10 YEARS OF BREAKTHROUGHS A HEALTHIER FUTURE

ZAPI Zoonoses Anticipation and Preparedness Initiative

FRIEDRICH-LOEFFLER-INSTITUT
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Novel peptide vaccines against Rift Valley fever virus

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Facts & Figures

Start date:	01.03.2015
End date:	28.02.2020
Contributions:	
IMI funding:	9 538 688 €
EFPIA in kind:	9 875 000 €
Other:	2 966 475 €
Total Cost:	22 380 163 €
Project website:	www.zapi-imi.eu

Challenge

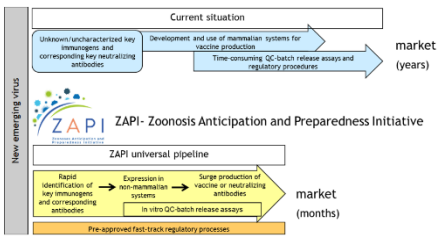


Fig. 1

The ZAPI project of the "innovative medicines initiative" aims to the establishment of a harmonized platform for the fast development of vaccines against new and emerging pathogens (Fig1.). There are three viruses as prototype within the project; MERS- Coronavirus, Schmallenbergvirus and Rift Valley fever virus(RVFV). The aim of our lab is the development of peptide vaccines and neutralizing antibodies (monoclonal as well as variable heavy chain of heavy chain only (VHHs) antibodies against RVFV.

Approach & Methodology

Innovative pipeline for fast-track identification and production of highly immunogenic

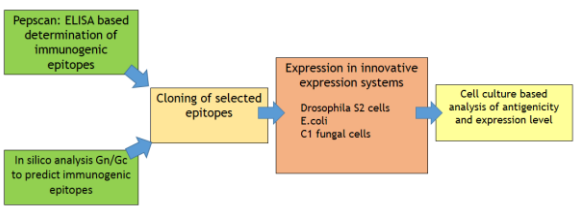


Fig. 2.: Workflow of the development of a possible peptide vaccine

Innovative antibody development pipelines:

Development and optimization of broad multi-specific antibody libraries:

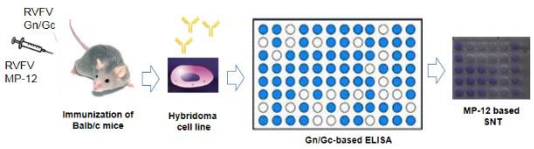


Fig. 3.: Workflow of generation of monoclonal antibodies (mabs)

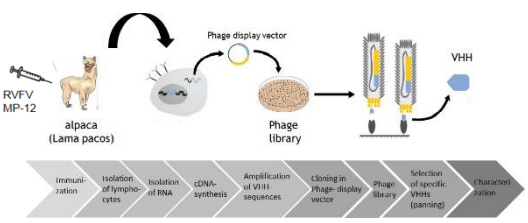
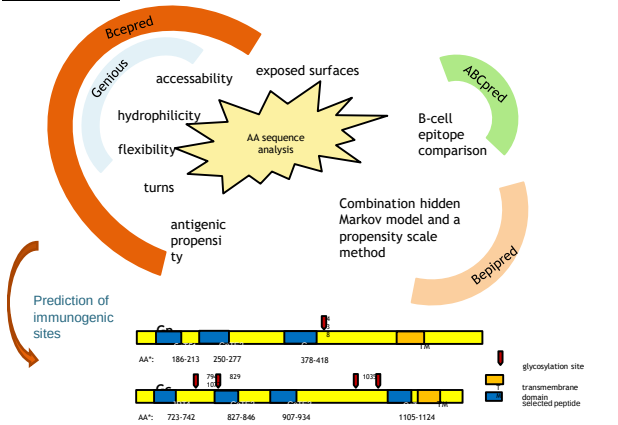


Fig. 4.: Workflow of generation of Alpaca VHHs (Variable domain of a heavy chain antibody)

Results

Key immunogens:



*: Amino acid numbering of polyprotein

Fig 5:Selection of key immunogens by in silico analysis of protein sequence

Key immunogen (peptide)	Scaffold	Innovative production system	Lab scale production	Immunization of mice	Antibody generation	Neutralizing activity
GnTE1	GFP	S2 Schneider Drosophila cells	P	P	P	No
	LS	E. coli	P	P	P	No
	MBP	E. coli	P	P	P	Weak (1:5)
GnTE2	GFP	S2 Schneider Drosophila cells	P	P	P	No
	LS	E. coli	P	P	P	No
GnTE3	GFP	S2 Schneider Drosophila cells	P	P	P	Weak (1:5)
	LS	E. coli	P	P	P	No
GcTE1	GFP	S2 Schneider Drosophila cells	P	P	P	No
GcTE2	GFP	S2 Schneider Drosophila cells	P	P	P	No
GcTE3	GFP	S2 Schneider Drosophila cells	P	P	P	No
JPT4	GFP	S2 Schneider Drosophila cells	P	P	P	No

Fig. 6: Expression of peptides on different scaffolds in different expression systems

Key neutralizing antibodies:

Anti-gens	mab RVFV +	SNT	Anti-gens	VHH RVFV +	SNT
Gc	5	-	RVFV MP-12	30	1
Gn	28	1			
RVFV MP-12	38	1			

Fig. 7.: Overview of generated mabs and VHHs against RVFV

mab	Minimal neutralizing concentraion [µg/ml]
Gn3	45
Gn3+Gn32c	22,5

Fig. 8.:Gn3 is the most potent neutralizing mab. (Derived from mice immunized with E.coli expressed Gn). A synergistic effect with the non neutralizing Gn32c shows an even higher neutralization.

Value of IMI collaboration

Thanks to the IMI- ZAPI project we had the possibility to collaborate with different researcher from a broad spectrum of scientific sectors as well as with industry partners. It has been of great benefit for the projects within the IMI-ZAPI consortium that all partners were willing to contribute and share their material and, even more, their specific knowledge of special parts of the projects to fulfill the working plans and reach outstanding effort. Furthermore, when facing problems, we always could exchange knowledge and experience with different partners. So thanks to IMI for enable such a great network.

Impact & take home message

Seven different immunogenic peptides could be predicted. They were successfully expressed with different scaffolds and in different expression systems, but only two variants showed a neutralizing effect. There are many parts that have an influence on the immunogenicity of the peptides. Nevertheless two promising variants could be detected and will be further tested in animal trials(mouse and sheep) for a proper protection.

In the second part different mabs and VHHs could be generated. Likewise with the peptides many factors play a role in detecting neutralizing antibodies. But the promising mab Gn3 and its combination will be further tested for protection in a mouse trial.

In the end the challenge of developing a fast pipeline for vaccine and antibody production could be successfully fulfilled. Although improvements have to be done, it is possible to develop a fast pipeline for vaccine and antibody production. This enables a quick intervention against outbreaks of new and emerging viruses. It can lower economic damages originated from the loss of susceptible animals(e.g. sheep in RVFV outbreaks) and maintenance human health.

imi innovative medicines initiative efpia

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