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Overcoming hurdles of HCMV vaccine development: Munich researchers claim progress

Recent patent publication introduces a viral vector that is both infecting endothelial cells and is eliciting an immune response

Munich, Infections by Human Cytomegalovirus (HCMV) are among the medically most significant herpesvirus infections. About 30 – 40.000 infants p.a. are born already infected in the USA alone, millions when including countries less developed. Individuals with a competent immune system cope with such infection, less so individuals that have experienced organ transplants or HIV. Such individuals then suffer life-threatening inflammatory diseases over and over again. The National Vaccine Committee of the US Institute of Medicine made an effective HCMV vaccine a highest level priority due to society costs in both morbidity groups.

No vaccine is commercially available, the therapy of choice is a single hit chemotherapy with known severe side effects. Searching for an effective HCMV vaccine has become a #1 priority in vaccine research.

One of the more promising strategies is viral vector based: live attenuated HCMV is being generated by multiple cell culture passages. When adapting HCMV to cell culture conditions it loses functional genes that make it less pathogenic to the host than in native state. The first such vaccine was based on the AD169 strain of HCMV that was cultured in human fibroblasts. The vaccine did work and elicited an immune response, it was found safe and generally well tolerated. The issue was common site reactions like fever, headache, fatigue and myalgia. A successor to AD169 was the so-called Towne strain which was phenotypically similar to AD169. Again, Towne strain worked well, unfortunately, the vaccine based protection was much less than natural immunity and was considered suboptimal. Other strains were tried out, some of chimeric nature.

Munich researchers discovered that Towne strain and related vaccines were incapable of efficiently infecting endothelial cells. In addition, proper antibodies against endotheliotropic HCMV strains were not being induced by Towne. The researchers discovered also that Towne strain is lacking genes when compared with clinical wild type HCMV isolates. Further work with replication-defective alpha-herpesvirus and single-cycle virus made clear that any effective HCMV vaccine better contains a beta-herpesvirus in such vaccine.

The recent patent publication introduces a viral vector that is both infecting endothelial cells and is eliciting an immune response. Even more, the neutralizing antibodies are targeted against beta-herpesvirus and CD4+ and CD8+ T-cells directed against epitopes of beta-herpesvirus . The immune response is being elicited by the beta-herpesvirus and more specifically the HCMV of the invention is spread deficient. Spread deficiency means that no viral particle is released from the infected cell making the vector a “safer” choice.

HCMV remains tricky: its genes encode gene products interfering with different immune mechanisms at all stages of the immune system. Evidence suggests that neither the humoral nor the cellular immune response alone is sufficient to control HCMV infection. The finding of

the Munich researchers is suggesting a new promising pathway that eventually may help coping with the complex issue.

About SIRION Biotech www.SIRION-Biotech.com

SIRION Biotech started in Munich in 2007 with the idea of enabling novel cell models closer to reality than ever before. This required the assembly of an all-encompassing, novel viral vector platform. Both, designing de novo viral vectors and the subsequent creation of custom cell models will pave the way for superior compound development in the life sciences. SIRION's technologies have been validated in over 300 single projects with more than 100 academic and industrial partners. As a result, cell models for drug discovery and development have become highly reliable, as have the use of new viral vectors in gene therapy and vaccine studies.

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