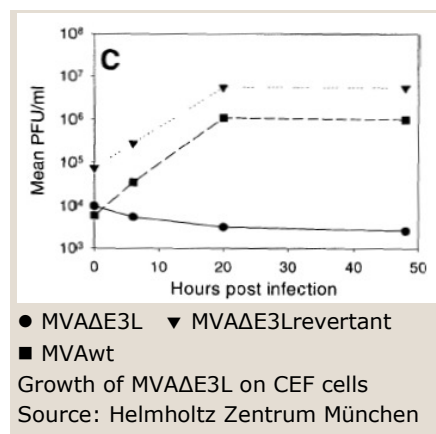


## Generation of recombinant MVA by E3L-selection

Reference Number: TO 01-00304

### Challenge

Absence of pathogenicity for humans, avirulence even in immuno-compromised hosts, high-level expression of foreign antigens and strong adjuvant effect make recombinant MVA (rMVA) an ideal vector for both prophylactic and therapeutic vaccination. The generation of rMVA relies on in vivo homologous recombination, a low-frequency event. rMVA must be purified from a large excess of parental non-recombinant MVA. Such isolation can be improved by selection with antibiotics, color screening, plaque-size restoration or plaque-forming capacity. The vaccinia viral protein E3L is an important interferon-resistance factor encoded by vaccinia viruses. So far, expression of the MVA E3L-orthologue ORF 050L was regarded as essential for the replication and production of infectious MVA virus particles in mammalian cells, but not in primary chicken fibroblasts (CEF).



### Technology

By knocking out the MVA ORF 050L or its dsRNA binding domain in MVA, the inventors found that E3L is essential for productive replication of MVA on CEF. Reconstitution of E3L leads to replication of MVA on CEF again.

Therefore, MVA lacking ORF 050L (MVAΔE3L) can be used for selection of rMVA, if along with a foreign gene of interest, ORF 050L is introduced into the MVAΔE3L genome. Only E3L expressing MVA (rMVA) grows on CEF and therefore can be selectively recovered e.g. by plaque purification. MVAΔE3L can be efficiently be

grown on Syrian hamster kidney BHK-21 cells.

### Commercial Benefit and Opportunity

The novel selection method allows the rapid identification and isolation of rMVA using an efficient host range selection system. The method can be performed with CEF cells (so far the only cells authorized by FDA regulations), thereby generating rMVA suitable for use in humans.

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

### Developmental Status

The function of MVA immunomodulatory genes like E3L in the context of infection of human cells is still a major focus of actual work.

### Patent Situation

Patents have been granted in the US (US7049145), Europe (EP1425404), and Germany (DE10144664), patent applications are pending in CA and JP.

### Relevant Publication

Fischer et al. (2006), Cell Death Differ. 13, 109-118; Ludwig et al. (2006), J. Gen. Virol. 87, 1145-1155; Ludwig et al. (2005), J. Virol. 79, 2584-2596; Hornemann et al. (2003), J. Virol. 77, 8394-8407.

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