Summary of the OFFLU Influenza Virus in Swine Regional Latin America Group Meeting 2018

XXIX Congresso Brasileiro de Virologia, Gramado, RS, Brazil, October 20th, 2018

Chairs: Ariel Pereda and Janice Ciacci-Zanella

Participants: Ariel Pereda (INTA, Argentina), Carine Kunzler Souza (USDA-ARS-NADC, USA), Daniel Perez (University of Georgia, USA and representing Universidad del Valle de Guatemala, Guatemala), Danielle Gava (Embrapa Swine and Poultry, Brazil), Érica Azevedo Costa (UFMG, Brazil), Gloria Ramirez (Colombia), Janice Ciacci Zanella (Embrapa Swine and Poultry, Brazil), Javier Cappuccio (INTA, Argentina), Lindomar José Pena (Fiocruz-PE, Brazil), Rafael Medina (Chile), Rejane Schaefer (Embrapa Swine and Poultry, Brazil).

OFFLU overview (Ariel Pereda):

Twenty experts around the world compose influenza in swine group.
OFFLU is a global, open network of expertise on animal influenza, established jointly in 2005 by the OIE and FAO to support and coordinate global efforts to prevent, detect, and control important influenzas in animals. The network encompasses the OIE and FAO Reference Centers, other diagnostic and research facilities, and world leading experts from a range of disciplines including diagnostics, classic, and molecular epidemiology, virology, animal production, and vaccinology. The vision of OFFLU is animal health community to provide early recognition and characterization of emerging influenza viral strains in animal populations and effective management. The objectives of OFFLU include: to share technical advice, training and expertise; exchange scientific data and biological materials; collaborate with the WHO related to human-animal interface; highlight influenza surveillance and research needs, promote their development and coordination. The network primarily works through special technical activities of primary interest. The newly established groups are the influenza in wildlife and the epidemiology. The outputs of the OFFLU network are listed on the website www.offlu.net. OFFLU also interacts with WHO on regular basis at the human-animal interface to provide zoonotic influenza data for pandemic preparedness, risk assessment and update on research agendas.

Surveillance in pigs by country-updated surveillance data and research activities:

All the representatives of the countries were invited to present:

- the groups, projects and capacities in each one
- swine production information per country
- advances in influenza surveillance and influenza in pigs research activities in each country

- data on isolation and genetic characterization of influenza virus detected in swine in each country
- main results, ongoing and future projects
- how each group can help coordinate influenza surveillance and research in pigs worldwide, harmonize approaches to diagnostics and surveillance, and provide a platform for data exchange.

Argentina (Javier Cappuccio):

In Argentina, research in influenza on INTA includes wild birds, equines and pigs. The swine production in Argentina, as in all Latin America differs per region of the country. Argentina has approximately 1.1 million sows, 40% of the farms are intensive production systems and 60% of the swine population are located in Buenos Aires, Cordoba and Santa Fé Provinces. Little research or investigation is done on wild boars.

A passive influenza A virus surveillance system is working since 2011. We processed almost 400 samples per year and almost 20% of them are rRT-PCR positive. Since 2008, INTA has characterized 59 viruses identified, and the pandemic H1N1 influenza virus (H1N1pdm2009) was the most frequent subtype detected (66%) in Argentina. Today, most of the identified influenza A viruses in swine have the H1N1pdm2009 internal genes.

A longitudinal study was performed which included 3 farms monitored for 1 year. Results showed detection of IAV in the same pig in several samples (differences of 70 days between positive rRT-PCR results). These positive samples were submitted to Dr Daniel Perez group at University of Georgia for NGS characterization.

Few studies were done in backyard farms. In 228 nasal and lung samples, studied viral detection was unsuccessful. However, most of the farms have antibodies against H1N1pdm2009 subtype.

Phylogenetic analysis of IAV isolates showed that Introductions of human viruses are not related to Brazilians or Chileans ones. It is important to mention that, Argentina only imported breeding stock from Brazil (1,500 pig/year).

There are 2 commercial vaccines in Argentina, both contain non-circulating antigens in Argentina. There is autogenous vaccine in use (sequencing and characterization is done in their lab in INTA sequenced).

Argentina can contribute and harmonize diagnostic protocol, proficiency panels.

Brazil (Rejane Schaefer):

Brazil has approximately 41 million swine and is the 4th largest swine producer and exporter.

There are limited data of influenza in pigs before 2009 (studies based in serology analysis with no further genetic characterization). Since 2009 there have been more frequent influenza outbreaks in pig farms. An investigation in seven Brazilian states in 2011 showed an influenza seroprevalence of 78% in pig herds.

Virus introductions in pigs - with segments of human origin, very different from viruses found in pigs in Argentina or USA.

H1N1pdm, human seasonal origin H1N2 and H3N2 circulate in swine in several Brazilian states. All H1N2 and H3N2 viruses sequenced so far have H1N1pdm2009 internal gene segments. Currently, there are 79 complete genomes; all of them harbor H1N1pdm2009 internal genes.

Sequences from 2009 – 2010, the H1N1pdm2009 was the most prevalent.

2010 - Today, H1N1 (1A.3.3.2/npdm), H3N2 and H1N2 (1B2.2/delta-like) or H1N1 (Other-Human 1B.2/ delta 2).
Vaccines: Commercial (H1N1pdm2009), autogenous, other companies bringing vaccines with US viruses (non-circulating antigens in Brazil).
Antigenic characterization of Brazilian IAVs is underway in collaboration with Dr. Amy Vincent (USDA-ARS-NADC, USA) and Dr Nicola Lewis (UC, UK).
Brazil can contribute and share data, diagnostic protocol, proficiency panels.

Chile (Rafael Medina):

Chile is the 6th meat exporter.
Surveillance and evolution of bird and swine influenza is funded by Mount Sinai.
There are 5 sites in Chile, sampled 39 farms (93% of all farms in the country) in collaboration with a major industry from December 2013 to January 2015. It was isolated more than 120 viruses and characterization showed 2 large clusters (very old). There are no delta flu in Chile and only 1 type of N2. Results showed that were 7 different introductions of pandemic N1. All internal segments are from the H1N1pdm2009. M gene is original pandemic segment. The NS showed distinct introductions.
Cartography studies showed 2 viruses, A and B, very distinct from the pandemic, those are old viruses. Used a panel of season human virus - H1N1 and H3N2. Serology compared the immune response and analyzed the year of birth of the people. The study included Chilean samples with human sera from 1915. In the 90's there was the reassortment. Today there are 4 subtypes, mainly after the introduction of the H1N1pdm2009. Future work will include historical samples (samples from Álvaro Ruiz). Also will work with farms that vaccinate and compare with those that do not vaccinate. All the sequencing is done in USA (free). Chile can share extraction protocol, direct sample sequencing and protocol for deep sequence.

Guatemala (Celia Cordon) – presented by Daniel Perez:

Guatemala started the first study in influenza in wild birds in 2005. In 2010 started to do serology and then virology analysis to detect influenza in pigs. From 2010 - 2011 3 H1N1pdm2009 and then human virus distinct from the vaccine virus. From 2016 - 2018 started the direct sequencing of the positive sample and now only H1N1pdm2009 detected. Ongoing work includes the sequencing of 141 flu samples. Future work associated to CDC includes the national study to establish which type of influenza virus is circulating and want to study the interaction with public health. Also the Guatemala group wants to work with Nicaragua and Honduras, consolidate a surveillance system of pig herds and convince producers that it is important.

USA (Daniel Perez and Daniela Rajão) – presented by Daniel Perez:

In Perez's lab there are 12 people working on flu. The lab is member of CEIRS, where Adolfo Garcia-Sastre is the principal investigator. Work with Guatemala (hotspot for migratory birds) and supports surveillance in Argentina and Guatemala. They want to collaborate making antigenic characterization, because the cost is to send the sample, Daniel does not charge. The lab sequences 500 viruses per year, approximately. One of the expertise of the lab is to make recombinant virus.

Fundamental to use vaccine that represents what is circulating.

Perez lab collaborate with Amy Vincent from USDA and are working with some vaccines that are being used in the US (Abente's work). Sent recombinant H9N2 for Amy to perform NA antigenic characterization studies. Can collaborate with all groups and can share protocols and help with sequence and antigenic analysis.

Colombia (Gloria Ramirez):

In Colombia there are no commercial vaccines for swine influenza. Specific studies in serology showed reactivity to H3N2 and H1N1 influenza virus in swine before 1970. From 2007-2011 the research group studied PCV2 and influenza in swine with government and the organization of swine producers.support. Fifteen virus were isolated from Antioquia, Valle, Cundinamarca, those from 2008 corresponded to (cH1N1), and the remaining were H1N1pdm2009 viruses.

Last study of flu virus detection and Isolation in samples from pig slaughterhouses showed presence of the virus in the same regions as in 2007, but the virus detected was the H1N1pdm2009. Partial sequencing of virus isolates demonstrated similarity to pandemic samples including Brazilian flu viruses.

Maria Antonia Rincon Monroy from ICA, shared information of a study that analyzed 186 farms, sampled 3-12 weeks pigs; nasal swabs were analyzed by RT-PCR resulting 30.6% positive for influenza A.

Colombia is interested in studies of infection dynamics and factors associated with subclinical infection and reinfection as well as in the characterization of influenza virus circulating in swine and human populations. Ongoing projects include risk factors, zoonotic infections, participation of other species in viral ecology (bats - seeking Orthomyxovirus).

USA (Amy Vincent) – presented by Carine Kunzler Souza:

Quantifying antigenic distance between swine and human seasonal vaccine strains can be used to indicate human population immunity and may indicate swine strains of increased risk for human outbreaks or pandemics. Antigenic cartography studies were conducted in collaboration with Nicola Lewis at Royal Veterinary College, primarily with North American IAV swine strains and human seasonal vaccine strains. Strains representing contemporary H3N2, H1N1, and H1N2 swine IAV circulating in U.S., Mexico (in collaboration with University of Minnesota and Mount Sinai School of Medicine) and Canada (in collaboration with University of Saskatchewan) were used in hemagglutination inhibition assays with swine reference anti-sera. Antigenic characterization of influenza variants (swine lineage IAV detected in humans) were also included. Antigenic characterization results were presented for H1s and H3s. H1s were classified according to the global H1 classification tool and representative strains were selected for antigenic characterization. North American 1A.1 α and 1B δ strains lineage had substantial distance from recent human vaccine strains (8-13 AU). H1 1A.3.3 γ and pdm strains (2010-13) were antigenically related to the current human vaccine strains, while later strains (2014-16) were 4-5 AU away. Multiple human seasonal H3N2 were introduced into pig populations worldwide, including major introductions in North America in the 1990s and 2010s. Swine H3.1990 strains were antigenically distinct from recent human vaccine strains, while H3.2010 lineages demonstrated closer antigenic relationships to recent human vaccine strains from the late 2000 and early 2010 decades. An automated global H3 classification tool, similar in concept to the H1 tool, based on the decade of human to swine virus introduction is in development. Ongoing work will also compare antigenic distance analyses generated from ferret anti-sera versus swine anti-sera. USDA has an influenza surveillance system in swine and many viruses are available for characterization from the National Veterinary Services Laboratories.

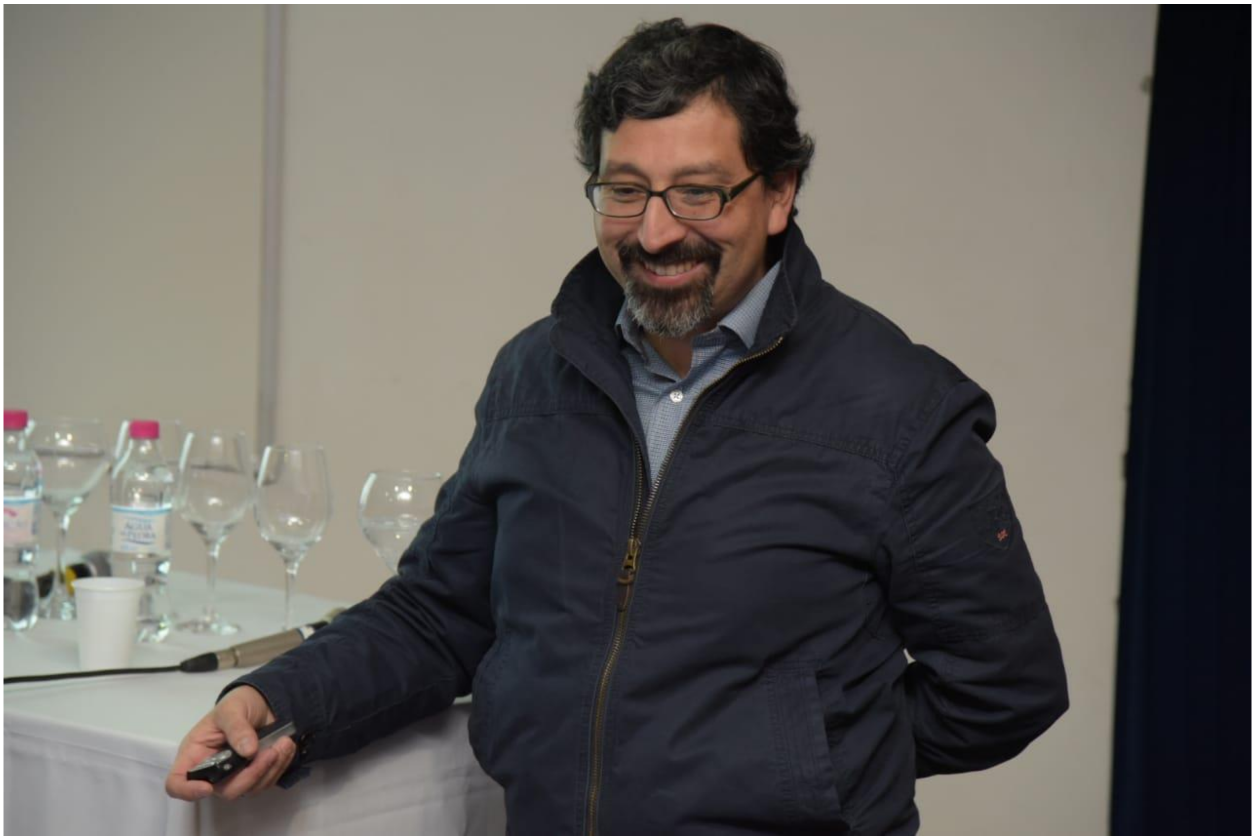
Tasks and action points for the group to work on:

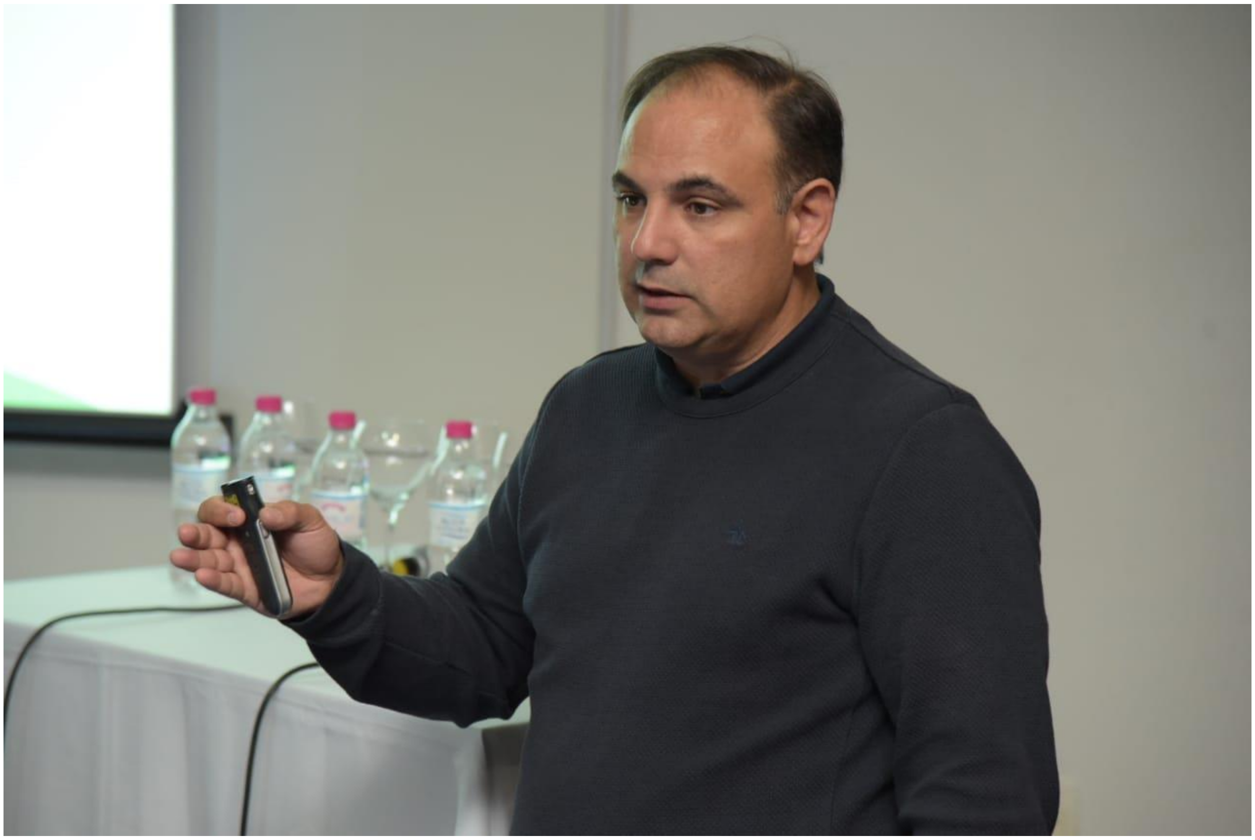
1. Labs share list of sera, list of viruses and diagnostic reagents available
2. Labs harmonize methods (MSPCR, phylogeny, cartography), produce antisera raised in pigs with strains of each region/country. Also it is very important to use the same methods (sera species, controls, reference antigens…) to have consistent HI tables for cartography analysis
3. The experts from the LA group will contact to obtain funding for training activities:
   - CEIRS - Rafael
   - OIE - IICA - Ariel
   - Fogarty International Center, NIH - Rejane
4. The experts from the LA group will write a paper with LA phylogeny and local sequences. Carine will talk to Tavis/Amy to ask for assistance (and of course be a co author) on phylogeny. Rafael will do a bullet list.
5. The experts from the LA group will make a draft manual with techniques (Javier).
6. The experts from the LA group will write a poster for the Emerging and Reemerging swine symposium in Chile (Janice and Ariel).
7. Contact and invite other labs working in Influenza in swine (all members)
8. Contact Alvaro Ruiz to see the possibility to hold the next meeting at the iserpd2019 (Ariel)

Summary - Janice

1) Minutes of the meeting
2) Send to OFFLU with the presentations
3) Email to Amy, Daniel, Adolfo - meeting brief
4) Put forward a group to start the paper - each country indicates the representative
6) Consolidate the group - give visibility
7) Set a location for the cartography (Brazil?) and MSPCR (Chile?) training in Latin America

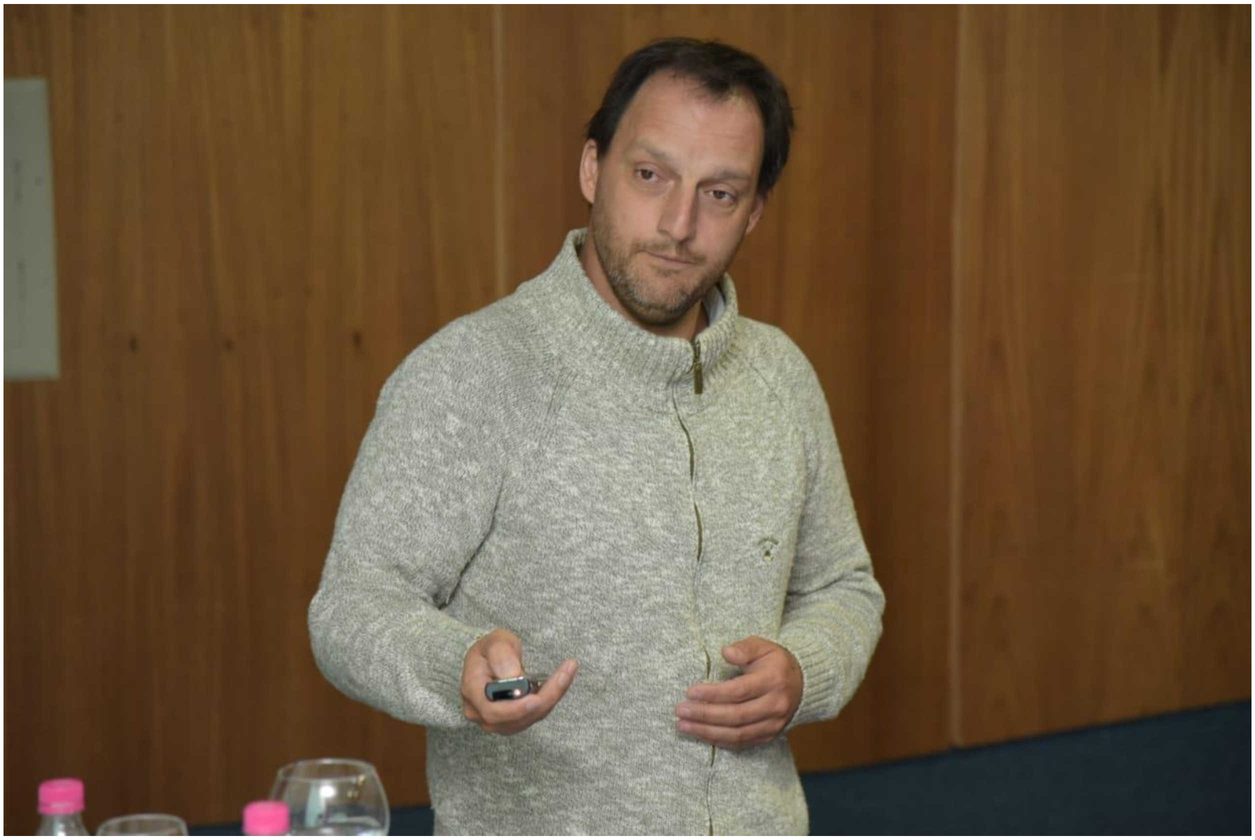
Rafael Medina - Chile

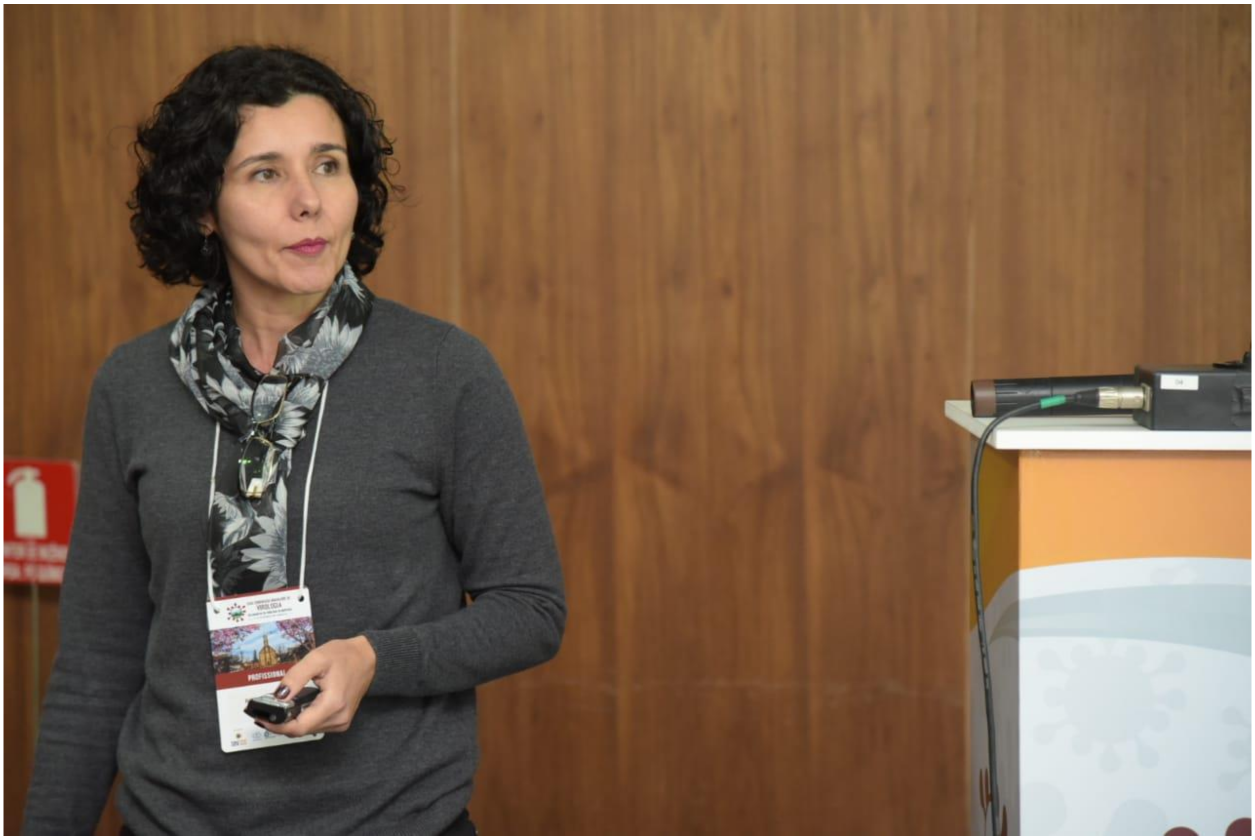




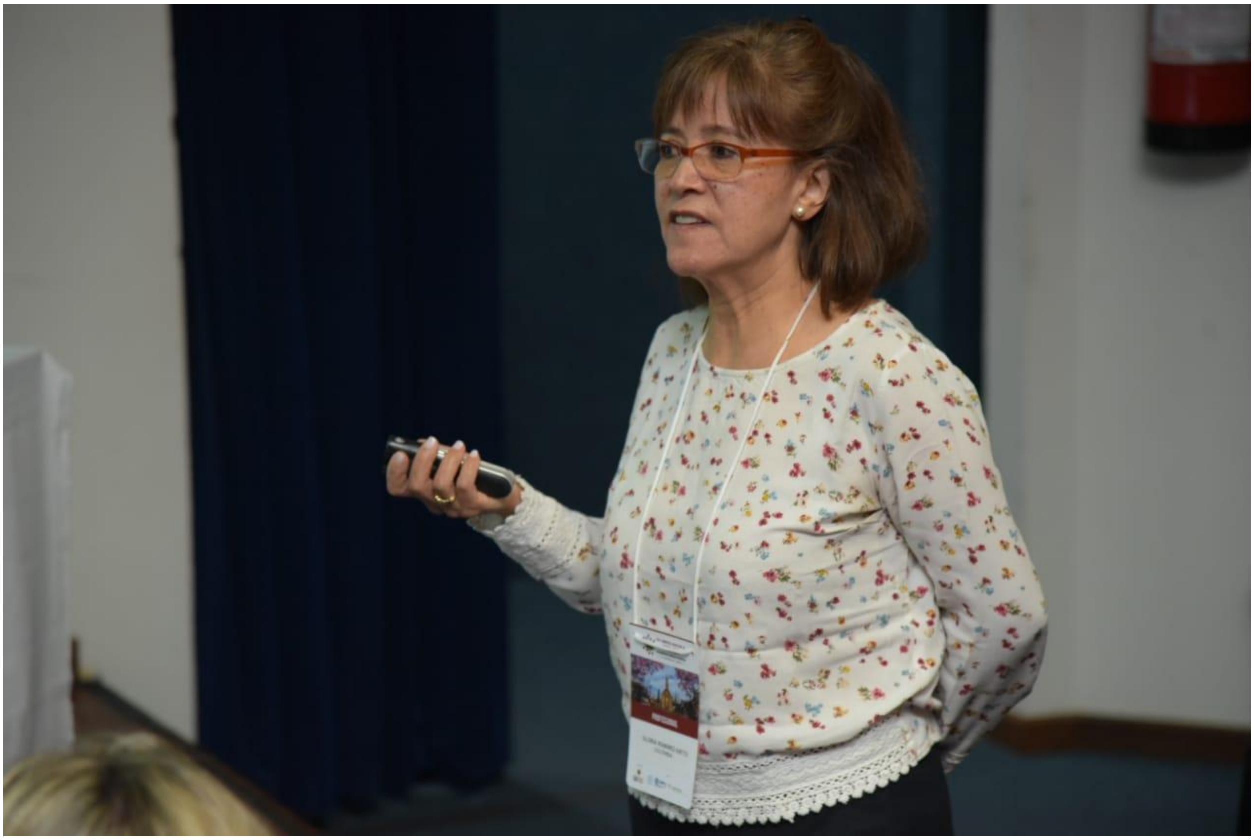
Ariel Pereda - Argentina

Javier Cappuccio - Argentina

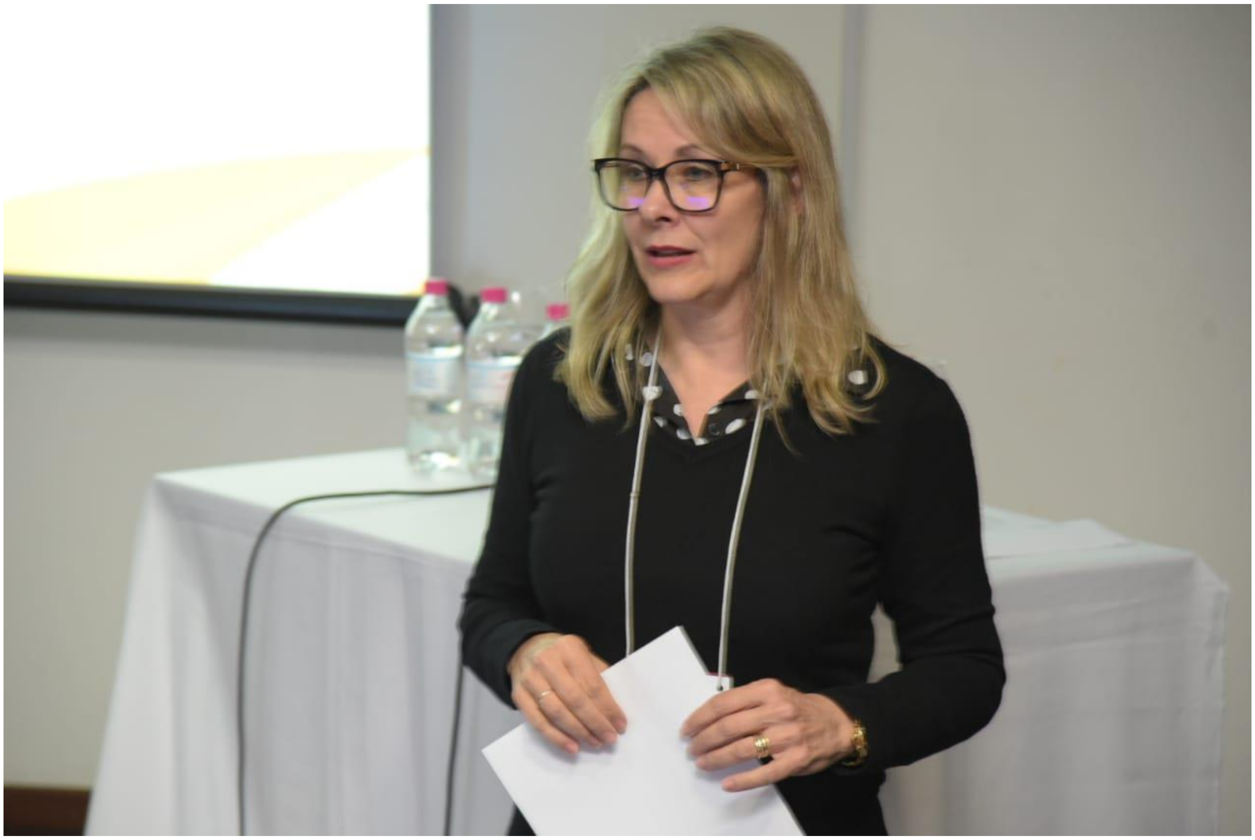




Rejane Schaefer - Brazil

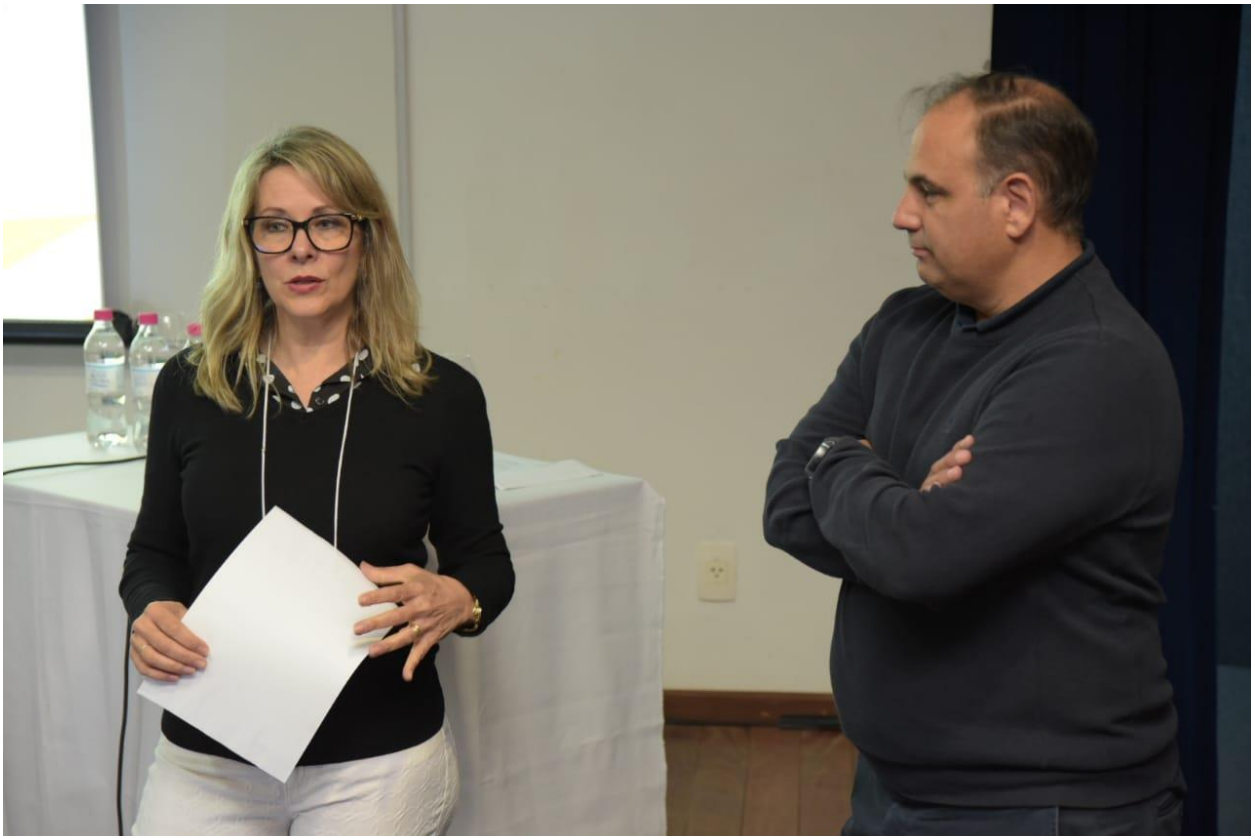


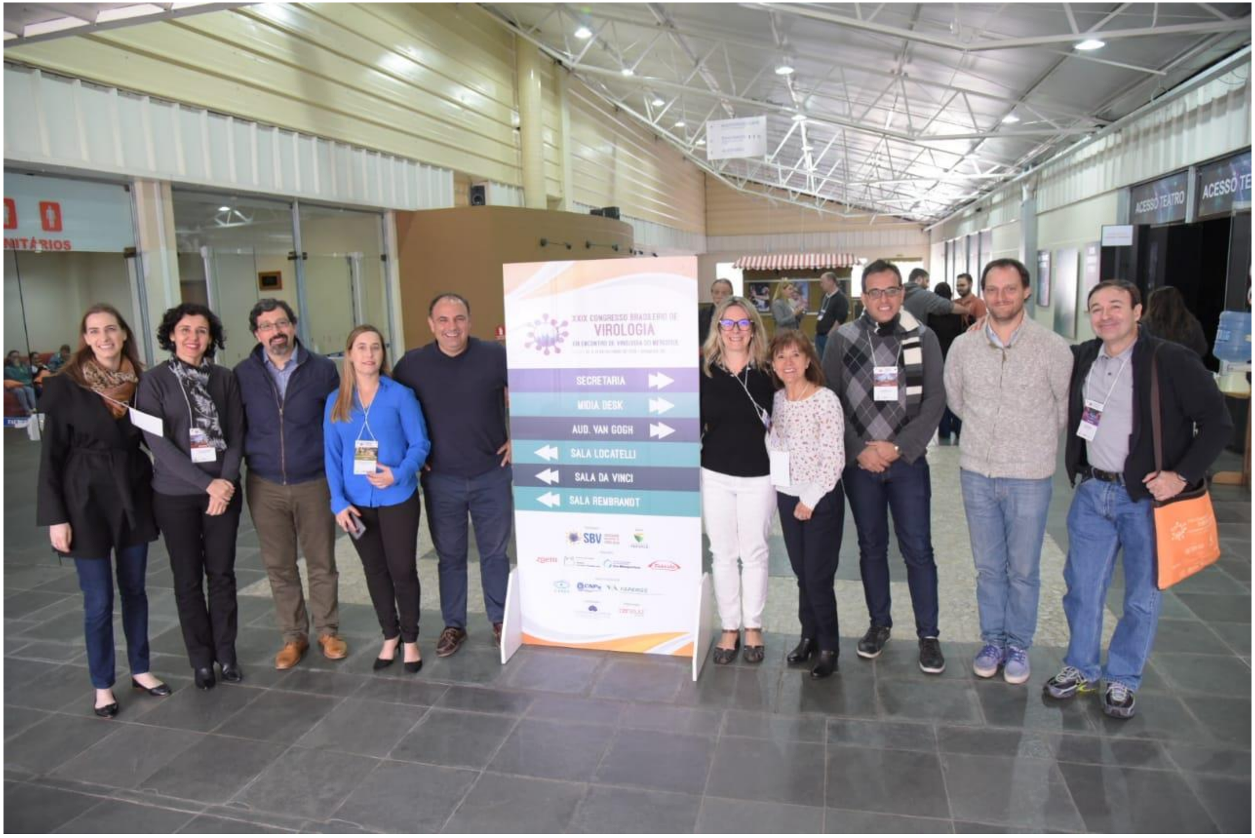
Gloria Ramirez - Colombia



Janice Ciacci Zanella - Brazil

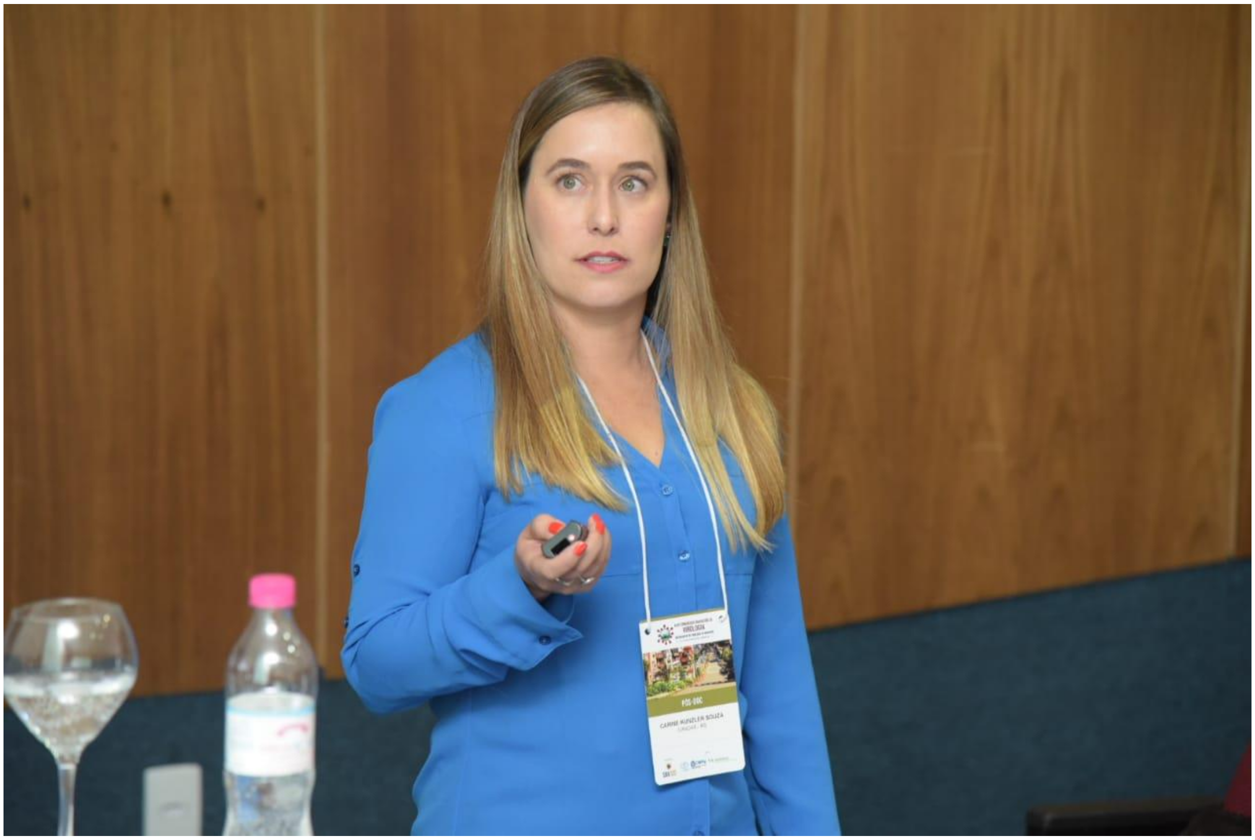
Janice - Ariel - Chairs



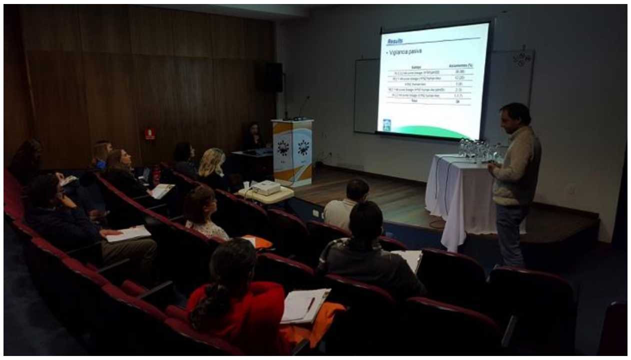


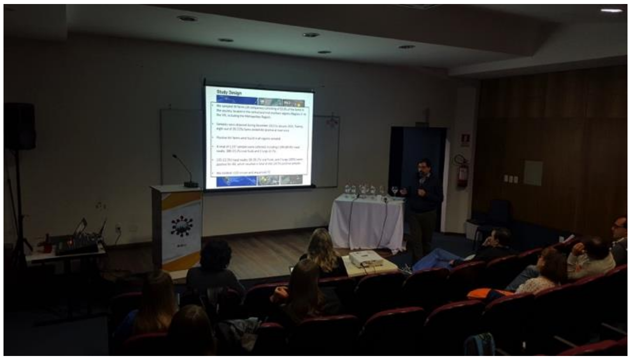
Daniel Perez - USA

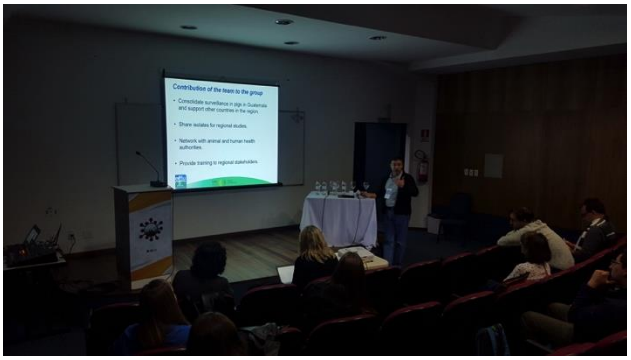
Carine Kunzler Souza - USA

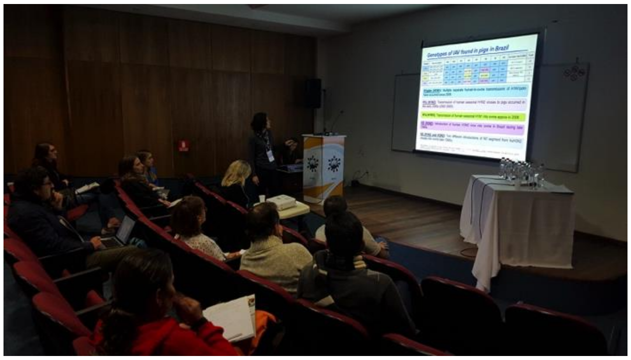


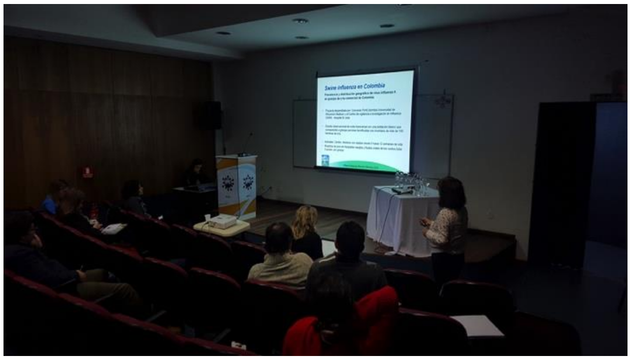
Pictures

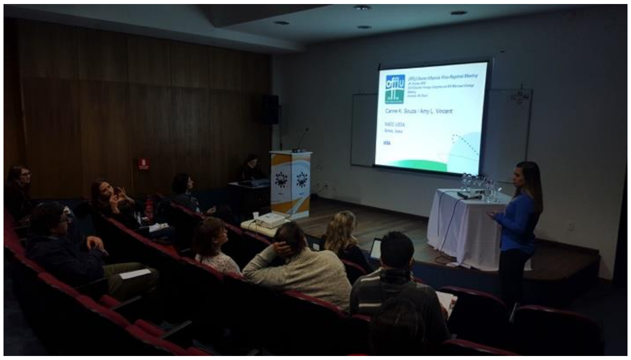

Results
Vigilancia pasiva


Study Design


Contribution of the team to the group
Consolidate surveillance in pigs in Guatemala and support other countries in the region.
Share isolates for regional studies.
Network with animal and human health authorities.
Provide training to regional stakeholders.


Genotypes of IAV found in pigs in Brazil


Swine influenza en Colombia


Carine K. Souza · Amy L. Vincent