GLOBAL ASF SITUATION and VACDIVA PROJECT UPDATE

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VACDIVA-862874
A Safe DIVA Vaccine for African Swine Fever Control and Eradication.

11st May 2022
Since 2007, the last exit from AFRICA, THE ASF VIRUS IS ALREADY IN 5 CONTINENTS

MORE THAN 50 COUNTRIES
8 EPIDEMIOLOGICAL SCENARIOS
ASF keeps being....
ASF situation in Africa

- West Africa
- East and South Africa
First time reported: Kenya 1921
24 genotypes
Vectors and reservoirs: wild pigs and ticks of the Ornithodoros spp (O. moubata, O. porcinus domesticus and O. porcinus porcinus)

→ Sylvatic and domestic cycles coexist
Europe

- Georgia, 2007
- Azerbajan, 2007
- Rusia, 2007
- Ucrania, 2012
- Bielorusia, 2013
- Lituania, 2014
- Polonia, 2014
- Estonia, 2014
- Latvia, 2014
- Moldavia, 2016
- Rumania, 2017
- Republica Checa, 2017
- Bulgaria, 2018
- Hungria, 2018
- Belgica, 2018
- Slovaquia, 2019
- Serbia, 2019
- Grecia, 2020
- Alemania, 2020
- Italy, 2022

2015-2020
Free ranging pigs
No positives since 2 years and a half
ASF situation in Europe

2 different scenarios

- 12.1% % ASF DP
- 87.9% % ASF WB

Species:
- % ASF DP
- % ASF WB
- Wild boar
WB habitat vs WB ASF notifications in EU: Interaction

Wild boar

38,875 ASF notifications in WB
(untill June 2021)

Agro-urban areas

Agroforestry areas

Natural areas

BIGGEST CONTACT WB - DP

HIGHEST WB POPULATION

68.1% ASF WB notifications in Natural areas
30.6% in Agroforestry

Bosch et al. 2016 TED

ADIS, 2021 - EU
NEW ATTENUATED ASF VIRUS

ILEGAL OR LEGAL VACCINES

LARGE AMOUNT OF VIRUS CIRCULATING

Emergence and prevalence of naturally occurring lower virulent African swine fever viruses in domestic pigs in China in 2020

Encheng Sun1, Zhenjiang Zhang1, Zilong Wang1, Xijian He2, Xianfeng Zhang1, Lulu Wang1, Wenying Wang1, Lianyu Huang1, Fei Xi1, Huoyue Huangfu1, Ghebremedhin Tsegay1, Hong Huo1, Jianhong Sun1, Zhijian Tian1, Wei Xia1, Xuewu Yu2, Fang Li1, Renqiang Liu1, Yuntao Guan1, Dongming Zhao1 & Zhigao Bu1

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2College of Animal Science and Technology, Inner Mongolia University for Nationalities, Taiyuan 026000, China

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A seven-gene-deleted African swine fever virus is safe and effective as a live attenuated vaccine in pigs

Weiyi Chen1, Dongming Zhao1, Xijian He2, Renqiang Liu1, Zilong Wang1, Xianfeng Zhang1, Fang Li1, Dan Shan1, Heifeng Chen1, Jiwen Zhang1, Lulu Wang1, Zhiyuan Wen1, Xijian Wang1, Yuntao Guan1, Jinxiong Liu1 & Zhigao Bu1

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17/28 countries and regions reported ASF outbreak in South-East Asia

Source: OIE WAHIS May, 2022

Affected
ASF Affected country
Free country
Emergence and prevalence of naturally occurring lower virulent African swine fever viruses in domestic pigs in China in 2020

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Attenuated ASF virus isolation

• ASFV were isolated from 7 provinces in 2nd half of 2020. 11/22 ASFV isolates had mutations or a deletion in CD2v.
These isolates were originated from Hubei, Hebei, and Heilongjiang province. Some of non-HAD isolates showed lower virulence, less mortality but were highly transmissible. Incubation period could be longer than 30 days. It caused partial death upon high-dose infection. It caused sub-acute or chronic disease upon low-dose infection.
So-called "African swine fever pilot vaccines, home-produced vaccines, and even smuggled vaccines."

ASF fake vaccine in 2019
Label: Harbin Veterinary Research Institute (Illegal use)
Contents: Vaccines for different diseases, such as Newcastle. Some of them are interferon.

Smuggled imported vaccines, such as the recently appeared Spanish and Vietnamese vaccines.

*Even some Chinese websites provide prescribing instructions for prophylactic use of vaccines.

https://kuaibao.qq.com/s/20190902A0HDQS00?refer=spider
https://wenda.zhihu.com/a/40966.html
THE ASFv CIRCLE

SWILL FEEDING
China’s ship route to the world

<table>
<thead>
<tr>
<th>Continent</th>
<th>No. of connected countries</th>
<th>Proportion of flows</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>26</td>
<td>63.9%</td>
</tr>
<tr>
<td>Europe</td>
<td>19</td>
<td>15.8%</td>
</tr>
<tr>
<td>North America</td>
<td>6</td>
<td>9.9%</td>
</tr>
<tr>
<td>Africa</td>
<td>15</td>
<td>5.2%</td>
</tr>
<tr>
<td>South America</td>
<td>7</td>
<td>4.4%</td>
</tr>
<tr>
<td>Oceania</td>
<td>8</td>
<td>1.0%</td>
</tr>
</tbody>
</table>
Inactivated Vaccines

Not induce immune response = No protection

Subunits Vaccines or DNA Vaccines

Weak immune response = No or weak protection

ATTENUATED Vaccines

Induce immune protection up to 92 to 100%
LET'S TO KNOW THE AFRICAN SWINE FEVER VIRUS (ASFv)

Complex virus, big size, large genome: 170-190 kb (170 genes)

Complex molecular structure, still not well known

GREAT Genetic variability*

NO production of significant neutralizing antibodies

NO GOOD LAB TESTs TO EVALUATE CROSS PROTECTION: Pigs trial is need

Lack of effective vaccine yet (several prototypes are under evaluation)

200 nm
More than 100 structural proteins

24 genotypes*
*The current genotype classification is not related with the virus virulence or protection (Mur et al. 2016)
## Comparison of ASFV with others virus

<table>
<thead>
<tr>
<th></th>
<th>Number of genes</th>
<th>Genoma size (kilobases)</th>
<th>Virion Size (nanometros)</th>
<th>Numer of virion proteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASFV</td>
<td>170</td>
<td>180</td>
<td>200</td>
<td>50</td>
</tr>
<tr>
<td>PRRSV</td>
<td>10</td>
<td>15</td>
<td>60</td>
<td>8</td>
</tr>
<tr>
<td>Parvo</td>
<td>2</td>
<td>5</td>
<td>22</td>
<td>2</td>
</tr>
<tr>
<td>PCV2</td>
<td>5</td>
<td>2</td>
<td>17</td>
<td>1</td>
</tr>
</tbody>
</table>

*Fuente: Viralzone*
Thirteen partners, two industrial Companies from EU
Three partners from non-EU countries

- Institute of Animal Science (IAS), Chinese Academy of Agricultural Sciences (CAAS)
- International Livestock Research Institute (ILRI)
- FGI Federal Center for Animal Health (FGI ARRIAH)

NOT ANY MORE
OBJECTIVES

1. To provide safe and effective vaccine(s) for wild boar and domestic pigs ready for registration.

2. To develop DIVA test to allow an accurate monitoring of the effectiveness of the vaccine.

3. To design ASF control and eradication strategies in different epidemiological scenarios worldwide and test the pilot vaccine in real environments (including buspigs and warthogs).
VACDIVA: Three LAV vaccine candidates

Lv17/WB/Rie1
- Genotype II
- Naturally attenuated
- Non-hemadsorbing
- Protection proved against genotype II
- Cell line adaptation in progress
- NGS, exclusive genome features

NH/P68
- Genotype I
- Naturally attenuated
- Non-hemadsorbing
- Protection proved against genotype II and I
- NH/P68-CCL adapted cell line
- NGS, exclusive genome features

DELETION MUTANTS:
SEVERAL MUTANTS FROM Rie1 and NH/68
Under in vivo evaluation

RESULTS OBTAINED UNTIL NOW WITH MUTANTS GIVED A PROTECTION OF 100% IN DP and WB and DIVA TEST
IN VIVO EVALUATION:
PRIORITY POINTS: SECURITY, DIVA and PROTECTION

- AT UCM Spain
  100%

- at PERUGIA
  Italy
  100%

- at CISA
  Spain
  100%
¿Cebos?
100% protection

100% protection
PROTECTION TO ARMENIA 07

10³ TCID50/ml

7/7

DIVA TEST

100% WITHOUT SIDE EFFECTS

DIVA TEST ON GOING

VACCINATED
INFECTED

MUTANTS ON GOING
DIVA assay: Interpretation (PCR and Ab)

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>Marker</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>-</td>
<td>INFECTED ANIMALS</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>VACCINATED ANIMALS</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>ASF NEGATIVE</td>
</tr>
</tbody>
</table>
Genetic stability in vitro and in vivo: partially done/ on going
Adaptation of the vaccine prototypes to tissue culture partially done/on going
Best dose for DP and WB immunization: done with mutants
WB Immunization with bait: done with mutants
Overdoses immunization in WB: done mutants
Duration of Immunity (DP and WB): on going
Immunization in domestic pig with a largest number of animals: on going
DIVA adaptation: done/for Ab and PCR
Bait conservation on different scenarios: done warm countries/on going low temperatures
Cross protection: partially done in WB and DP/on going with another different isolate
Our goal: A world free of ASF