New broad-spectrum vaccine to prevent cervical cancer induces strong responses in animals

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Mice and rabbits immunized with a multimeric-L2 protein vaccine had robust antibody responses and were protected from infection when exposed to human papillomavirus (HPV) type 16 four months after vaccination, according to a new study published in the May 26 online issue of the *Journal of the National Cancer Institute*.

Current HPV L1-based vaccines are almost 100% protective against infection by the two HPV types that are responsible for 70% of all cervical cancer cases world wide. However, the existing vaccines provide limited protection against the other HPV types that cause cancer. With that limitation in mind, Richard Roden, Ph.D., of the Johns Hopkins University in Baltimore, and colleagues have been working on an alternate vaccine that is based on the HPV minor capsid protein L2, which is highly conserved between HPV types. Previous experiments showed that the L2 protein induced only a weak antibody response in animals.

In the current study, Roden and colleagues linked together a short segment of the L2 protein from several HPV types to generate a single multimeric L2 fusion protein. They tested the ability of this multimeric-L2 protein to induce antibody responses in animals and its ability to protect them from subsequent infection with HPV type 16.

Mice immunized with the multimeric L2 vaccine developed robust

antibody responses against all of the HPV types tested, although the antibody titer was still lower than the type-restricted responses following vaccination with an existing HPV L1-based vaccine. When a multimeric L2 vaccine was delivered with a potent adjuvant to stimulate the immune response, such as alum, the vaccinated animals were able to resist infection by HPV16.

"Clinical studies are warranted to assess the safety and immunogenicity of multitype L2 vaccines in alum and other adjuvant formulations," the authors write. "If an L2 vaccine were proven effective in people, its simpler manufacturing process could make the local production of such a vaccine highly feasible, which might achieve the goal of producing it at sustainable prices in emerging countries and lead to its widespread implementation in the developing world."

In an accompanying editorial, F. Xavier Bosch, M.D., Ph.D., of the Catalan Institute of Oncology, in Barcelona, Spain, reviews the strengths of the current HPV vaccines but notes that they are too expensive to be used in much of the world and do not protect against enough HPV types. A broad-spectrum vaccine, such as the one being developed by Roden and colleagues, could solve those problems. The new data represent a meaningful step forward, Bosch says.

"The results open the door to a novel family of second generation HPV vaccines with significant potential value in the public health horizon," the editorialist writes. "As soon as appropriate, Phase 1 trials in humans should be initiated."

The clinical evaluation of new products, however, will likely take years. During this time, the currently available vaccines should be used as widely as possible, according to the editorialists.

More information:

Article: Jagu et al. Concatenated Multitype L2 Fusion Proteins as Candidate Prophylactic Pan-Human Papillomavirus Vaccines. J Natl Cancer Inst 2009, 101: 782-792.
Editorial: Bosch, F.X. Broad-Spectrum Human Papillomavirus Vaccines: New Horizons but One Step at a Time. J Natl Cancer Inst 2009, 101: 771-773

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