Rice researchers seek better vaccine procedure

September 8 2009

As manufacturers work furiously to make a vaccine to protect against 2009 influenza A (H1N1) virus, a Rice University bioengineer is trying to improve the process for future flu seasons. The goal is to shorten the time it takes to identify targeted flu strains and manufacture the vaccines for them.

In a paper published this summer in the journal *Protein Engineering, Design & Selection*, Rice researchers described a new method to predict the efficacy of H1N1 vaccines.

Michael Deem, Rice's John W. Cox Professor in Biochemical and Genetic Engineering and professor of physics and astronomy, and his group are using a formula they developed several years ago to more accurately predict which vaccines can halt ever-evolving strains of the flu, including the novel H1N1 variety that the World Health Organization has tagged as a pandemic virus.

Deem has identified the dominant epitope regions of hemagglutinin, a part of the virus that the immune system recognizes, as the best candidates for comparison by the formula. Epitopes are antigens, short for antibody generators. They're bits of viral protein the body recognizes when the flu attacks, and they prompt the immune system to make antibodies, destroy the virus and be on guard against future infection by the same microorganism.

Deem's technique compares amino-acid sequences of the epitope regions

of two strains of H1N1 -- or any other influenza A virus -- and marks the differences. The fewer the differences, the more likely it is that one strain engineered into a vaccine will help prevent the other from infecting a person.

Vaccines work by introducing weak versions of live or inactivated viruses into the body and give the immune system fair warning that a flu virus with a particular epitope may attack. If a vaccine's epitopes are a perfect match to those of the virus, it should be effective in stopping the flu.

That does not always happen.

Vaccines typically contain protection against what scientists consider the three most likely strains of influenza A and influenza B to hit during flu season. But the flu is a master of disguise and can evolve between the spring, when such decisions are made, and the fall, when shots are administered.

"The virus mutates quite a bit," Deem said. "Normally, when we're doing rational drug design, we're trying to do it against a target protein that is not changing, and we're trying to find something that fits very nicely in the pocket of that protein.

"For the flu, these epitopes change. So rational drug design against one strain of the flu virus would only be useful for that one year, and then the virus would mutate the next year."

Deem wants to cut the amount of time between the analysis of flu strains and the manufacture of vaccines to fight them. He and graduate student Keyao Pan can predict the efficacy of H1N1 vaccines by estimating the antigenic "distance" -- the degree of difference between the epitopes -- for any two strains of virus.

Deem's technique assigns a numerical value to the antigenic distance between two strains. That tells researchers just how effective a virus might be. But it also offers a tipping point: If a value of zero is the perfect H1N1 vaccine, a value above roughly 0.4 indicates a vaccine that offers no protection at all.

That means there's a real incentive to formulating the vaccine as close to flu season as possible. It also means choosing strains of the virus that can be produced in high quantities but which are also as close as possible to the virus strain expected to hit. The current process is time-consuming: The novel H1N1 vaccines are incubating in hens' eggs -- the traditional method -- right now, and the United States expects to have 40 million doses in hand by mid-October, with 20 million doses arriving weekly thereafter, said Deem.

His calculations provide incentive to refine cell-based approaches that could shorten manufacture time. "In the United States government, this has been recognized, and there's investment now in new technologies," he said.

"I think modeling has already had an impact on the World Health Organization, and this type of modeling -- and our model in particular -- will have an impact."

More information: Read the paper at: peds.oxfordjournals.org/cgi/content/short/22/9/543

Source: Rice University (news : web)