

## Novel MVA mutant eliciting enhanced T cell memory

Reference Number: TO 01-00440

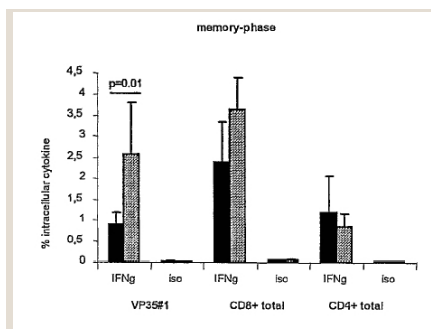
### Challenge

Absence of pathogenicity for humans, avirulence even in immunocompromized hosts, high-level expression of foreign antigens and strong adjuvant effect make recombinant MVA (rMVA) an ideal vector for both prophylactic and therapeutic vaccination.

Interleukin 1 $\beta$  (IL1 $\beta$ ) is an important regulator of inflammatory responses and contributes to host immune defense against infection. MVA and other orthopoxviruses encode a viral soluble IL1 $\beta$ -receptor (IL1 $\beta$ R), which modulates the acute-phase host response to infection and might influence the induction of immune responses against virus-associated antigens. Due to conflicting data from experiments after deletion of the IL1 $\beta$ R gene in vaccinia virus, the role of MVA IL1 $\beta$ R gene in modulation of MVA life cycle and host response to MVA is still unclear.

### Technology

IL1 $\beta$ R deficient MVA (MVA- $\Delta$ IL1 $\beta$ R) shows the same growth characteristics as wtMVA on



Memory response in HHD mice  
Source: WO 05/030971

chicken embryonic fibroblast cells. As shown by intranasal infection of mice with high doses of MVA- $\Delta$ IL1 $\beta$ R, the mutant virus is as safe as wtMVA. After vaccination of mice, MVA- $\Delta$ IL1 $\beta$ R or wtMVA induced similar acute-phase immune responses. Importantly, in the memory phase, MVA- $\Delta$ IL1 $\beta$ R elicits significantly higher MVA-specific total CD8+ and peptide-specific T-cell responses. Moreover, 4–6 months after vaccination, MVA- $\Delta$ IL1 $\beta$ R provided higher levels of protection against lethal challenge infection with virulent vaccinia virus strain Western Reserve compared with wtMVA. These data suggest that deletion of the viral IL1 $\beta$ R gene may amplify the virus-

specific CD8+ memory T-cell response and duration of protective immunity obtained after MVA vaccination.

### Commercial Benefit and Opportunity

The work so far recommends deletion of the viral IL1 $\beta$ R gene as a first step towards the development of a new generation of MVA-based vaccines. The improved vaccine properties of MVA- $\Delta$ IL1 $\beta$ R is particularly promising, since it demonstrates the possibility of obtaining more efficacious MVA vaccines through rational genetic engineering.

The technology is available for non-exclusive licensing. Parties interested in collaborative research and development are highly welcomed.

### Developmental Status

The novel MVA mutant is currently used as vector in murine vaccination studies using MVA-nef as rMVA.

### Patent Situation

Patent applications are pending in AU, BR, CN, EP, IN, and US.

### Relevant Publication

Staib et al. (2005), J. Gen. Virol. 86, 1997-2006.

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