UMS developing DNA-based vaccines

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KOTA KINABALU: Two researchers at the Biotechnology Research Institute of Universiti Malaysia Sabah (UMS) are currently embarking on a project to produce DNA-based vaccines against animal diseases.

Dr Clarence M. Ongkudon and Dr Kenneth F. Rodrigues, who are experts in high throughput DNA purification and DNA vaccine optimisation, hope to address the challenge faced by the aquaculture industry, which is the mitigation of the looming vaccine crisis in the event of a pandemic.

"The long-term objective of this research is to contribute to the public health and biological security in Malaysia and to offer an alternative to currently existing vaccines which have to be imported at a very high cost," they said in a statement.

UMS Researchers Focus on Development of DNA Vaccines Viruses, they said, have evolved alongside humanity for millennia and are responsible for global pandemics, some of which have been thoroughly documented.

Foremost among these is the Spanish Flu of 1918, which infected approximately 500 million individuals and resulted in 50 million deaths over a period of six months, they said.

The outbreaks of influenza such as the 2009 flu pandemic, they said, resulted in over 18,000 deaths worldwide.

To this, they said evolution is central to the existence of viruses.

"The small genome and rapid rate of multiplication in a specific host offer plethora of opportunities to mutate, evolve and eventually develop resistance to therapies which are currently practised by the global healthcare community.

" Vaccination against viruses is one of the most widely accepted practices, which results in a cell-mediated immune response in the human host," they said.

Currently, there are three generations of vaccines that are available to the community, they said.

The first generation is based on killed or attenuated viruses while the second generation is based on recombinant proteins from viruses and the third generation is DNA vaccine, they said.

One of the major challenges facing the healthcare community in the event of a pandemic, they said, is the limited production capacity of traditional vaccine production platforms.

In a typical situation, they said the emergence of a new variant of a common virus would require the rapid development of a vaccine to mitigate the threat in a very short time interval.

"First generation vaccines are produced using virus free fertilised chicken eggs.

"The virus is cultured within the egg, purified and subsequently combined with an adjuvant in order to improve its efficiency," they said.

However, this method is time consuming and the production capacity is limited, they said.

Second generation vaccines, on the other hand, are produced by cloning of the gene encoding the viral coat protein in a bacterial host, which produces large volumes of proteins in a very short period of time.

It can be produced within a period of days in industrial fermenters, following which they can be purified and delivered directly to healthcare providers, they said.

However, they said that recombinant proteins produced in bacteria may not possess the correct physical and biochemical structure to elicit appropriate immune responses.

"In addition to that, the production cost is also high due to the complex protein purification steps involved," they said.

Third generation DNA vaccines, they said, are based on small sections of DNA derived from the virus itself.

These DNA molecules are then developed into vaccines, which can be delivered directly into the human host, they said.

They said that extensive research done on the biosafety of DNA vaccines reveals that DNA vaccines do not pose a threat to human beings.

"The low effective dose and rapid production time of DNA vaccines make them an antigen of choice for the present and future disease prevention.

"A DNA molecule encoding the viral coat protein, or antigen, is injected into the human host, and upon entry into the nucleus, the DNA molecule produces the viral antigen, which in turn elicits a range of immune responses.

"The DNA is subsequently degraded by the enzymes, which are present in the human cells and is not passed on to subsequent generations," they said.

Hence, they said that production and purification of DNA based vaccines can now be carried out at a laboratory scale and a pilot scale.

These vaccines can be lyophilised and stored for indefinite periods of time, they said, unlike first and second-generation vaccines, which require refrigeration and special conditions for storage.

The process of vaccine development, they said, commences with the design of the plasmid DNA construct, which comprises the viral antigen engineered to express as a protein in the animal cell.

"Subsequently, these plasmids are tested in animal cell lines to ensure that the correct antigen is produced," they said.

But hundreds of candidate plasmids have to be screened in order to produce the correct combination of antigen and promoter DNA molecules, they said.

The viable candidates are then produced in bacterial hosts, which serve as microbial cell factories and generate millions of copies of plasmids within 24-48 hour period.

Following this, the DNA molecules are purified using dedicated affinity columns, which result in ultrapure DNA vaccine that is free from any adventitious agents.

But plasmid DNA vaccines have to undergo extensive testing and need to comply with statutory norms such as biosafety laws and FDA regulations prior to their administration into the animal population.

In a nutshell, Dr Ongkudon and Dr Rodrigues said the amount of impurities (e.g. RNAs, gDNAs, nicked pDNAs, endotoxins, proteins and other medium residuals) remaining in the final DNA vaccine product should represent less than one (1) per cent by mass volume of the total vaccine.

To this end, they said the Biotechnology Research Institute is currently developing a vaccine to treat Grouper Iridovirus, a major causative agent of mortality in the aquaculture industry.