



PILGRIM NEWSLETTER No 1 / 2010

Welcome

The spread of infections in hospitals poses a considerable risk to patients and therefore is of public health concern. Prevention and control measures are urgently needed.

The EU-funded project PILGRIM investigates a specific bacteria that can occur in hospitals, called methicillin-resistant *Staphylococcus aureus* (MRSA). MRSA occur in hospitals throughout Europe. It can also be found in animals from where it can spread to humans and through the community, and sometimes reach health care settings. In order to develop measures and tools for reducing infections caused by MRSA in humans, we need to better understand their epidemiology and spread in different environments.

The PILGRIM consortium brings together public health specialists, microbiologists, veterinarians and engineers from academia and innovative industry to explore the epidemiology of resistant bacteria, especially MRSA. As a truly multi-disciplinary team we will provide solutions for infection prevention and control.

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"The three-year project had a flying start and after only one year, many activities are on their way. First results have already been published and the highlights of the first project phase are presented in this newsletter."

Prof Katharina Stärk, *PILGRIM* Coordinator,
Prof Veterinary Public Health,
the Royal Veterinary College London (RVC)

Enjoy your reading!

Facts and Figures

The PILGRIM research and development comprises different methodologies, including epidemiological and physiological studies, *in vivo* and *in vitro* experiments as well as molecular-genetic analysis.

- Title: “Preventing community and nosocomial spread and Infection with MRSA ST-398 instruments for accelerated control and integrated Risk Management of antimicrobial resistance”
- Start: 1 January 2009
- Duration: 3 years
- Funding: ~3 million euro
- Programme: 7th Research Framework Programme of the EU (FP7)
- Consortium: 12 organisations from 6 countries

PILGRIM ranked 5th among all Antimicrobial Drug Resistance projects and 2nd of 11 proposals submitted to the Molecular Epidemiology topic launched by the EU within FP7 in 2007.



Experts of five EU member states and one associated country closely collaborate to make this project a success.

Meticillin-resistant *Staphylococcus aureus* (MRSA) is among the key pathogens of concern. The new pig-adapted strain ST398, first reported in 2003, has been spreading in pig populations throughout Europe and other parts of the world. It has caused severe infection and disease in humans.

The PILGRIM project investigates the epidemiology of zoonotic, resistant bacteria with a focus on this particular strain. It also develops and evaluates new technologies which could be used for infection control in agricultural and hospital settings.

PUBLIC HEALTH News

Epidemiological studies

During the first year the PILGRIM consortium successfully started a longitudinal and several cross-sectional epidemiological studies in agricultural settings to be continued throughout the project duration.

Objectives

Several extensive studies are being carried out in Belgium, Denmark and The Netherlands. Their objectives are:

- To determine the patterns of MRSA human carriage inside and outside the farming environments
- To investigate the transmission routes between farm animals and humans

Professor Andreas Voss supervises the studies with the aim to decipher the epidemiology and ecology of MRSA-ST398 in farm and community environments. Brigitte van Cleef (NL), Cristina Garcia-Graells (BE) and Jesper Larsen (DK) are in charge of the public health related tasks. One study intends to identify the number of human MRSA-ST398 carriers not having had direct contact with livestock in areas of high pig densities in The Netherlands. The findings have been published recently by Van Cleef et al.



“The PILGRIM-studies shed light on veterinary MRSA, which seems to be abundantly present in animals, environments and humans, but is not as virulent as its hospital-associated brother until now. Scientists fear that new virulence genes can be acquired by the bacterium, with the result of a widespread virulent multiresistant strain. Therefore, studies examining veterinary MRSA are of vital importance to public health and healthcare.”

Dr Brigitte van Cleef, AIO Veterinaire MRSA, VUmc Amsterdam, RIVM Bilthoven

Procedure

This cross-sectional study was conducted in three municipalities in The Netherlands with a high pig population density of approximately 3000 pigs per square kilometre. Adults were sent randomly an electronic questionnaire and a nose swab.

Results

Figure 1 shows the study procedure and major results. Of the 534 people without livestock contact, one was positive for MRSA (0.2%; 95% confidence interval, 0.01–1.2). Of the 49 people who did indicate to be working at, or living on a livestock farm, 13 were positive for MRSA (26.5%; 95% confidence interval, 16.1–40.4). All spa-types belonged to CC398.

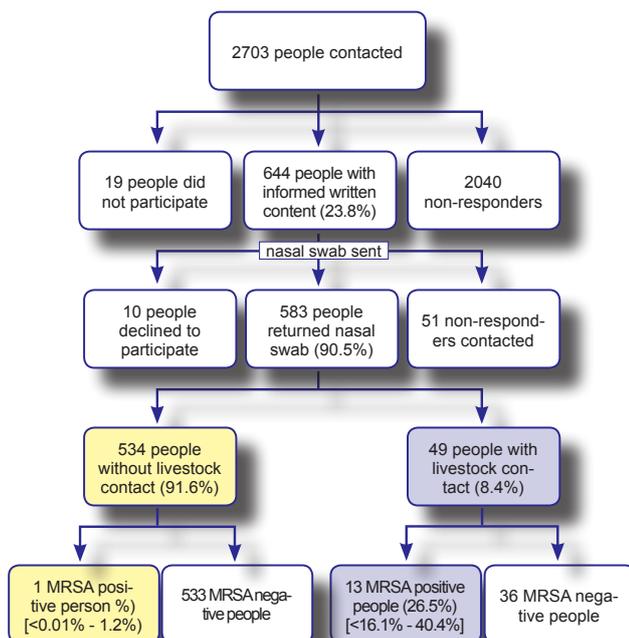


Figure 1. Flow Chart of the study procedure. (Van Cleef et al. 2010)

Although livestock-associated MRSA has a high prevalence in people with direct contact with animals, the bacteria has not spread from the farms into the community in The Netherlands. The findings of this study have been recently published in PLoS One. 2010 Feb 25;5(2):e9385.

VETERINARY News

Animal studies

In parallel to the human studies, researchers at the University of Copenhagen developed an *in vivo* porcine model for MRSA colonization studies. The model is based upon perinatal transmission of MRSA (see Figure 2).

Background

It is well known that the ability of bacteria to adhere to host tissue is an important process of colonization and subsequent invasion. Regarding *S. aureus*, nasal colonization has been shown to be a risk factor for the development of human infections. Better understanding of the colonization dynamics may provide valuable information that can be used to develop decolonization strategies. Animal models can be used to study both bacterial and host factors that influence nasal colonization by *S. aureus*, including MRSA strains. Current murine *S. aureus* colonization models are not ideal as they require anesthetization of the animals prior to inoculation, and rodent nares differ from human nares. The anatomical and physiological similarities between porcine and human skin makes the pig a suitable model for human *S. aureus* colonization.



"We have developed an easy method to obtain MRSA-colonized piglets having the same genetic background. The model can be used as a tool for future studies of MRSA-host interaction during colonization. This could have important implications for the possible development of MRSA eradication programs in pig production."

Dr Luca Guardabassi, Associate Professor, University of Copenhagen

Objectives

One of the objectives in PILGRIM is to develop a pig model for studying *S. aureus* colonization.

Procedure

Previous attempts to colonize pigs artificially by introducing MRSA into the nares failed, indicating that the indigenous bacterial flora exerts an antagonistic effect and prevents acquisition of the newly introduced strains. An alternate approach, the sow vaginal inoculation model, was used in which MRSA were implanted in the vagina of a MRSA-negative pregnant sow six days prior to farrowing. The carriage status of the piglets was monitored over 28 days after birth using a selective enrichment procedure for MRSA isolation.

Results

Naturally colonized piglets were successfully obtained by vertical perinatal transmission and MRSA carriage was stable over the entire 28 days of the experiment. Implantation of *S. aureus* in the vagina shortly before farrowing is an easy method to obtain naturally colonized piglets without using invasive procedures. The study also provides useful epidemiological information on the dynamics of MRSA transmission in pig production systems as it shows that MRSA lineage ST398 is efficiently transmitted from contaminated sows to their offspring.



Figure 2: The sow vaginal inoculation model: MRSA inoculation of the vagina of a pregnant sow results in natural colonization of the offspring.

TECHNOLOGY News

Surface MRSA decontamination

Researchers at the Royal Veterinary College London, together with experts from the Institute of Chemical Technology Prague (ICT Prague), have developed and investigated antimicrobial agents for surface MRSA decontamination.

Background

In both veterinary and human medicine, disinfection of surfaces is required to reduce numbers of potentially infective bacteria in order to prevent bacterial transmission and infection. Conventional disinfection methods are limited because they have short-term effects, are labour intensive and cannot be easily standardized. This study investigated the potential of using photocatalytic surfaces for the reduction or elimination of MRSA ST398.

Procedure

A range of commercially available or custom made ultraviolet (UVA) activated photocatalytic surfaces (tiles, paints) were tested *in vitro* against MRSA ST398 in a custom made chamber (Figure 3). Photocatalytic surfaces were tested for their antimicrobial potency against bacterial suspensions by serial dilution as well as against dried suspension by surface swabbing.



Figure 3. Test chamber developed at ICT Prague. Test materials held on tables are exposed to UVA from above. The illustration shows the chamber with the lid, holding the UVA lamps, open. Gloves attached to the two ports enable aseptic handling of contaminated test surfaces in the chamber.



Results

A linear correlation was found between the time of exposure and the inactivation of the MRSA bacteria in suspension on the tested surfaces. The most effective candidate surfaces were white photocatalytic facade paints that are used for outdoor/indoor coatings based on an organic polymer binder with inorganic titanium dioxide. Findings from these studies will be used in follow up studies *in vivo* in farm-style chambers. Suitability for prevention and control of MRSA ST398 transmission in health-care settings will be established in future studies.

Technology Testing Platform (TTP)

There is a lack of validation possibilities for products targeted at the control of MRSA under healthcare environments conditions.

The idea of the TTP has already been presented to selected companies in Europe and Asia who have expressed their strong interest and are committed to use the testing environment. The TTP will be made commercially available to companies as of 2011.

This year, a testing platform will be developed by some of the PILGRIM partners with the aim to provide a "natural" MRSA infected environment for product testing.

Are you also interested in getting to know more about the TTP or testing your products? Please contact Ms Joanna Cocker (jcocker@rvc.ac.uk), scientific PILGRIM assistant, at the Royal Veterinary College London, or Mr Mike Simonds (msimonds@rvc.ac.uk), Business Manager, at the RVC Enterprise London.



Team of the RVC Enterprise London

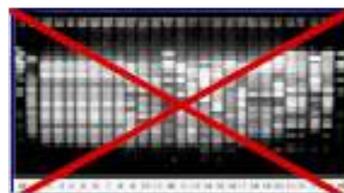
Business Opportunities

Diagnostic test for MRSA CC398

A novel Multiplex PCR test allows cheap, rapid and accurate detection of CC398 (*hdsS*) and methicillin resistance (*mecA*) genes simultaneously.

Thanks to the technology, jointly developed by three PILGRIM partners (University of Copenhagen, St George's Hospital Medical School, Statens Serum Institut), this invention can be applied by newer technology (microarray or deep-stick) to develop a solid-based assay for MRSA-typing.

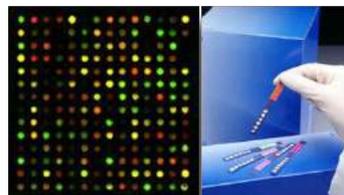
Advantages of our useful tool for MRSA surveillance and control:



No need for fingerprinting!



No need for sequencing!



Potential for solid-based assays for MRSA typing using microarray or deep-stick technology!

Companies and organisations can accelerate the current procedure for MRSA typing (three to four days) by 50% and reduce costs substantially.

Licenses can be acquired from the Tech Transfer Office at the University of Copenhagen. Please contact Ms Dorte Wissing Kaznelson (dwk@adm.ku.dk).

Communication

Presentations

Members of the PILGRIM consortium have successfully presented the initial project findings at the following scientific conferences.

3rd Symposium on Antimicrobial Resistance in Animals and the Environment (ARAE2009).

June 1-3, 2009, Val de Loire, France

- Poster: Objectives and potential applications of PILGRIM
- Presenter: Dr Efstathios Giotis



ASM-ESCMID Conference on Methicillin-resistant Staphylococci in Animals.

September 22-25, 2009, London, United Kingdom

- Paper: Multistrain *S. aureus* Microarrays to Investigate Host Specificity
- Presenter: Dr Jodi A. Lindsay and Dr Alex J. McCarthy



20th European Congress of Clinical Microbiology and Infection Diseases.

April 10-13, 2010, in Vienna, Austria

- Poster: Major achievements of the PILGRIM project to date
- Presenter: Dr Cristina Garcia-Graells



6th European Meeting on Solar Chemistry and Photocatalysis: Environmental Applications.

June 13-16, 2010, Prague, Czech Republic

- Poster : Ability of photocatalytic TiO₂ surfaces to destroy MRSA ST398 under controlled UV light conditions
- Author: Assoc. Prof Petr Kluson



Publications

The following dissemination material has been delivered to date:

- **Publication:** van Cleef BA, Verkade EJ, Wulf MW, Buiting AG, Voss A, Huijsdens XW, van Pelt W, Mulders MN, Kluytmans JA. Prevalence of livestock-associated MRSA in communities with high pig-densities in The Netherlands. PLoS One. 2010 Feb 25;5(2):e9385.
- **Factsheet:** The first factsheet is available in six different languages ([English](#), [French](#), [Dutch](#), [German](#), [Danish](#) and [Spanish](#)). It explains why MRSA is a major public and animal health concern in Europe and beyond.

All publications and other documents are available on www.fp7-pilgrim.eu.

Outlook

A number of exciting opportunities for the PILGRIM partners to present the project findings and project activities are foreseen in the coming months:

- Set up of an Exploitation and Dissemination Panel (EDP) with external experts from both areas – veterinary and public health to advise the project partners on the potential use of the R&D results
- Annual meeting in Gent, December 1-2, 2010

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For further information on the latest project activities please visit our project website or send us an email.

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