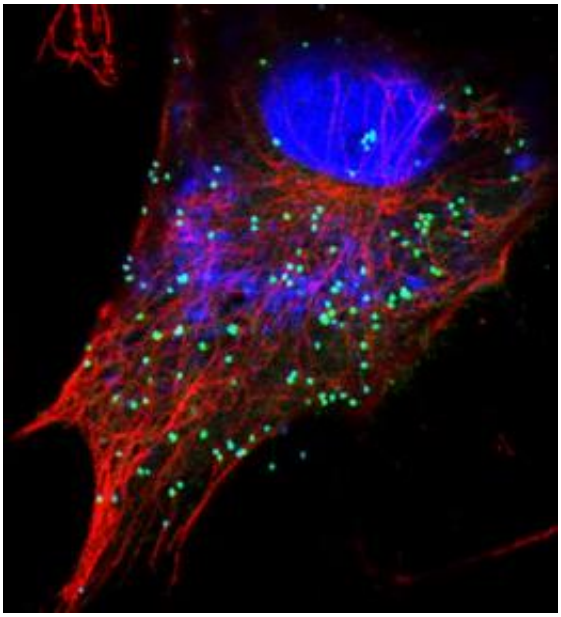
Avian flu vaccine on the brink

January 10 2011



Pox virus infecting avian cells - image captured using confocal microscopy in the Central Laser Facility. Credit: STFC and Oxford Brookes University

A collaboration between BBSRC and STFC-funded scientists has been using a new form of low energy microscopy to observe how poxviruses interact with components inside live cells. Genetically modified fowlpox viruses have been used extensively in Mexico and southeast Asia to vaccinate chickens against bird flu and the scientists hope that the technique will help them develop more effective vaccines that reduce the chances of healthy birds acting as a reservoir for influenza virus. The research was published in the December 2010 edition of the *Journal of Virology*.

Dr. Ananya Jeshtadi, from Dr. Mike Skinner's group at Imperial College London, carried out the study as part of the BBSRC Combating Avian Influenza initiative, which aims to increase understanding of how avian influenza interacts with its animal hosts in order to control its spread more effectively.

Dr. Skinner said: "The current generation of fowlpox-based vaccines are really good at stopping chickens from getting ill when they come into contact with flu but they don't always stop the birds from getting infected. Because of this, around a quarter of vaccinated birds still act as carriers of the disease and pass it on to others. Our hope is that we can engineer a new vaccine that makes this much less likely."

Since being introduced in Mexico in the mid 1990s, fowlpox-based vaccines have become an important weapon in the fight against avian influenza (more than 2 billion doses have been used) and are currently being used as part of a massive campaign to protect some 5 billion poultry in China. The so-called 'recombinant vaccine' is based on a fowl pox virus that has been modified to display an influenza protein on the surface of the infected cell. The immune system of a vaccinated chicken is primed to respond to the influenza protein, meaning that the bird can successfully combat flu when subsequently exposed to it. With recombinant vaccines, farmers can also test whether chickens have been given the vaccine or have been exposed to the influenza virus, which is less easy with flu-based vaccines.

Dr. Skinner continued: "The problem with current influenza vaccines is that they don't stimulate the part of the immune system that would normally clear out any infected cells when the chickens are exposed to flu. What we hope is that this work will enable us to identify factors in the fowlpox-based vaccines that prevent chickens from mounting responses to eliminate infected cells. Once we know what these are, we may be able to develop an improved vaccine that would counter this

problem of vaccinated chickens harbouring the virus".

Dr. Stan Botchway of the STFC Rutherford Appleton Laboratory who developed the advanced microscopy technique and worked on the study said: "The type of microscopy we used to study the viruses interacting with the chicken cells is particularly valuable for several reasons. For example, by using near infra red laser light we are able to see deeper into cells and tissues and observe them for a long time, even over days without damaging them. This allows us to observe how all of the different proteins interact without disturbing the process by firing high energy lasers at them. Also, the technique doesn't require us to extract the proteins from the cells before we determine the protein interaction, which is the method used in nearly all laboratories currently."

Improved vaccination against bird flu is especially important because the current H5N1 type is both highly contagious and has a high mortality rate in birds. It is widely estimated that at least 200 million domestic birds have either died or been culled as a result of H5N1. H5N1 virus also presents a risk to human health. Over 500 cases have been identified in people, resulting in 300 deaths. Most of the cases so far have been in rural Asian populations where cases may be under-reported and there is an ongoing fear that the virus may evolve the capacity to spread from person to person causing an influenza pandemic.

A vaccine which is able to block transmission would be especially beneficial in the UK where 25% of chickens are free-range. It is often necessary to house free-range chickens indoors when a serious communicable disease has been detected within a defined radius. Such a vaccine would increase the likelihood that a flock could remain outside during outbreaks of influenza.

Provided by Science and Technology Facilities Council