NEWS IN BRIEF

THE FIRST SUCCESSFUL MALARIA VACCINE

Making a vaccine against a parasite is more complex than against bacteria or a virus. Joe Cohen, scientist at Glaxo Smith Kline, who has been in search of a vaccine against the ubiquitous malaria parasite for 23 years, could testify to this. It could also explain why there were tears in the eyes of the team when results of the large scale trial of the most successful vaccine against malaria so far came out.

"It's been a long time coming, and indeed we are still not there yet, but it is becoming increasingly clear that we really do have the first effective vaccine against a parasitic disease in humans." says Nicolas White, in a recent editorial in the NEJM. WHO has indicated that if all goes well the RTS,S/AS01 *Plasmodium Falciparum* malaria vaccine should be available for use in 3 years. RTS,S/AS01 is a hybrid construct of the hepatitis B surface antigen fused with a recombinant antigen derived from part of the circumsporozoite protein derived from the sporozoite stage of the parasite. The success of Cohen's vaccine lies in its ability to stimulate the immune system with several molecules for a multi-pronged attack and the proprietary adjuvant AS01.

The NEJM has just published an interim report of a large, multicenter phase 3 trial of this vaccine in which 15,460 children in two age categories — 6 to 12 weeks and 5 to 17 months — were enrolled. There was a 55% reduction in overall episodes of clinical malaria and a 35% drop in cases of severe malaria. Inexplicably there was an increased incidence of bacterial meningitis in the cases who received the vaccine and this needs further observation. It still remains to be seen how long the protection lasts especially with declining malaria transmission (*NEJM October 8, 2011*).

THE NOBEL PRIZE FOR MEDICINE 2011

The Nobel Prize in Medicine goes to 3 scientists who have uncovered the secrets of how organisms sense attack by microbes and activate innate immunity initially and adaptive immunity later.

Jules Hoffman was working in The University of Strausburg, France on how fruitflies combat infections. When he infected them he found that flies who had mutations in a gene named *Toll*, all died. *Toll* mutants died because they could not mount an effective defense. He concluded that the product of the *Toll* gene was involved in sensing pathogenic microorganisms and *Toll* activation was needed for successful defense.

Across the Atlantic, Bruce Beutler in the University of Texas, Dallas, was working from a different angle. He was trying to understand how lipopolysaccharide (LPS) which is a bacterial product, sometimes causes septic shock. Mice resistant to LPS had a mutation in a gene that was quite similar to the *Toll* gene of the fruit fly. This *Toll*-like receptor (TLR) turned out to be the elusive LPS receptor. When it binds LPS, signals are activated that cause inflammation and, when LPS doses are excessive, septic shock ensues. These findings showed that mammals and fruit flies use similar molecules to activate innate immunity when encountering pathogenic microorganisms.

The third person to share the Nobel this year was Ralph Steinman of the Rockfeller University, New York. There was intense speculation whether the award would be withdrawn since he died 2 days before the announcement of the award. However the Nobel Committee got to know of it 3 hours after the award announcement. So although the Nobel Prize is never awarded posthumously, this time the honor has not been withdrawn. It is tragic that Steinman died battling pancreatic cancer for which his life had been extended using immunotherapy of his own design. Steinman discovered the dendritic cell and speculated that it had a key role in activating T cells. In cell culture experiments he showed that the dendritic cell is responsible for developing an immunological memory against various substances which on later encounters will induce an exaggerated response by T cells. This interesting cell is also involved in decisions regarding mounting attacks on self and non self antigens (*Scientific American 3 October 2011*).

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