Meeting report for PALE-Blu Kick off meeting:

Centre for Virus research Glasgow 5th -6th November 2017

Introduction :

The Kick –off meeting for PALE-Blu was held at the Centre for Virus Research in Glasgow and was well attended by EU representatives and most of the partners (apart from Tunisian colleagues who had problems with visas).

The meeting was structured as a series of talks to include input and views from all partners and the EU commission, as well as information concerning finance from the coordinating partner (Geoge Rose – Partner 1). The meeting agenda is presented below along with the abstracts that are available for individual talks. Links to the slide presentations from each speaker will also be included.

On the second day the afternoon session was devoted to round-table discussions concerning the specific objectives. Overall it was a very successful and helpful meeting and we hope for real progress towards objectives and milestones in the coming years.

Agenda for PALE-Blu meeting to be held at the Centre for Virus Research (CVR), Glasgow University, September 5th and 6th September 2017

Day1 (5th September 2017)		
Time	**Speaker and (Institution)**	**Title of talk**
9:00-9:30	**Registration and Coffee**	
Session 1 :	**Chair: P. Mertens**	
9:30 – 09:45	Peter Mertens (Coordinator) (UNott – UK)	**Talk 1:** "PALE-Blu: welcome and introduction: Aims of the meeting and project" (Abstract : Slides)
9:45 -10:00	George Rose (UNott – UK)	**Talk 2**: "PALE-Blu : short financial presentation" (Slides)
10:00 - 10:15	Bernd Hoffmann (FLI - Germany)	**Talk 3**: "Identification and characterization of atypical bluetongue viruses" (Slides)
10:15 - 10:35	Giovanni Savini Annamaria Conte Giuseppe Mancini (IZSAM – Italy)	**Talk 4**: "Recent advances in the circulation of Bluetongue virus serotype 3 in Tunisia and detection of new small ruminant adapted BTV strains" (Slides)
10:35 - 10:55	Thomas Belenghien , Renaud Lancelot, Karine Huber, Serafin Gutierrez, Julie Reveillaud (CIRAD - France)	**Talk 5:** "Animal movements and interactions between the environment and *Culicoides* populations" (Abstract : Slides)
10:55-11:30	**Coffee break**	
Session 2 :	**Chairs: Stephan Zientara & Bernd Hoffmann**	
11:30 -11:50	Lucilla Steinaa and Nicholas Svitek (ILRI –Kenya)	**Talk 6**: "Bluetongue in South-Saharan Africa". (Abstract : Slides)
11:50- 12:10	בכר עדי [Adi Behar] (KVI – Israel)	**Talk 7:** "Bluetongue in Israel". (Slides)
12:10-12:30	Mirazimi Ali (SVA – Sweden)	**Talk 8**: "Virus – host cell interaction" (Slides)
12:30-12:50	Zati Vatansever (KAU – Turkey)	**Talk 9**: "Current situation of *Culicoides* distribution in Turkey". (Abstract : Slides)
12:50-13:10	(IAV - Morocco)	**Talk 10**: "situation of BTV in Morocco" (Abstract : Slides)
13:10 - 14:10	**Lunch break**	
Session 3:	**Chair: Piet Van Rijn & David Haig**	
14:10-14:30	Karin Darpel (TPI - UK)	**Talk 11:** "*Culicoides* saliva effects on BTV infectivity in ruminant hosts and insect vectors" (Abstract : Slides)
14:30-14:50	Massimo Palmarini (UGLA-UK)	**Talk 12:** "Host acute immunosuppression in the pathogenesis of bluetongue" (Slides)
14:50-15:10	Richard Urbanowicz & Jonathan Ball (UNott - UK)	**Talk 13:** Strategy to identify serotype cross-protective neutralising antibodies. (Slides)
15:10-15:30	David Haig UNott	**Talk 14:** Vaccination strategy for cross-serotype BTV control (Abstract : Slides)
15:30-16:00	**Coffee break**	
Chair: David Haig & Piet Van Rijn		
16:00 – 16:20	Piet van Rijn (WBVR/CVI)	**Talk 15:** The BT DISA vaccine platform for European serotypes (Abstract : Slides)
16:20 - 16:40	Houssam Attoui & Fauziah Mohd Jaafar (Anses / INRA - France)	**Talk 16:** "Animal movements and interactions between the environment and *Culicoides* populations" (Slides)
16:40 – 17:00	Javier Ortego (INIA - Spain)	**Talk 17:** ¨Development of universal BTV vaccines¨ (Abstract : Slides)
17:00 – 17:20	Sarah Sebastian (Jenner Institute – Oxford UK)	**Talk 18:** Creating vectored subunit vaccine candidates for BTV (Abstract : Slides)
End of Scientific session for Day 1		
Dinner: 19:30 At the Oran Mor Restaurant in Glasgow		

Day 2 - Session 4 :	**Chair: Roman Biek & Massimo Palmarini**	
09:00-09:20	Kyriaki Nomikou (UNott - UK)	**Talk 19:** Next generation sequence analyses of Bluetongue and other dsRNA viruses (Slides)
09:20-09:40	Josh Singer & Robert Gifford (UGLA - UK)	**Talk 20:** BTV-Glue database (Abstract : Slides)
09:40-10:00	Roman Biek & Maude Jacquot (UGLA -UK)	**Talk 21:** "Molecular evolution and phylogeography of BTV". (Abstract : Slides)
10:00-10-20	William Wint (ERGO - UK)	**Talk 22:** "PaleBlu spatial data and modelling". (Slides)
10:20-10:40	Marius Gilbert (ULB – Belgium)	**Talk 24:** "Bluetongue statistical spatial spread models". (Slides)
10:40-11:20	**Coffee**	
Session 4 (continued:	**Chair: Massimo Palmarini & Roman Biek**	
11:20 – 11:40	Assane Gueye FALL & Mamadou Ciss (ISRA – Senegal)	**Talk 23:** "Bluetongue in Senegal: current knowledge" (Slides)
11:40-12:00	Stephan Zientara (Anses / INRA – France)	**Talk 24**: "BT situation in France and in Corsica" (Slides)
12:00-12:20	Jose Manuel Sanchez-Vizcaino Rodriguez & Cecilia Aguilar (UCM - Spain)	**Talk 25: Evolution of BTV in Spain. *Culicoides* suitability areas and periods for spread and introduction. Futures challenges (Slides)**
12:20-12:40	Thomas Belenghien, Renaud Lancelot, Karine Huber, Serafin Gutierrez, Julie Reveillaud CIRAD - France	**Talk 26: "Animal movements and interactions between the environment and *Culicoides* populations" (Slides)**
12:40-13:00	Lesley Bell-Sakyi (University of Liverpool – UK)	**Talk 27:** "Novel arthropod cell line establishment – the Tick Cell Biobank experience" (Abstract : Slides)
13:00 - 14:00	**Lunch break**	
14:00 – 16:30 **Discussion of collaborations for Objectives 1 to 6 (up to 30 minutes each)** **Initiated by 5 minute talk by each work package leaders**		
Objective 1: (WP1 & WP2) (Chairs Kyriaki Nomikou & Roman Biek) Develop a more detailed and up-to-date molecular-epidemiology map of BTV strains circulating in domesticated and wild ruminants in Europe and neighbouring countries:		
Objective 2: (WP3 & WP4) (Chairs Thomas Belenghien & Marius Gilbert) Map interactions between the environment, the composition of the *Culicoides* species community, the genetic characteristics of Culicoides populations and their microbiomes, to quantify connectivity between midges and virus sub-populations:		
Objective 3: (WP5) (Chairs: Peter Mertens and Stephan Zientara) Develop innovative multiplex diagnostic tools for BTV identification and typing:		
15:00 - 15:30	**Coffee**	
Objective 4: (WP6, WP7, WP8, WP9) (Chairs: Houssam Attoui & Karin Darpel) Characterise orbivirus-related genetic control of infection and horizontal transmission in vertebrate hosts, as well as infection replication and vector competence in European Culicoides spp.:		
Objective 5: (WP10, WP11) (Chairs: David Haig & Massimo Palmarini) Develop novel BT vaccines, vaccination strategies and antiviral approaches for BTV:		
Objective 6: (WP12) (Chairs: Peter Mertens David Haig) Project management, coordination and communications:		
16:30 End of meeting		
14:10-14:30	Héla Kallel & Sofien Sghaier (IPT)	"Bluetongue survey and vaccine development in Tunisia" (Partner unable to attend)

Please note: **Partners are responsible for booking their own travel and accommodation in Glasgow**

The 'Arboviruses and their vectors' meeting will be held on the 7th and 8th of September in Glasgow. This is likely to be relevant to the scientific objectives of PALE-Blu.
If you wish to register for 'Arboviruses and their vectors' please visit website:
https://www.microbiologysociety.org/event/society-events-and-meetings/focused-meeting-2017-2nd-international-meeting-on-arboviruses-and-their-vectors-imav-2017.html

Below is a list of hotels near the CVR which would be suitable for the meeting participants.

Glasgow Hilton Grosvenor (Around £95 per night): http://www3.hilton.com/en/hotels/united-kingdom/hilton-glasgow-grosvenor-GLAGRHN/index.html

There is also the Glasgow Pond Hotel (around £60 per night) http://www.glasgowpondhotel.com/

or either of the Premier Inn's in Bearsden or Milngavie (around £35-£45 per night):
http://www.premierinn.com/gb/en/hotels/scotland/strathclyde/glasgow/glasgow-bearsden.html

http://www.premierinn.com/gb/en/hotels/scotland/strathclyde/glasgow/glasgow-milngavie.html

Useful Maps

The best way to travel from the hotels or airport to the CVR at the Garscube Campus is by taxi:

Map of the CVR at Garscube campus in Glasgow: **http://www.gla.ac.uk/media/media_396829_en.pdf**

Map of showing route from Glasgow Hilton Grosvenor to University of Glasgow Garscube Campus (by car or taxi):
https://www.google.co.uk/maps/dir/Hilton+Glasgow+Grosvenor,+Grosvenor+Terrace,+Glasgow/464+Bearsden+Road,+Bearsden/@55.8900902,-4.3260955,14z/data=!3m1!4b1!4m14!4m13!1m5!1m1!1s0x488845c955552e81:0xce421ce04def1787!2m2!1d-4.291097!2d55.8779004!1m5!1m1!1s0x48884598d4c7557d:0x5f62819476c55087!2m2!1d-4.3203018!2d55.8991316!3e0

Map of showing route from Premier Inn Milngavie to University of Glasgow Garscube Campus:

https://www.google.co.uk/maps/dir/Premier+Inn+Glasgow+Milngavie,+Main+Street,+Milngavie/464+Bearsden+Road,+Bearsden/@55.9169592,-4.3381119,14z/data=!3m1!4b1!4m14!4m13!1m5!1m1!1s0x4888453971a83c15:0x2aeffef953bf073c!2m2!1d-4.3156038!2d55.9348405!1m5!1m1!1s0x48884598d4c7557d:0x5f62819476c55087!2m2!1d-4.3203018!2d55.8991316!3e0

Map of showing route from Premier Inn Bearsden to University of Glasgow Garscube Campus:

https://www.google.co.uk/maps/dir/Premier+Inn+Glasgow+Bearsden,+Milngavie+Road,+Bearsden/464+Bearsden+Road,+Bearsden/@55.9151386,-4.3381119,14z/data=!3m1!4b1!4m14!4m13!1m5!1m1!1s0x4888453e5d5a360d:0xc6982cbda2402c79!2m2!1d-4.317722!2d55.931113!1m5!1m1!1s0x48884598d4c7557d:0x5f62819476c55087!2m2!1d-4.3203018!2d55.8991316!3e0

Map of showing route from Glasgow Pond Hotel to University of Glasgow Garscube Campus (by car or taxi)

https://www.google.co.uk/maps/dir/Glasgow+Pond+Hotel,+Great+Western+Rd,+Glasgow+G12+0XP/464+Bearsden+Road,+Bearsden/@55.8933428,-4.3260571,15z/data=!3m1!4b1!4m14!4m13!1m5!1m1!1s0x488845bf0c484b67:0xf662f21ce185d922!2m2!1d-4.3120794!2d55.8844037!1m5!1m1!1s0x48884598d4c7557d:0x5f62819476c55087!2m2!1d-4.3203018!2d55.8991316!3e0

PALE-Blu: participants/Contact/Mailing list: * indicates contributors not attending the meeting

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Partner 11: KVI – Israel

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Abstracts

Talk 1: PALE-Blu: welcome and introduction: Aims of the meeting and project

Peter Mertens (coordinator)

School of Veterinary Medicine and Science, University of Nottingham, Sutton Bonington Campus,

LE125RD, UK

First of all I want to welcome all of you, as colleagues and partners to this first meeting of the PALE-Blu consortium. I hope that the three years funding for work on Bluetongue and its vectors in Europe and surrounding areas will not only generate invaluable scientific data and publications that will help us to understand and control the disease but will also continue to support and establish new long term working links between us as individuals and between our separate organisations.

This is the first of several meetings of the consortium over the three and a half years of the project and I look forward to seeing how the science progresses during that time. I have asked each of the partners to present a brief description of their work so that you we can better understand the expertise and research capability within the consortium. This will be followed by a brief discussion of the different project objectives on day 2. I ask partners within the individual work-packages to make contact with each other and use time during coffees lunch and dinner to discuss ways of working together.

PALE-BLU will explore*:*

- Full-genome sequence-analyses to increase the accuracy of BTV outbreak-strain identification and molecular epidemiology studies.
- Development of more effective and cross-serotype subunit-vaccines that are DIVA assay compatible, based on a better understanding of immune responses to BTV.
- The distribution of different Culicoides vector species / populations and develop novel cell lines as tools to determine the genetic basis for the vector competence of emerging outbreak-strain.
- The use of antiviral agents to induce immediate protection post vaccination.
- More effective diagnostic systems to better detect mixed infections.
- The movements and reassortment of individual BTV genes, generating novel and emerging virus lineages.
- These studies will provide a better understanding of incursion risks for different BTV strains, supporting effective control strategies.
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Underlying all of these activities is 'communication and dissemination of results and sharing of data. The project will generate a web page, which I hope you will use as part of your communication strategies.

"For epidemiology studies of Bluetongue virus, it is vital to accurately record and store the different virus samples and isolates. For several years this has been done using the Orbivirus Reference Collection at Pirbright, but there is no reason, provided the isolation data is shared, why these samples need to be all stored in one location. The BTV-GLUE database (http://btv.glue.cvr.ac.uk/) which is being developed at Glasgow – see Talk 20) will make it possible to record and share the incidence and genetic lineages of BTV strains from around the world between partners, improving our ability to identify novel strains, serotypes and reassortants more rapidly and accurately than before. BTV-GLUE could also be further developed to record the storage locations (wherever they are held) of specific samples and isolates that will be of value for future molecular studies, vaccinology and diagnostic assay development."

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http://www.paleblu.eu/project-documents

Talk 2: "PALE-Blu : short financial presentation"

George Rose University of Nottingham, LE12 5RD

Abstract not available

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Talk 3: "BT situation in France and in Corsica"

Stephan Zientara
Animal Health Laboratory-ANSES/INRA/ENVA, 14 rue Pierre et Marie Curie, 94700 Maisons Alfort, France

Abstract not available

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Talk 4: "Identification and characterization of atypical bluetongue viruses"

Bernd Hoffmann
FLI - Germany

Abstract not available

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Talk 5: "Recent advances in the circulation of Bluetongue virus serotype 3 in Tunisia and detection of new small ruminant adapted BTV strains"

Giovanni Savini
IZSAM – Italy

The whole genome characterization of two different BTV-3 strains identified in clinically affected sheep originating from different regions of Tunisia will be described and their possible repercussions on the livestock industry of northern Africa and Europe will be discussed. Recent advances in the research on new small ruminant adapted BTV strains will also be presented with particular focus on the BTVX ITL2015 isolated in Sardinia in 2015, on a BTV-26 like strain identified in asymptomatic Tunisian sheep imported from Libya and on a BTV-25 like strain detected in goats in an area of the Piedmont region close to the Swiss border.

Giovanni Savini g.savini@izs.it
http://www.paleblu.eu/project-documents

Talk 6: "Bluetongue in South-Saharan Africa".

Lucilla Steinaa & Nicholas Svitek
International Livestock Research Institute, Animal and Human Health Program, Kenya E-mail:
l.steinaa@cgiar.org and n.svitek@cgiar.org

Bluetongue has been reported in several countries in Sub-Saharan Africa, such as Sudan, Kenya, Tanzania, Ethiopia, Mozambique, Botswana, Namibia and South Africa but there appear to be a lack of reporting by many countries as scientific publications do not match records by OIE. BTV seems to be less problematic in Africa compared to Europe when comparing overt disease, likely due to the sheep breeds used. However, it

has been suggested that indirect losses associated with loss of body weight and condition, drop in milk production, poor reproductive performance and restriction of international trade with livestock and germplasms may have greater economic impact than direct effects of the disease.
ILRIs contribution to this project will be to assess prevalence of BTV in selected locations in Kenya and possibly in other Sub-Saharan countries, assessed using cELISA and PCR and to provide full genomic sequences from the region. Serotypes will be determined using serotype specific primers and full genomic sequences will be sequenced by isolating the virus followed by sequencing of segment overlapping PCR amplicons and/or by NGS.
BTV positive samples will be attempted collected from various sources: previous project samples, Kenyan department of veterinary services (DVS), upcoming projects and from the present project. In addition to sampling field animals, it is the plan to put sentinel animals at strategic locations in order to isolate virus and perform genomic sequencing.
We are new in the BTV field so efforts in the beginning will be focused on setting up necessary methods for diagnosing BTV, isolation and virus and strategy for sequencing. Some prevalence studies has previously been done by other groups at ILRI, finding high seroprevalence in Kenya (0.942, 95% CI) and a prevalence of 88.9% was found by real-time RT-PCR in 51 week old cattle.
Kenya E-mail: l.steinaa@cgiar.org & n.svitek@cgiar.org

http://www.paleblu.eu/project-documents

Talk 7: "Bluetongue in Israel".
בבר עדי [Adi Behar]
KVI – Israel

Abstract not available

Adi Behar (adibehar@gmail.com); בבר עדי[Adi Behar] Adib@moag.gov.il

http://www.paleblu.eu/project-documents

Talk 8: "Virus – Host cell interaction "
Mirazimi Ali
SVA – Sweden

Abstract not available

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Talk 9: "Current situation of Culicoides distribution in Turkey".
Ahmet DENIZ, Central Veterinary Control and Research Institute Etlik, Ankara, Turkey
Zati VATANSEVER, Kafkas University,Kars, Turkey

Bluetongue virus is known since 1944 in Turkey. Up to date 3 serotypes, namely BTV4, BTV9 and BTV 16 are known to circulate. BTV4 live attenuated vaccine (Blu-T4 Evac) is produced and used in sheep since 1977. In case of an outbreak all sheep in the affected area are subjected to vaccination at least for 3 years. In last yers a total of 5360608, 4712700 and 1578845 doses of vaccine was applied in 2015, 2016 and 2017 respectively.

Little is known about population dynamics, distribution and vector competence of Culicoides species in Turkey. A recent project, which is led by Central Veterinary Research Institute in Ankara, is focused on research of Culicoides distribution and seasonal abundance. Since 2015 112 Onderstepoort type light traps were placed all around Turkey and monitored at least for one night twice a month (Fig 1). Collection are identified by 8 Veterinary Control Institutes. A total of 70224 and 85462 Culicoides specimens were collected and identified in 2015 and 2016 respectively (Table 1).

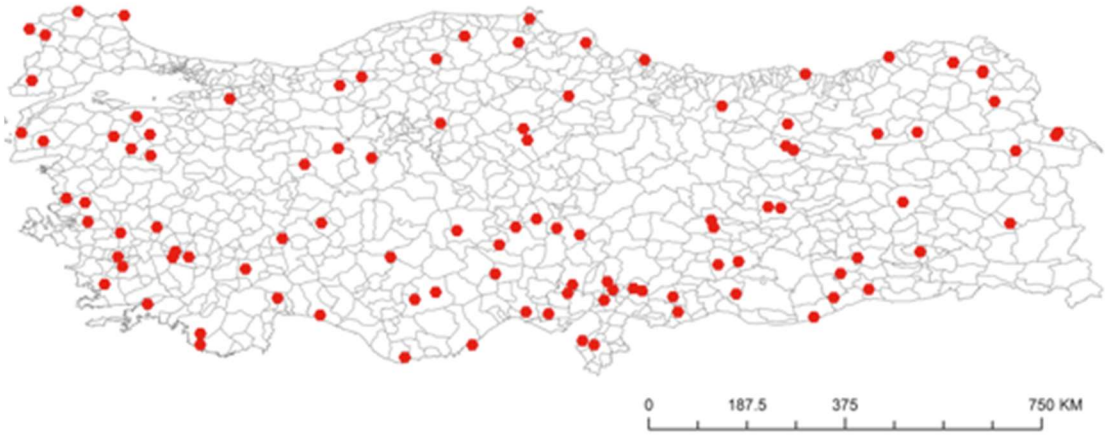

Fig 1. Places where traps were places.

Table 1. Species composition of *Culicoides* spp. collected in 2015 and 2016

	2105		2016	
	n	%	n	%
Obsoletus group	28736	40.92	9381	10.98
C. imicola	9125	12.99	7460	8.73
C. newsteadi	6980	9.94	1499	1.75
Schultzei group	5541	6.89	61900	71.43
C. punctatus	3054	4.35	932	1.09
Nubeculosus complex	1301	1.85	411	0.48
C. pulicaris	595	0.85	76	0.09
C. circumscriptus	558	0.79	648	0.76
others	14334	21.42	3155	4.69

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Talk 10: Monitoring of Bluetongue virus in Morocco in asymptomatic camels and cattle

O Fassi Fihri. K Drif. C Loutfi. M El Harrak
IAV Hassan II, Rabat Morocco: Tel: 00212661179955

This survey focused on the extent that camels and cattle can be used in Morocco to detect the presence of the serotypes of bluetongue virus (BTV) currently present in the Mediterranean Basin. In 2012, 278 camels from the south Morocco and 214 cattle from the west were tested for the presence of antibodies against the BTV serotypes, (BTV-1, -4, -6, -8, -11, -14 and -16 for camels and 1, 4 and 8 for cattle). This serological survey based in viral neutralization assay report for the first time the emerging of BTV-8 in both cattle and camels, furthermore, antibodies against BTV-16 was detected in camels reaching 60% whish can suggest a silent circulation of this serotype among cattle. Moreover, the founding reveals as well a higher co-infection rate in both species mainly between BTV8 and 1.

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http://www.paleblu.eu/project-documents

Talk 11: "Culicoides saliva effects on BTV infectivity in ruminant hosts and insect vectors"

Karin Darpel, Lyndsay Cooke & Simon Carpenter

"*Culicoides* saliva effects on BTV infectivity in ruminant hosts and insect vectors"

Orbivirus Research Group, Entomology Group and Non-vesicular Reference Laboratory (NVRL)
The Pirbright Institute, Ash Road, GU240NF

Arthropod saliva contains numerous bioactive molecules to counteract the vertebrate coagulation response, thereby facilitating uptake of a blood-meal in hematophagous species. Vertebrate hosts often respond to the injury caused by arthropod mouthpart insertion and respective saliva inoculation with a local inflammatory and wound healing response, further modulated by specific arthropod saliva components. The effect of arthropod saliva is of particular interest in those arthropods that serve as a biological vector of a pathogen since numerous studies have highlighted how vector saliva enhances pathogen infectivity, dissemination and virulence in vertebrate hosts. While arthropod saliva induced enhancement of pathogen infectivity is generally attributed to the indirect effect of local immune modulation, interestingly it has been demonstrated that *Culicoides sonorensis* saliva can directly modify the BTV particle by proteolytic cleavage of the outer coat protein VP2. Proteolytic cleavage of VP2 is known to generate infectious subviral particles (ISVP), which display a greater infectivity for *Culicoides* spp. and *Culicoides* derived cells. So far cleavability of BTV VP2 by *Culicoides* saliva has only been demonstrated for strains from 2 serotypes. Furthermore it is unknown if saliva modified BTV particles would also demonstrate changed infectiousness in ruminant derived target cells. Within this project our objective is to assess VP2 cleavability by *Culicoides* saliva and control proteases across a range of BTV strains from numerous serotypes. The subsequent consequence on particle infectivity for *Culicoides*, as well as ruminant derived target cells, will be assessed with a specific focus on particle membrane binding and cell entry mechanisms. We are particularly interested to assess the potential impact of VP2 cleavage resistance on subsequent infectivity, either by identifying or generating a cleavage resistant BTV strain which remains intact as virus particle in the presence of serine-proteases. Additionally the team will contribute to ongoing efforts of vector competence assessment trials across different *Culicoides* species (

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Talk 12: "Host acute immunosuppression in the pathogenesis of bluetongue"
Massimo Palmarini
UGLA-UK

Abstract not available

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http://www.paleblu.eu/project-documents

Talk 13: Strategy to identify serotype cross-protective neutralising antibodies.
Rich & Jonathan Ball
UNott – UK

Abstract not available

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Talk 14: Vaccination strategy for cross-serotype BTV control

David Haig
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Current vaccines to protect animals against Bluetongue raise neutralising antibodies (nAbs) against outer capsid proteins, particularly VP2. They are effective at preventing disease but are neither DIVA compatible nor do they protect against more than one BTV serotype. Previous studies have shown that cross serotype nAbs can be generated following immunisation, and that cell-mediated immune (CMI) responses against non-structural proteins (e.g. NS1) can afford a degree of cross-serotype protection. Our objective is to generate

a cross-serotype protective vaccine /vaccines that are DIVA compatible and exploit both the VP-2 specific nAb response and CMI to NS1. This will improve efficiency of BT diagnosis and vaccine deployment and reduce costs. Sheep will be sequentially immunised with plant-derived VP2s and plasma cells isolated to generate ovine recombinant monoclonal antibodies. This is a powerful technique used by Jon Ball's group at Nottingham to identify low abundance antibodies that may have cross-serotype reactivity, allowing identification of suitable VP2s for vaccine inclusion. Furthermore, the adenovirus prime and MVA boost viral vectors of Sarah Gilbert's group (Jenner, Oxford) are proving highly effective in the field and generate potent CMI and nAb responses to vaccine antigens. These will be used as a delivery method for our vaccine antigens (NS1 with and without VP2s) in this study. We will liaise with others in WP10 to develop a comprehensive BT control strategy.

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Talk 15: The BT DISA vaccine platform for European serotypes

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Talk 16: Species barrier to orbivirus replication in mammals and arthropods and control strategies

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Talk 17: ¨Development of universal BTV vaccines¨

Javier Ortego
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Current BTV vaccines are mainly based in the induction of neutralizing antibodies serotype-specific. This limits the rapid availability of the appropriate vaccine serotype for outbreaks caused by different serotypes and therefore delays their deployment, leading to more costly production and inefficient vaccination strategies. There are no highly effective vaccines for infections in which Th1 CD4+ T cells, CD8+ T cells, or both play also critical roles in pathogen control or elimination, such as bluetongue virus. We wish to exploit recent advances in rational vaccine design to produce vaccines that are easy and economical to produce rapidly, with the appropriate BTV protective antigens that are more broadly cross-reactive (cross-serotype) and tailored for specific disease outbreaks with DIVA capability.

The main objective of our proposal is the generation of novel universal BTV vaccines based on the conserved non-structural protein NS1 of the virus that induce a protective cellular immune response and the development of efficient vaccination strategies that elicit long lasting protection: We propose to explore cross reactivity among serotypes and topotypes, using BTV antigens/epitopes from the non-structural

protein NS1 delivered in viral vectored vaccines to stimulate cell-mediated immunity and long lasting multiserotype protection. The vaccine efficacy will be further evaluated in the murine model characterized in our laboratory and in sheep, its natural host. This project will contribute to the rational further development and improvement of BTV vaccines (DIVA, more potent, safer and cross reactive) for development of more effective control strategies.

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Talk 18: Creating vectored subunit vaccine candidates for BTV0
Sarah Sebastian & Sarah Gilbert
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Talk 19: Next generation sequence analyses of Bluetongue and other dsRNA viruses
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Talk 20: BTV-GLUE: a bioinformatic resource for bluetongue virus sequence data
Josh Singer & Robert Gifford
MRC-University of Glasgow Centre for Virus Research, Stoker Building Room 117, Garscube Campus, 464 Bearsden Road, Glasgow G61 1QH

Bluetongue virus (BTV) is an insect-borne virus within the Orbivirus genus of the Reoviridae family. It causes a severe hemorrhagic disease (bluetongue) in domestic and wild ruminant species. The last two decades BTV has expanded its geographical distribution worldwide and the biggest ever recorded outbreak caused by BTV-8 starting in 2006 threatened livestock industries in northern Europe.

The virus has ten double-stranded RNA (dsRNA) segments which encode 7 structural and 6 non-structural proteins. Reassortment involving all genome segments has been well documented. The segments encoding the outer capsid proteins VP2 and VP5 have a complex evolutionary history; 27 published and more putative serotypes are in circulation, which complicates ongoing surveillance and vaccination programmes.

We have created BTV-GLUE, a new bioinformatic sequence data resource for bluetongue virus. We collated several thousand BTV sequences from the NCBI nucleotide database and added complementary contextual metadata alongside each sequence. These were integrated together inside GLUE, a data-centric software package for capturing virus sequence data and organising it along evolutionary lines.

Each of BTV's 10 segments is allocated a separate phylogenetic data structure. Each sequence is held within a multiple sequence alignment specific to the segment and clade. Reference sequences with genome feature annotations are defined for each segment clade.

While BTV-GLUE can be used offline in a conventional bioinformatics context, some aspects of its functionality, including access to sequences, metadata and alignments, have also been made available via a public web server (http://btv.glue.cvr.ac.uk). This will help the wider BTV community accurately study the ongoing evolution and epidemiology of the virus worldwide, whilst also allowing analysis of reassortment and other phenomena.

http://www.gla.ac.uk/researchinstitutes/iii/staff/joshsinger
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Talk 21: "Molecular evolution and phylogeography of BTV".
Roman Biek & Maude Jacquot
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Talk 22: "PaleBlu spatial data and modelling".
William Wint
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Talk 23: "Bluetongue in Senegal: current knowledge"10:20-10:40
Assane Gueye Fall & Mamadou Ciss
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Talk 24: "Bluetongue statistical spatial spread models".
Marius Gilbert
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Talk 25: "Evolution of BTV in Spain. *Culicoides* suitability areas and periods for spread and introduction. Futures challenges"
Jose Manuel Sanchez-Vizcaino Rodriguez & Cecilia Aguilar
UCM - Spain

The ruminant population of Spain has been constantly affected by different serotypes of Bluetongue virus (BTV) since 2000. These serotypes include BTV-1, BTV-4, BTV-8 and, to a lesser extent, BTV-2 (de Diego et al., 2014). The continuous presence and recurrent incursions of BTV in the last two decades represents a constant threat to animal health in Spain and Europe.
Our research group point to vector transported by wind currents from affected areas in North Africa as the possible cause of virus introduction in Spain. In fact, previous studies showed a high correlation between Saharan dust depositions over specific BTV infected locations from affected North African territories. Due to the small size of Culicoides, this suggests that they may have been carried by the wind among sand particles (Martínez-López et al., 2009). Furthermore, a preliminary comparison between Spanish outbreak locations and a model of occurrence of C. imicola and the Obsoletus complex on the field also showed a high

correlation between each serotype affecting national territory and the predicted occurrence of different species of the genus Culicoides.
Our contribution to the PALE-Blue project will cover the epidemiology of the disease, combining phylogeografical, environmental, anthropogenic and vectorial information. Moreover, sequencing analysis of the circulating Spanish strains and the development of a multiplex assay for BTV serotyping focusing on the serotypes circulating on European and North of African territory, will be developed. Finally, a wind model simulation tool will be developed in order to identify the areas and periods at high risk of wind-borne Culicoides introduction, especially from North Africa to Spain, but configurable to any other European-African countries.
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Talk 26: "Animal movements and interactions between the environment and *Culicoides* populations"
Thomas Balenghien, Renaud Lancelot, Karine Huber, Serafin Gutierrez, Julie Reveillaud
CIRAD – France

During this talk, I will briefly present our research group, which has a long experience in bluetongue study (including activities in entomology, epidemiology and virology). Then, I will detail the implication of Cirad in the PALE-Blu project, mainly in WP3 on animal movements and in WP4 on *Culicoides* population structure.
During previous research projects and collaborations with national veterinary services, we collected and gathered data on animal movements at national and regional scales in Western Africa and in Maghreb. We used these data to carry out network analysis, or to develop risk mapping and metapopulational models. During PALE-Blu, we aim to harmonize these data and to collect additional data to provide broad-resolution connectivity matrices between the different epi-zones based on animal movements. More precisely, we aim to establish a raster map of the "most likely paths" between origins and destinations of transhumant or trade movements (based on friction/cost map and movements modelling), a R0 raster map and an “effective” meta-population model for bluetongue in Western Africa (in collaboration with ISRA).
Moreover, during the PALE-Blu project, we aim to determine which environmental factors are driving the *Culicoides* population structure at the community level, at the population level and at the microbiome level. We hypothesize that *Culicoides* population structure are important contributors to the existence and definition of bluetongue epi-zones. These activities will lead to strong interactions with WP3.

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Talk 27: Novel arthropod cell line establishment – the Tick Cell Biobank experience
Lesley Bell-Sakyi
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The Tick Cell Biobank (TCB) is the world’s largest repository of continuous tick cell lines, and the only culture collection specialising in establishment and maintenance of cell lines derived from ticks and other arthropod vectors. The TCB has been supplying cell lines and associated training to the international scientific research community since 2009, but the expertise behind tick cell line generation spans a much longer period. Techniques developed over the past 60+ years have led to the large portfolio of cell lines now available from hard and soft ticks of veterinary and medical importance. In the PALE-Blu project, this expertise will be blended with the small amount of published literature on midge cell culture to generate novel *Culicoides* spp. cell lines that will complement the one currently-available *C. sonorensis* cell line, KC. The emphasis will be on bluetongue virus vector and non-vector *Culicoides* spp. from Europe, the Middle East and Africa, provided by other PALE-Blu participants; resultant cell lines will be shared with consortium members and, after the end of the project, made available to the wider scientific research community through the TCB.
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Bluetongue survey and vaccine development in Tunisia"

Héla Kallel & Sofien Sghaier

IPT- Tunisia

Speakers unable to attend due to visa problems:

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