SPIDVAC

Newsletter No 5

December 2024

Dear reader,

The last project year is just around the corner and we are still working hard to achieve the goals we have set ourselves.

Whether in the lab or in the barn, at meetings or conferences, in person or online, we are discussing and planning, devising new strategies and even throwing one or two overboard. Of course, all this doesn't just happen in a quiet little room and in the 'home' lab. Conferences have given us the opportunity to get in touch with other scientists and to present SPIDVAC. As always, we want to bring you closer to our work and keep you up to date on exciting topics. A highlight of this half year is certainly the launch of our SPIDVAC socio-economic survey on vaccination against Peste des Petits Ruminants in Senegal.

And our project also won an award…

We hope you enjoy reading and look forward to your feedback!

Author: S. Weber

A re-empowered weapon: the use of cryo-EM for vaccine development

Obtaining the 3D structure of viruses is crucial for accelerating the development and design of vaccines. X-ray crystallography has been instrumental in solving many high-resolution viral structures. Tobacco mosaic virus (TMV) was the first one to be structurally described, thanks to the efforts of renowned scientists such as Wendell Stanley, John Desmond Bernal, Erwin Fankunchen, Rosalind Franklin and Aaron Klug. Later, Stephen Harrison and Michael G. Rossmann, pioneers in the field, contributed with numerous viral structures, including human infecting ones [1].

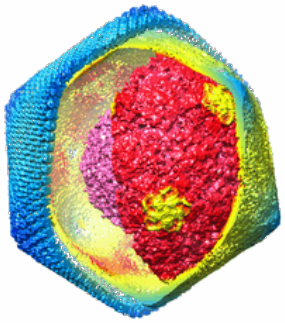

Figure 1 Overall structure of 2,080 Å diameter African swine fever virus (EMD-10346). From outside to inside, the virus contains an outer membrane (not shown), outer icosahedral capsid (blue), an inner membrane (yellow), inner capsid (red) and nucleoid (pink).

Since 2014-2015, there has been a revolution in the field of cryo-electron microscopy (cryo-EM) for 3D structure determination [2]. With advancements in microscopes, detectors and data processing algorithms, cryo-EM has emerged as one of the leading techniques for solving atomic-resolution structures of proteins and macromolecular complexes. We are in the golden age of this technique. According to the Protein Data Bank, 22,205 structures have been solved by cryo-EM, with over 80% of them deposited in just the last 4 years. One of its key advantages is that it requires less sample material, which does not need to be in crystal form as required in X-ray crystallography, and, in structural virology field, it can be used for a wider range of samples, such as enveloped viruses like Zika virus or giant viruses with diameters exceeding 1,000 Å (Fig 1).

Averaging particles embedded in vitreous ice in different orientations is at the basis of this technique. Thousands of cryo-electron 2D micrographs of the vitrified sample are collected, particle boxes are extracted, and their contrast is enhanced by averaging. Various software programs can be employed to obtain a cryo-electron density map of the particle, which is then used to generate a tridimensional atomic model of the targeted protein or virus. These models guide rational vaccine design and help in understanding antibody recognition or immune evasion. The whole virion structure aids in identifying surface exposed proteins and their epitopes, especially when interacting with Fabs. The recent COVID-19 pandemic has demonstrated how quickly cryo-EM can elucidate structures [3]. The acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike protein was rapidly solved, both alone and in complex with its cellular receptor or with neutralizing antibodies (NAbs). These structures unraveled several conformational states and the interaction interfaces with its receptor or NAbs. These studies provided the molecular basis for understanding conformational dynamics, glycan shield, vaccine development, and drug design in the fight against COVID-19 [3, 4, 5] (Fig 2).

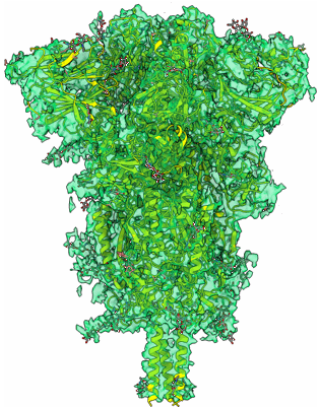

Figure 2. Fitted model of SARS-CoV-2 spike protein trimer inside the electron density represented in green colour (EMD-14621). Glycans can be observed on the surface of the spike protein even at medium resolution.

Furthermore, cryo-EM is an essential tool for particle characterization. New vaccine platforms, such as virus-like particles and lipid or inorganic nanoparticles undergo quality control for size, morphology, integrity and encapsulation state. This provides a direct method for assessing the physical state and for iteratively improving vaccine preparations. Even 3D reconstructions of nanoparticles with attached antigens on their surface can offer insights into their decoration level and ligand exposure. For example, a candidate SARS-CoV-2 vaccine based on SpyTag/SpyCatcher technology was proved to contain the receptor binding domain attached to the surface of the VLPs as confirmed by cryo-EM [6]. In gene therapy using adeno-associated viruses (AAVs), the morphological characterization of fully DNA packaged particles containing the therapeutic gene is crucial for the clinical release of efficient vectors [7].

In summary, cryo-electron microscopy has demonstrated to be a powerful tool for vaccine development, and it is evolving into a standard technique for rapidly determining the structure of emergent viruses, and soon even under conditions that approach those in native cells. In-situ cryo-electron tomography, a promising variant of cryo-EM, opens a new and exciting window into understanding biological processes inside the cell, which are essential for comprehending the virus life cycle and for the search for new therapies against viral infections.

Yet, this is just the beginning of an even more thrilling journey ahead!

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SPIDVAC Annual Meeting in Lyon 2024

At the beginning of November, a large part of the SPIDVAC consortium met at Boehringer Ingelheim in Lyon for this year's annual meeting. Again, we were also able to welcome the members of the Scientific Advisory Board and the Ethics Committee. Over the course of three days, young colleagues in particular presented their work from the laboratory and the stables, and also more experienced scientists reported on their work over the past year. In addition to many discussions about the results already achieved, the future direction of the project was also discussed. And once again, there was no shortage of socialising. Whether it was an exciting game of table football during the coffee break or a delicious dinner in a cosy atmosphere, the team spirit was strengthened and everyone got in the mood for the final year of the project. We are already looking forward to the next reunion in 2025.

5 Facts about BTV

1. Bluetongue virus (BTV), like African horse sickness virus (AHSV), is a member of the Sedoreoviridae family (Genus Orbivirus). There are 9 AHSV serotypes and many BTV serotypes of which 24 are notifiable.
2. BTV can infect domestic ruminants including cattle, sheep and goats, along with wild animals such as buffalo, deer, antelope and camels. BTV is present in all continents except Antarctica.

3. BTV is mainly spread between ruminants through the bite bites of competent Culicoides midges
4. Signs of bluetongue include fever, excessive salivation, depression, and difficulty breathing. The lips and tongue may be very swollen, the tongue is often bluish in color, giving the disease its name.
5. There is no effective treatment for bluetongue. Vaccines are available for certain types of the disease and are used in Africa and Asia.

Working internationally - Socioeconomic SPIDVAC survey on vaccination against Peste des Petits Ruminants

The first phase of the socioeconomic SPIDVAC survey on vaccination against Peste des Petits Ruminants was conducted in October 2024. A team of 8 enumerators of ISRA was deployed in a pastoral area located in North Senegal with the objective of interviewing 200 small ruminant farmers.

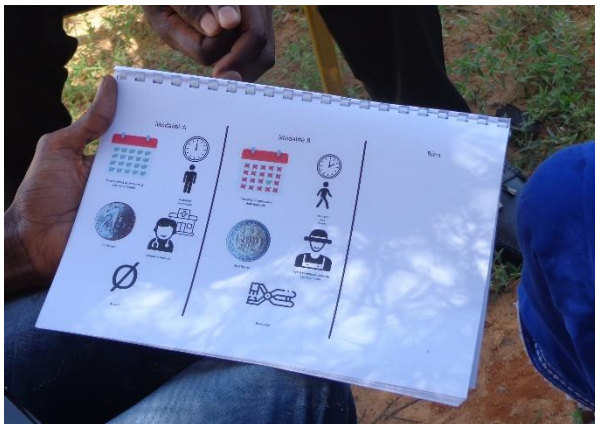


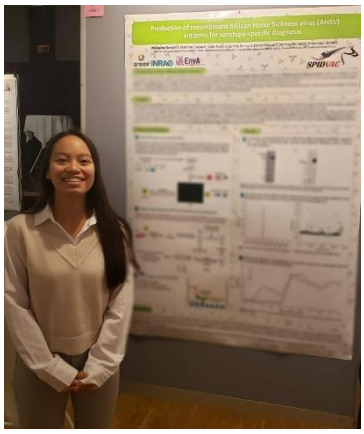
Figure 1 A questionnaire is used to determine which criteria, and which combination of criteria, are important for farmers to vaccinate their sheep against PPR.

The objective of this study is to evaluate the willingness-to-pay for vaccinating sheep and goats against Peste des Petits Ruminants (PPR) among rural farmers. PPR is a viral disease caused by a morbillivirus genetically close to the now-eradicated rinderpest virus of cattle. Its control through vaccination programs is critical for protecting the livelihood of rural households of the Sahel region and for ensuring the food security of a large part of sub-Saharan Africa. In spite of the efforts engaged by governments as well as the international community to enhance the production of efficient vaccines providing lifelong immunity, the vaccination coverage against PPR remains limited.

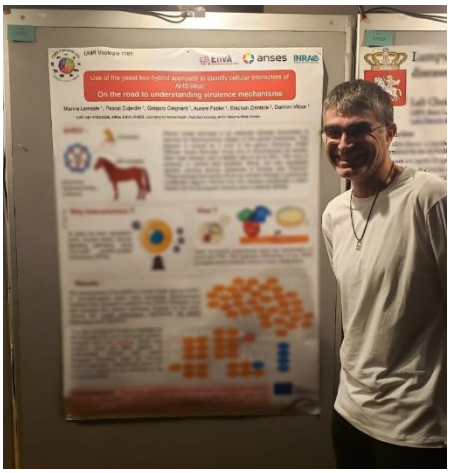
In the framework of the SPIDVAC project, CIRAD, ISRA and ID-Vet are developing innovative technologies to foster PPR vaccination programs, including DIVA vaccines and diagnostic tests - differentiating infected from vaccinated animals - as well as metaphylactic vaccines, the latter enabling the use of emergency vaccination in herds experiencing a PPR outbreak. The socioeconomic study aims at evaluating the effect of these technological changes on the likely adoption of vaccination by farmers and the price they will consent to pay for it. Among the key assessed features are the possibility to vaccinate animals when PPR outbreaks occur, and the phase out of the physical marking of vaccinated animals - a practice that is rejected by a fraction of the small ruminant farmers. To fulfill this objective, researchers of CIRAD and ISRA BAME have opted the use of discrete choice experiment, a well-known method of ex-ante valuation of goods and services commonly used in consumption economics.

Author: A. Delabouglise

Outside the lab - SPIDVAC goes to meetings



Uppsala. The 16th annual EPIZONE meeting was held from September 25 to 27 in Uppsala, Sweden, at the Swedish Veterinary Agency. EPIZONE European Research Group (ERG) is an international network of veterinary research institutes focusing on epizootic animal diseases, including those with zoonotic potential. Its main aim is to prevent, detect, and control infectious animal diseases to safeguard both animal and public health globally. Globalization and climate change have increased the risk of spreading diseases like bluetongue, swine fever, and tick- or midge-borne illnesses. EPIZONE fosters international cooperation by bringing together scientists to develop innovative tools and strategies. EPIZONE focuses on infectious diseases in animals (poultry, swine, fish, livestock, wildlife) and zoonotic agents. Its goals include improving diagnostic methods, vaccines and intervention strategies, surveillance and epidemiological studies and risk analysis.
It was therefore all the more important that the SPIDVAC consortium was also represented by some of its members to present initial project results on posters and in presentations. The abstracts of the meeting can be downloaded here: https://www.epizone-eu.net/en/home/am-2024.htm



With a presentation on the topic 'To cast virus before pigs and still not make them sick: The unsuccessful story of intra-oropharyngeal infection with foot-and-mouth disease virus', Saskia Weber presented some of the work carried out at the Friedrich-Loeffler-Institut. Piet van Rijn (Wageningen Bioveterinary Research Institute) enriched the EPIZONE with his two presentations on African horse sickness and the development of Disabled Infectious Single Animal (DISA)-DIVA vaccines.

But the members of the SPIDVAC consortium had not only travelled to Uppsala with presnentations.

Philippine Toneatti from Anses-animal health laboratory (France) presented the poster "Production of recombinant African horse sickness virus (AHSV) antigens for serological diagnosis" (Pic 1).

Damien Vitour from the same ANSES lab presented the poster "Use of the yeast two-hybrid approach for the identification of cellular interactors of AHSV: on the road to understanding virulence mechanisms" on behalf of Marine Lemesle, post-doctoral position, on the identification of new cellular interactions for African horse sickness virus to better understand pathogenesis mechanisms (Pic 2).

At the gala dinner on the third evening of the conference, Saskia Weber was delighted to win one of the two poster prizes that are awarded each year (Pic 3). In her poster 'SPIDVAC - Safe Priority Infectious Diseases VACcines', she presented the project and gave a brief insight into the various animal diseases that are being addressed in the project.

Authors: S. Weber, S. Zientara

Outside the lab - SPIDVAC goes to meetings

Deauville. From 30 September to 4 October 2024, the International Equine Infectious Diseases Conference (IEIDC2024) was held at the Centre International de Deauville, France. The IEIDC, which is organised every four years attracted over 350 participants representing 33 countries with 160 oral presentations and 27 invited speakers, including our own Stéphan Zientara from Anses.

Stéphan Zientara gave two presentations: one on emerging viral diseases or those at risk of emergence in Europe, and the other on the specific risk of emergence of the African horse sickness virus. He stressed the need to develop tools to combat and prevent this disease and presented the objectives of the SPIDVAC project.

Piet van Rijn was also at the meeting with two presentations and two posters on the development, safety and immunogenicity of African horse sickness Disabled Infectious Single Animal (DISA)-DIVA vaccines in horses and IFNAR-/- mice. Alix Carpentier and Oceane Mercier (IDvet) presented a poster on the new AHSV VP7 indirect ELISA.

Madrid. The 2024 EU National Reference Laboratories Annual Meeting for African Horse Sickness and Bluetongue took place on October 22 and 23, 2024 in Parador de Alcalá de Henares, near Madrid. Philippine also presented the SPIDVAC project and was invited to give a talk on the serotype-specific ELISA test for AHSV. Further, Piet presented an overview of his development of AHS Disabled Infectious Single Animal (DISA)-DIVA vaccines.