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Armour against attack

Softwares now help biologists make better vaccines. **G.S. Mudur** reports

Another needle prick: All available vaccines are not foolproof

Many years ago, when he was forced to dissect a frog in his 10th grade biology class, Gajendra Pal Singh Raghava made up his mind to abandon biology altogether. 'It was a messy dissection and I hated doing it,' says Raghava who hasn't ever worked in a 'wetlab' since then. He has neither poured biological reagents into test-tubes nor even peered through a microscope to watch organisms on a glass slide.

But Raghava, who works at the Institute of Microbial Technology (IMTECH), Chandigarh, is now doing work that can help biologists make better vaccines. After five years of research, he and his colleagues at the IMTECH have teamed up with a small software company in New Delhi to release a set of programme for the computer-aided design of vaccines.

BioMantra, the life sciences division of the First eLearning Quest, a knowledge management company, has just released the software called VaxiPred. It can help biologists develop vaccines that are more effective and have lower risks of side-effects than existing vaccines. Traditional vaccines are based on killed or weakened organisms. The immune res-ponse generated by these vaccines protect people from the disease when they get infected.

'But you don't need a whole organism to immunise people,' says Raghava. Over the past decade, vaccine-designers have come closer to the concept of using small portions of organisms ' specifically small fragments of their proteins ' as vaccines to trigger an immune response. 'The key question is which fragments of proteins will generate an immune response. Our software predicts those fragments,' he says.

Raghava may have decided not to study biology in his 10th grade but once at IMTECH, his interest in the subject perked up. He began to apply his computer skills to predicting the shapes of proteins. All proteins are made of a small set of amino acids and predicting the three-dimensional shape of proteins is crucial in many applications, such as deciphering the functions of proteins, designing new drugs, or fathoming the complex interactions between organisms and cells in the body.

Five years ago, Raghava and his colleagues decided to build a database of known fragments of proteins of organisms that stimulate an immune response in humans. When a virus enters the human body, it encounters two types of immune responses. To tackle the invasion, a class of white blood cells, called B cells, trigger the production of antibodies that attack the virus circulating in the blood.

But many organisms escape this antibody attack by invading specific human cells. The body organises a second type of response, called T cell immunity, which is orchestrated to destroy these infected cells as well as to store a memory of the invading organism to protect against future infections.

Inside an infected cell, the organism releases its own proteins that are recognised as 'non-human' by special molecules in the cell and chaperoned to the surface of the infected cell.

'The infected cell with a small foreign protein fragment sticking out of its surface is a tagged cell, marked for destruction by T cells themselves and by cell-killing chemicals released by T cells,' says Raghava. The software developed by IMTECH helps predict specific fragments of proteins on organisms that can trigger both the B cell and T cell immunity. The identity of such fragments called antigens can help biologists make better vaccines.

The IMTECH researchers scanned over 10,000 scientific papers from all over the world in which biologists had reported finding regions of antigens that elicit B cell and T cell immunity, also known as B cell and T cell epitopes. They first created a database of 24,000 entries, covering known T cell epitopes and 3,000 known B cell epitopes. They developed software that uses rules to exploit this database to predict other new, and likely, epitopes.

To find the latter on a protein with 200 amino acids, biologists create 192 fragments of

nine amino acids in each, and test each one individually in the laboratory. However, the new software will choose four or five specific fragments as the most likely epitopes. Biologists will have to authenticate this in a laboratory, but it will save them enormous time.

The versions of the software created by the IMTECH researchers weren't too friendly for busy users. It would not support a large number of parallel users and tend to slow down or deliver inaccurate results. BioMantra reengineered the programme to achieve greater stability and faster processing and to make it more user-friendly.

'We've now got an enhanced package tailored for commercial applications,' says Madhulika Tripathi, who studied pharmacology and management, but has spent over two dec-ades in the information technology industry. 'It's also easier to use because all epitope prediction methods have been integrated into a single programme,' she says. VaxiPred will be available through BioMantra as a product. Si-nce its launch last week, many scientists have logged on to test the new software. Hits on the website have come from the University of Ma-ryland, University of Virginia, Imperial College, London, and several institutions in Australia, Brazil, France, Germany and Japan.