Towards a subunit vaccine for African swine fever

Background

In late 2018, the International Livestock Research Institute (ILRI) received funding from GALVmed for a research project for the development of a subunit vaccine for African swine fever. African swine fever is a disease that is present in approximately 26 countries in Africa where it poses a problem for pig farmers due to the frequent wipeout of herds, which happens regularly in some areas. In addition, the disease has grown to pandemic proportions in Europe and Asia, including China.

There is no vaccine against African swine fever virus (ASFV) and current control is based on culling and biosecurity measures. Therefore, a vaccine could significantly contribute to this control and alleviate the problems for African farmers.

The disease

African swine fever (ASF) is a devastating hemorrhagic pig disease originating from Africa, first described in Kenya in 1921. It is currently a major problem in Eastern Europe, Asia, China and India where it has spread since it escaped to Georgia from Africa in 2007 (Iglesias et al. 2017). African swine fever virus (ASFV) is present in about 26 countries in Africa, where it poses a serious constraint for pig farmers due to the recurrent wipeout of whole pig herds.

There is no vaccine; therefore, control of the disease is dependent on biosecurity and culling of animals. The virus infects domestic pigs, wild boars in Europe and Asia and wild pigs (i.e. warthogs and bush pigs) in Africa. It is transmitted by the soft ticks of the Ornithodores genus in Africa. The transmission system is very complex with several farm risk factors associated such as, lack of fences and routine cleaning of pens (Dione et al. 2017). This complex transmission system complicates the control measures.

The virus is a large DNA virus belonging to the Asfaviridae family, sharing some similarities with the pox viruses. It encodes between 151 and 167 genes depending on the isolate. ASFVs are divided into 24 genotypes, all of which have been detected in Africa (Quembo et al. 2018).

The project

One of the goals in the project is to identify antigens from ASF which are responsible for the immunity seen using the whole virus for vaccination. It has been shown previously that modified viruses by deletion of genes can confer immunity. Therefore, an attenuated version of ASF isolate was used for immunization of pigs followed by peptide screens using overlapping peptides (pieces of protein) covering the whole virus. The ASF virus which was used was isolated at the border between Kenya and Uganda during an outbreak and was determined as a genotype IX isolate (Gallardo et al. 2007 and Onzere et al. 2018). The virus had a deletion of one gene called the CD2v gene, which was generated in another project.

Three groups of pigs (including European and Kenyan local breed pigs, 22 animals in total) were immunized with the modified live virus followed by testing of immune cells. Cells were either white blood cells (PBMC) or a fraction of these, the CD8 cells, which are known as killer cells. They recognize virus-infected cells and kill them. The recognition of the infected cells happens due to small pieces of protein (peptides) of the virus, which are located on the outside of the infected cells. These peptides can be recognized by the immune cells and get killed.

In order to determine these peptides which are recognized by the immune cells, the cells are cultured together with pools of known peptides from the virus. If the cells recognize them, they will produce a substance called interferon-gamma (IFN-γ). That can be measured in an assay called enzyme-linked immunospot (ELISpot) assay.

The cells from the three groups of pigs were tested in ELISpot for recognition of peptide pools corresponding to each gene of the virus. Of the 217 peptide pools tested, 153 pools were recognized by PBMC of at least one animal (2.8 animals/pool +/- 3.6, range 1–17 animals) of which 42 pools were also recognized by CD8 T cells of at least one animal (1.7 animals/pool +/- 1.5, range 1–6). There were 47 pools corresponding to 41 genes, which were recognized among members of all three groups (6.8 animals/pool +/- 3.9, range 3–17). Among these highly immunogenic genes, there were known immunogenic genes, as well as genes that have not previously been identified as immunogenic.

Eleven genes have initially been selected for testing immunogenicity and protection against ASF in pigs. The selected genes are recognized by cells from 5–17 animals out of the 22 pigs for the PBMC. The CD8 cells recognized fewer pools with the best antigen recognized by six animals.

The antigens are currently being inserted into viral vectors for vaccination of pigs. The viral vectors are human adenovirus 5 (AdHu5) and modified vaccinia virus (MVA), which are both replication-defective, meaning that they don't multiply after injection. Each pig will receive a pool of AdHu5 with selected genes from African swine fever. Then, they will receive a booster with the recombinant MVA with the same antigens inserted as in the AdHu5 vectors. Following this immunization, they will be challengd with the virus to monitor if the vaccine is effective.

Expected outcome

The first generation ASF vaccine will probably be a live attenuated vaccine, whereas a second- generation vaccine could be a subunit vaccine, which likely will be far safer. Accesses to a vaccine will have a major impact on pig farming in Africa, where many farmers are discouraged from staying in the pig business due to recurrent problems of ASF. A vaccine would greatly improve income and livelihoods for African farmers, which translates to other actors in the value chain.

Photo credit: ILRI/Apollo Habtamu

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