viruses. This target is the M2e protein which is constant in sequence and therefore, is the same in the different influenza strains which infects people.

Comment
In summary, this universal vaccine no longer takes into account the two imposing surface proteins, the highly mutant H & N but rather a small, much more stable protein M2e - shown here in red.

ITV Xavier Saelens - Dept. for Molecular Biomedical Research - University of Ghent
We have seen if we vaccinate mice so far with a M2 based protein, a recombinant vaccine that only present the M2 to the immune system, that then we get a protection against a influenza infection regardless of the strain that we use.

Comment
At this stage, the vaccine still has to undergo clinical testing. In time, the vaccine will have a much wider coverage and will come in a nasal spray form. Probably five years from now, when it will be produced on an industrial scale.
The universal vaccine involves a response at the level of the antibodies. The immune system has another way of reacting - via the T cells of the patient. Here in Rotterdam, they are the focus of « NOVAFLU », a European project that brings together six partners in The Netherlands, France, Germany and the United Kingdom

**ITV John Oxford**
The T-cell response who is very important in virus recovery but is particularly directed -for reasons that are not to clear- against the internally structure, the M2, the M and nuclear protein.

**ITW Albert Osterhaus, Director of the National Influenza Centre, Head of the Department of Virology, Erasmus University Rotterdam**

T-Cells can be generated against these internal proteins and they work in a different way. So they actually kill infected cells that have been recognized. The good thing about the T-cell responses is that generally speaking they are much more conserved, meaning that the proteins have much less variations there than at the surface of the proteins.

**Comment**
And this is what happens: Our T cells, shown in diagrammatic form here have, on their surface, receptors which can attach themselves to residues found on the surface of infected cells; these residues come from the internal proteins of the virus. Once the patient’s T-cell comes up against the infected cell, it destroys it.

**ITV Albert Osterhaus**
We have been doing a lot of studies on the possibilities to elicit the T-cell response with the internal proteins and also trying to elicit them against the most conserved structures that we know. And for that, we know a number of additional techniques like the use of reverse genetics, the use of certain vectors, also the use of adjuvant.

**Comment**
These techniques will allow vaccines to be produced in a much quicker and less expensive way than conventional vaccines. And, what's more, produced on a massive scale. Which is crucial when you realise that today, only about 200 million doses of vaccine can be produced whereas there are more than 6 billion people in the world. The outlook for NOVAFLU is optimistic. The vaccine formula could be finalised three years from now.

Off to Leuven in Belgium now. Here they are not working on the preventive aspects like vaccines, but on the therapeutic approach, that is to say antivirals. One of them is already well-known by the general public, Tamiflu. It is on this anti-viral approach that the European VIZIER project is concentrating, - a network of 22 laboratories spread across nine countries in the Union plus one in Russia.

**ITV Johan Neyts- Rega Institute for Medical Research - Katholieke Universiteit Leuven**
So from the moment that the cell is infected with influenza and new particles are produced these newly formed particles have to disappear from the cell. Once they liberated from the cell they remain stuck to it for a moment. Neuraminidase, a viral enzyme, cuts the viral part of the cell like a pair of scissors.

**Comment**
What are Tamiflu or Relenza doing, seen here in white? These antivirals attach themselves to the neuraminidase and stop it acting, in such a way that the virus cannot detach itself from the cell to infect others. The cell dies, and the process of infection stops.

**ITV Johan Neyts**
We know that with Tamiflu used to combat the traditional winter flu, the virus can become resistant to the medicine.

**Commentary**
Existing antivirals do act on neuraminidase, an external protein which promotes the dissemination of the virus. The VIZIER researchers are concentrating on the interior of the virus, the part which allows its replication. The genetic material is copied and assembled by several proteins, of which the last three, larger ones serve as the virus’s engine. If you can manage to stop them functioning it would put an end to the replication mechanism. And therefore an end to the virus itself.

VIZIER, Universal Vaccine and Novaflu: these three projects are allowing the Europe of 25 to come up with complementary strategies for the production of better vaccines and antiviral drugs. This will help us to prepare for a possible mutation of the avian flu virus, H5N1, to a virus which can be transmitted by humans. And so to prepare itself for a pandemic.

**ITV John Oxford**
I think that the power of this sort of project is refer to it is started several years ago before we reached this crisis. The EU scientifically has been preparing itself and generating new data in anticipation of this event. Not many countries or regions of the world just had this foresight. So I find that pretty pleasing.