Supplement Table 2. Examples of vaccine candidates against infectious agents based on plant virus carriers (updated from Balke I., Zeltins A. (2019) Adv.Drug Deliv. Rev. 145:119-129)

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Anthrax *Bacillus anthracis* protective antigenic peptides CPMV Plant Partial toxin neutralization in mice [1]

Canine N-terminal fragment of L2 protein (AA 61-171) TMV Plant Streptavidin-L2 fragment bound to TMV [2]

papillomavirus enhances the immunogenicity in mice

Canine CPV VP2 protective epitope (15 AA) PPV Plant CPV neutralizing antibodies in mice [3,4]

parvovirus and rabbits

CPV VP2 protective epitope (AA 3-19) CPMV Plant CPV protective antibodies in mice, dogs [5-7]

protected after subcutaneous or intranasal

vaccination

CPV VP2 protective epitope (15 AA) PRSV  *E. coli* Strong immune response against epitope [8]

in mice

Different neutralizing and T-cell epitopes PhMV  *E. coli*  Protective antibodies against CPV [9]

of CPV in guinea pigs and dogs

Classical swine CSFV E2 peptides (40 and 70 AA) PVX Plant Positive Western blots using antibodies [10]

fever virus from immunized rabbits

Cottontail rabbit CRPV L2 (AA 94-122) TMV Plant Strong protection against experimental [11]

papillomavirus papillomavirus infection

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Dengue virus EB4 protein domain (45 AA) CGMMV Plant data not found [12]

type 2

Foot and mouth FMDV VP1 epitope (25 AA) CPMV Plant Epitope-containing VLPs react with specific [13-15]

disease virus sera

FMDV VP1 peptides (AA 144-152 and 142-150); TMV Plant Vaccination protects guinea pigs and swine [16,17]

fused epitope (AA 200-213 and 142-150) against FMDV infection

Different FMDV epitopes PhMV *E. coli* Epitope-containing VLPs react with sera [18]

from infected animals

FMDV VP1 epitope (AA 128-164) BaMV Plant Vaccination protects against FMDV [7]

challenge

Different FMDV VP1 peptides TNV-A Plant Strong immune response against VP1 [19]

epitopes in mice

*Francisella* OmpA (47 kDa), DnaK (70 kDa), Tul4 (17 kDa) TMVPlant Multiconjugate vaccine partially protects [20]

*tularensisis* mice against lethal doses of *F.tularensis*

Tetra-antigen vaccine, CpG as adjuvant TMV Plant (TMV) Two vaccine doses protect 80% of mice [21]

*E.coli* (antigens) from lethal pathogen challenge

Hepatitis B HBsAg (AA 111-141) CGMMV Plant VLPs stimulate *in vitro* cultured human [22]

virus PBMC from pre-immunized donors

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

HBV preS1 epitope (AA 20-41) PVY *E. coli* Strong immune response against [23]

preS1 epitope in mice

Hepatitis C HCV neutralizing “mimotope” R9 (27 AA) CMV Plant VLPs react with immune sera from [24-28]

virus HCV-positive patients (>80%)

HCV E2 epitope (AA 511-530) PapMV *E. coli* Humoral response in mice depends on [29]

antigen multimerization;

VLPs react with immune sera from

HCV-positive patients

HCV neutralizing “mimotope” R9 (27 AA) PVX Plant VLPs react with immune sera from [30]

HCV-positive patients (35%)

Human immuno- HIV-1 gp41 epitope (AA 731-752) CPMV Plant VLPs stimulate the formation of [31-34];

deficiency virus neutralizing antibodies in mice

HIV-1 gp120 V3 loop (13 AA) TBSV Plant VLPs react with immune sera from [35]

HIV-1-positive patients

HIV-1 gp41 epitope (6 AA) PVX Plant sera from VLP-immunized mice [36]

demonstrate HIV-1-neutralizing activity

HIV-1 gp41 epitopes CdMV *E. coli* VLPs react with immune sera from [37]

HIV-1-positive patients

HIV-1 gp41 epitope (6 AA) AMCV Plant data not found [38]

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Human HPV16 E7 peptide (AA 44-60) PVA Mammalian DNA vaccination protect mice [39]

papilloma virus (293T cells) against tumor development,

HPV E7ggg oncoprotein, PVX  *E. coli,* plant Strong immune response against L2 [40-43];

L2 peptide (AA 108-120) epitope in mice

Human HRV-14 VP1 epitope (AA 85-98) CPMV Plant VLPs are immunogenic in rabbits [44,45]

rhinovirus

Infectious IBDV VP2 epitope (AA 207–224) BaMV Plant VLPs protect immunized chickens from [46]

bursal disease virus challenge

virus

IBDV neutralizing epitopes PhMV *E.coli* VLPs recognized by IBDV antibodies [47]

Influenza Influenza M1 epitope (AA 57-65); PapMV *E. coli* M2e-VLPs adjuvanted with unmodified [48-54];

viruses Influenza A (H1N1) VLPs lead to 100% protection against;

M2e peptides (AA 2-24 / 6-14); lethal challenge in mice; stable

HA11 epitope (9 AA); NP epitope (AA 147-155) VLPs are more immunogenic;

M2e-VLPs serve as efficacious adjuvant for

trivalent inactivated flu vaccine

Nucleoprotein (NP), M2e peptide PapMV *E.coli* Combination of the NP nanoparticles [55]

with the PapMV-M2e nanoparticles

protects mice from infectious challenges

by influenza strains H1N1 and H3N2

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Influenza Nucleoprotein (NP) PapMV *E.coli;* NP coupled to PapMV VLPs [56]

Viruses Sortase A improved significantly the humoral

mediated and CTL immune response

coupling

Influenza A NP peptide (AA 336-374) PVX Plant VLPs activate specific CD8+ cells [57]

Influenza M2e peptides AltMV Plant data not found [58]

Influenza M2e peptide (24 AA) CCMV *E. coli;* data not found [59,60]

*P. fluorescens*

Influenza M2e peptide MaMV *E. coli* OmpC porine-adjuvanted VLPs increase [61]

the immune response in mice and dogs

Influenza HA protein (ca. 60 kDa) TMV Plant Squalene-adjuvanted HA-VLPs lead to [62]

100% protection against virus challenge

in mice

Influenza AH1N1 HA peptide (AA 87-120) PRSV *E. coli* VLPs demonstrate strong adjuvant [63]

properties in immunized mice

*Yersinia pe*s*tis* Virulence factors F1 (17.6 kDa) TMV Plant Chemically conjugated LcrV and F1 [64]

and LcrV (37 kDa) proteins to viral particles protect

mice against lethal challenge

Japanese JEV envelope protein PhMV *E. coli* Refolded VLPs generate neutralizing [65]

encephalitis epitopes (42 AA) antibodies in mice

virus

JEV EDIII domain (ca 12 kDa) BaMV Plant EDIII-VLPs generate neutralizing antibodies [66]

in mice

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Lymphocytic LCMV p33 CTL epitope (9 AA) PapMV *E. coli* p33-VLPs induce protective cell-mediated [67]

choriomeningitis antiviral immunity

virus

Malaria *P.vivax* and *P.yoelii* peptides from TMV Plant Specific mAb’s react with peptide [68]

imunodominant protein containing TMV

*P. falciparum* Pfs25 (25 kDa) AlMV Plant Pfs25-VLPs block *P.falciparum* transmission [69]

in mice

*P. falciparum* Pfs25 (25 kDa) AlMV Plant Produced under cGMP Pfs25-VLPs induced [70]

10% of antigen Pfs25-specific IgG in a dose dependent

incorporation manner; 44 human participants in Phase 1

study; low transmission reducing activity

*P. vivax* TRAP protein (AA 25-493) CMV *E. coli* (VLPs) Chemically conjugated TRAP to VLPs [71]

Mammalian protects mice against *P. berghei* challenge

(TRAP)

Mink enteritis MEV VP2 epitope (AA 3-19) CPMV Plant VLPs protect minks against virus challenge [72]

virus

Murine hepatitis MHV 5B19 epitope (AA 899-913) TMV Plant 5B19-VLPs protect mice against lethal [73]

virus virus challenge

Newcastle NDV F epitope (AA 65-81) and CMV Plant Polyclonal antibodies obtained after [74-76]

disease virus HN (AA 346-353) chicken immunization with HN-VLPs

recognize native NDV

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Poliovirus PV type 3 VP1 epitope (8 AA) TMV *E. coli* Epitope-containing VLPs induce the virus- [77]

neutralizing antibodies in rats

PV type 1 peptide (15 AA) derived TMV Plant VLPs induce antibodies against [78]

from VP1 and VP3 from peptide in immunized mice

Porcine PCV type 2 CP epitope (AA 19-28) PRSV *E. coli* Strong immune response against peptide [79]

circovirus in mice

PCV type 2 CP epitope (AA 224-233) CMV Plant Immunized pigs partially protected [80]

against PCV challenge

Porcine neutralizing epitope of PRRSV glycoprotein 5 CGMMV Plant no data found [81]

reproductive 10% of antigen

and respiratory incorporated

syndrome virus

*Pseudomonas* OM-F protein tandem peptide (34 AA) CPMV Plant Peptide specific mice antibodies [82,83]

*aeruginosa* recognize all immunotypes of

*P.aeruginosa;* immunized mice are

partially protected against challenge

OM-F protein peptides TMV Plant Peptide specific mice antibodies [84,85]

recognize all immunotypes of

*P.aeruginosa;* immunized mice are

protected against challenge

|  |  |  |  |  |  |
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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Rabies Antigenic peptide Drg24 / T-cell epitope 31D AlMV Plant Peptide-containing VLPs elicit [86,87]

(AA 253-275 / AA 404-418) virus-neutralizing antibodies; edible

vaccine serves as oral booster in

human volunteers

Adjuvant for rabies vaccine TMV Plant VLPs enhance the protection of mice [88]

spherical VLPs against rabies

Respiratory RSV RhoA protein peptide (AA 80-94) AlMV Plant data not found [89]

syncytial virus

Ricin toxin Ricine toxin chain A peptide (16 AA) TBSV Insect Antibodies from immunized mice recognize [90]

native toxin

Rubella virus RV E1 tetrapetide (32 AA x 4) TMV Plant Strong humoral immune response in mice [91]

against rubella

*Staphylococcus* FnBP D2 peptide (AA 1-38) PVX Plant Sera from peptide-VLP immunized mice [92]

*aureus* inhibit the binding of fibronectin to

immobilized FnBP

FnBP D2 peptide (AA 1-30) CPMV Plant Sera from peptide-VLP immunized rats [92]

inhibit the binding of *S. aureus*

to immobilized FnBP

*Streptococcus* S9 peptide mimicking capsular CCMV Yeast *P. pastoris* Peptide conjugated VLPs elicits [93]

group B polysaccharide (13 AA) Th1 response

S9 peptide mimicking capsular CPMV Plant Peptide conjugated VLPs elicits [93]

polysaccharide (13 AA) Th1 response

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| **Vaccine candidate** | **Antigen** | **Plant virus / VLP** | **Expression system** | **Immunological data** | **Reference** |

Zika virus ZIKV envelope protein CMV *E.coli* Vaccine induces high levels of [94]

domain III chemical specific IgGs able to neutralize

coupling ZIKV *in vitro*

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