MultiBac IC-BEVIS for Producing VLP-based Vaccines

DCVMN 19th Annual Meeting Kunming 2018

Imre Berger
University of Bristol
BrisSynBio Centre
MultiBac – Complex Production Technology

DNA Cargo: >150 kb

Bieniossek et al. TiBS 2012
MultiBac Platform @ Berger Group: 100+ projects per year
MultiBac – Complex Production Technology

Pelosse et al. BMC Biology 2017

Reich et al. Nature 2014
Crepin et al. COSB 2015
Creating a Better BV Genome

- Genome stability
- Autodeletion
- Scale-up limitations

Vijayachandran et al., *Bioengineered* 2013
SynBac: Designing a Better BV Genome

Pelosse et al., *BMC Biology* 2017
Customized Baculoviral Genomes (SVNs)

Entry site on viral backbone facilitates functionalization
Tailored genomes with tailored properties

Synthetic Viral Nanosystems (SVNs) for:
Protein folding, High-content screening (HCS), Humanized Glycosylation, Reprogramming, Genome Engineering, VLPs...
Customized Genomes

Synthetic Viral Nanosystems (SVNs)

- **MultiBac**: Target Gene(s)
- **Kinase Factory**: Hop, HSP40, P23, PPID, AHSA1, CDC37, HSPA5
- **VLP Factory**: Flu H1N1 M1, mCherry
- **MultiBacTAG**: M. Mazei PylRS, U6^{Sf21} / tRNA_{Pyl}

Pelosse et al. *BMC Biology* 2017
Influenza VLPs
VLP Factory: Influenza Virus-like particle array

Influenza Virus

Synthetic Influenza Virus Like Particle (VLP)

infectious

safe
VLP Factory: Influenza Virus-like particle array

Live Influenza Virus

VLP-factory™

MultiBac

Influenza HA5, HAB

Sari-Ak et al., Meth. Miol. Biol. 2018
VLP Factory: Influenza Virus-like particle array

Influenza VLP array of HA wild-type and mutants in VLP-factory™

Small-Scale Purification
- Sedimentation
- Gradient Centrifugation

Functional Assays
- Hemolysis
- Animal models

M1 only
HA5 M1
HAB M1

(CMV)
The ADDomer
Emerging infectious disease: Chikungunya

- Humanitarian consequences
- Economic consequences
- No efficient treatment
- No prophylactic vaccine

2006: La Réunion
Cost of epidemic: 65 M €

- Medical check-ups: 17 M €
- Medication: 8 M €
- Hospitalization: 10 M €
- Economic shortfalls: 30 M €

Source: CHU La Reunion

2025: FRANCE
5 Billion Euros!
Our technology: The ADDomer

Adenovirus is the most widely used viral vector in clinical trials (FDA approved).

- We discovered a SINGLE COMPONENT of human Adenovirus that spontaneously forms a superparticle, the ADDomer.
- ADDomer is exceptionally suited for multi-epitope peptide/protein display to combat a wide range of diseases.

ADDomer:

✓ Synthetic protein scaffold
✓ Safe (no DNA/RNA inside)
✓ Thermotolerant (no cold chain)
✓ Scalable
✓ Highly soluble (high dose)
✓ Broad range of applications
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‘Plug-n-play’

Customizing ADDomer: Vaccines

Immunogenic epitope
(i.e. Chikungunya neutralizing antigen)

ADDomer-CHIK:
ADDomer displaying nature-like ‘exposed’ neutralizing peptide antigen epitope
(120 copies per ADDomer)

ADDomer-CHIK by EM

DCVMN Kunming 2018 – Imre Berger
ADDomer: Chikungunya Vaccine Candidate PoC

Chikungunya Immunization

**ADDomer-CHIK**
(120 copies, ‘exposed’ neutralizing CHIK epitope)

**Efficient internalisation**
(ADDomer-CHIK)

**Strong humoral response**
(Prime/Boost)

**ADDomer-CHIK** vaccine candidate confers robust immune response in mice and outperforms competitor product!
ADDomer: Chikungunya Vaccine Candidate PoC

Chikungunya Immunization

**ADDomer-CHIK**
(120 copies, ‘exposed’ neutralizing CHIK epitope)

Efficient internalisation (ADDomer-CHIK)

![HeLa cells stained with fluorescent antibody](image)

**Strong humoral response**
(Prime/Boost)

- ADDomer
- ADDomer-tevCHIK (TEV cleaved)
- Diluent

Specific Serum IgG ELISA Titre

○ after 1st immunisation
● after 2nd immunisation

ADDomer-CHIK vaccine candidate confers robust immune response in mice and outperforms competitor product!
Application 2: Skin Cancer Vaccine

Melanoma (skin cancer) mouse model

ADDomer-MEL
(120 copies, melanoma model peptide epitope ‘ova’)

Efficient internalisation

Specific cellular response

Robust humoral response

ADDomer-MEL vaccination achieves >90% tumour clearance!
Thank you!
Thank you!

Join us - have fun!
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