Understanding pathogen, livestock, environment interactions involving bluetongue virus

Reporting

Project Information

PALE-Blu

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Project closed

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Periodic Reporting for period 3 - PALE-Blu (Understanding pathogen, livestock, environment interactions involving bluetongue virus)

Reporting period: 2019-12-01 to 2021-11-30

Summary of the context and overall objectives of the project

Bluetongue is an economically important disease that since 1998 has invaded Europe, particularly southern and central countries. These changes linked to climate change appear unlikely to be reversed. The disease causes major economic losses due to fatalities in livestock (>25% in sheep), loss of reproductive performance and milk/meat production, restrictions in animal movements & trade & costs of control measures.
The PALE-Blu Project brings together 19 different Partner organisations in fifteen countries to generate data concerning the distribution & interaction of genetic variants of the bluetongue virus with insect vector & host populations to inform control & prevention strategies The project analysed interactions between different virus strains, insect vectors & vertebrate hosts at the population, individual & molecular levels. Transmission mechanisms have been analysed to help inform the ways in which risks can be evaluated, modelled & mitigated. In particular the project identifies & maps different virus & vector populations & the environmental factors that determine their incidence & distribution to understand how genetic variations can determine transmission of different BTV serotype / strains in different regions. Databases have been created to help in the global identification of different BTV variants based on sequence analyses. The project has developed diagnostic assays to maintain and improve current diagnostic & surveillance capabilities. These specifically include the recently identified 'novel' serotypes (BTV-25 upwards) to ensure that they can also be rapidly & sensitively detected. The project has sought to generate additional cell lines for European & Africa Culicoides species for further studies of transmission mechanisms & differences between different vector populations / species.Cross reactive antigens & epitopes were identified for different BTV serotypes to develop safe multivalent or cross-reactive vaccine candidates against different BTV serotypes.The project has developed & maintained communication & project management through websites periodic meetings & publications/presentations to both scientific & lay audiences.

Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

BTV sequences have been collected, annotated & curated & introduced into the BTV-GLUE website. The beta version of the BTV-GLUE dataset is available via a public web server (http://btv.glue.cvr.ac.uk) including an automated genotyping tool for all segments. A comprehensive database of Culicoides vector abundance, covering most of Europe & neighbouring countries, has been generated to define epizones with different insect vector populations. Updated livestock maps (cattle, sheep, and goats) have helped define epizones based on ecoclimatic data. Diagnostic tools for the novel BTV serotypes, as well as multiplexed assay systems have been developed & evaluated.Continuous cell lines for an additional Culicoides species have been developed, maintained & made generally available to the scientific community. Rescued mono-reassortant BTV strains were generated to explore the molecular basis for contact transmission & insect vector transmission as well as other viral properties, including interactions with the innate immune response & inhibition by interferon. Antiviral activity of statin derivatives & calcium channel inhibitors were further explored.Project outputs & data have been & will continue to be disseminated through one or more of the four websites that have been established or associated with the project:http://www.paleblu.eu the general project website, which provides project details,

presentations, publications & deliverables .This includes kick off project meeting in Glasgow 2017: http://www.paleblu.eu/system/files/2019-01/2017-09-06-MeetingReportFor1stPALE-BluMeetingCVRGlasgow-LR%20update.pdf & the 2nsed meeting in Rabat 2018: http://www.paleblu.eu/system/files/2019-01/2018-09-19-20-2ndPALE-BluMeetingMorocco.pdf See WP1 above.https://www.edenextdata.com/: the project spatial data archive, see also WP3 above. http://mapserver.izs.it/gis_oiemaps/: a site which displays global BTV distributions. A newly developed haploid embryonic stem cell library, was used to characterize cellular genes & pathways essential for productive BTV-8 infection.

Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the project so far)

BTV-GLUE has helped the BTV community to study BTV biology, evolution & outbreaks to distinguish the properties of BTV strains circulating worldwide. The addition of the Culicoides distribution data to epizone maps already developed, has helped to identify risk areas for BTV transmission. A model of wind-borne Culicoides movements also helps to characterise natural barriers to vector dispersion. Collectively these models help us understand & identify pathways & risk factors in BTV incursions & epidemiology. Work is ongoing to maintain a comprehensive set of diagnostic assays to detect current & known BTV serotypes that represent outbreak risks. Work towards multiplexing assays using novel platforms like MagPlex has helped to automate throughput. Recent developments in sequencing technologies provide opportunities to identify viral pathogens using a metagenomics approach. Development of cell lines from additional midge species has helped to support studies to improve our understanding of the molecular characteristics that determine if a particular midge species is a competent vector for a specific BTV strain.Investigations of viral genetic control of infection, replication & vector competence in European Culicoides species has enhanced our understanding of viral, insect & host factors that enable BTV insect-transmission. This may help us to predict vector transmissibility of BTV strains directly by interrogation of the virus genome. Identification of virus-related genetic control of horizontal transmission (HT) in the ruminant host might allow us to predict non-vector transmissibility of BTV strains by interrogation of the virus genome. The data obtained will improve control measures & provide advice to policy makers concerning the risks posed by novel BTV strains.The development of a library of BTV specific monoclonal antibodies for BTV, was intended to support the identification of VP2 regions/epitopes involved in the protective response. They would also facilitate the development of serotype specific serological assays (e.g. ELISA). However these studies were unsuccessful in sheep & were therefore transferred to a bovine system. The delays caused by the Covid 19 outbreak delayed many aspects of the PALE-Blu studies, & the work on monoclonal antibodies is still progressing.
The generation and validation of novel vaccines, vaccination strategies & antivirals that are compatible with existing surveillance methods/assays & potentially ‘cross-serotype’ has potential to enhance our ability to respond rapidly to disease incursions. Developing effective & broad-range antiviral strategies for dsRNA viruses using the orbiviruses, could be a step towards controlling dsRNA virus replication in infected animals, including potentially humans.The PALE-Blu websites provides project related data to project members. They have a combined hit rate in excess of

3000/month.The project have also generated fact-sheets, regular e-newsletters & a short series of videos describing project outputs & impact. Like the websites, these are aimed at a wide audience, not just professionals and planners.

Figure WP6.1 Demonstration of the method for processing midge eggs for primary cell culture at ISRA, October 2018

processing-midge-eggs-for-primary-cell-cultures.png

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Permalink: https://cordis.europa.eu/project/id/727393/reporting

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