

Final academic report for the UCPH Excellence Programme for Interdisciplinary Research.

UC-Care



MEMORANDUM

26 JANUAR 2018

Re: Final academic report

Administrative officer in charge:

RESEARCH & INNOVATION

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1. Basic Information

<i>PI and Co-PI's</i>	PI: Professor Luca Guardabassi Co-PI and coordinator: Professor Anders Miki Bojesen Professor Peter E. Nielsen Professor Niels Høiby Professor Lars Bjerrum Professor Jens Peter Nielsen Professor Fredrik Björkling Professor Charlotte Reinhard Bjørnvad Professor Anders Løbner-Olesen Professor Jørgen Dejjgård Jensen Professor Hanne Mørck Nielsen Assoc. Professor Lisbeth Rem Jensen Assoc. Professor Carsten Strøby Jensen
<i>Project title</i>	University of Copenhagen Research Centre for Control of Antibiotic Resistance (UC-CARE)
<i>Amount granted</i>	32.627.000 DKK

2. Research excellence and international impact of the project

2.1 Excellence in research based on interdisciplinary collaboration: Scientific discoveries and achievements

Give an account of the most important scientific discoveries and achievements of the project. Describe how interdisciplinary collaboration has influenced the discovery described and the potential significance for the research fields involved. (maximum 4800 keystrokes/2 pages including a brief summary introducing the highlights).

Given the diverse nature of the research activities these have been ordered according to the work package they mainly associate to.

Drug discovery and translational research

We have developed two novel cell based screens for identifying inhibitors of the chromosomal DNA replication initiation in bacteria. Subjecting the screens to a library of 400 microbial extracts, identified the iron chelator, deferoxamine, as a compound that rescues the growth of over-initiating cells. Substantiating the model that oxidative DNA damage and its repair promotes the lethal action of hyper-replication.

We have constructed and verified a novel high throughput, cell based, fluorescence screen for inhibitors of chromosomal replication initiation in bacteria. The screen utilizes an *E. coli* mutant that is resistant to replication initiation inhibitors and holds a fluorescence reporter system that is activated by DNA replication initiation inhibition. This screen was also subjected to the above-mentioned library of microbial extracts, though it did not lead to any positive hits.

Alternative control strategies

Aiming at identifying immunogens that had the potential to induce serotype-independent protection against bacterial pathogens characterized by broad antigenic diversity we applied a rational approach on the pathogens *Gallibacterium anatis* and *Actinobacillus pleuropneumoniae*. We successfully developed and tested a set of *G. anatis* vaccine prototypes in the relevant host species, the chicken. A subset of prototype vaccines is currently developed further for commercialization in collaboration with an international company.

The results showcase how broad-scoped bacterial vaccines can be developed and represent a real alternative to antibiotic treatment.

An alternative vaccine platform technology based on an adenoviral vector backbone including a modified MHCII associated invariant chain able of inducing increased antibody responses against a broad panel of microbial antigens appears to be a platform technology with a great potential. The

technology has been tested using protozoal (malaria), viral (hepatitis) and bacterial (*G. anatis* and *A. pleuropneumoniae*) antigens and showing very promising immunization results.

The principle has been filed in a patent application, which already has been co-licenced by a Danish and a UK based company, respectively.

Optimisation of antibiotic therapy.

Using *in vitro* and *in animal* models we have shown that the non-antibiotic OligoG can break the *P. aeruginosa* biofilm matrix and facilitate killing of the released bacteria by polymorphonuclear leucocytes and antibiotics. We have found that the bactericidal effect of colistin on *P. aeruginosa* is independent of hydroxyl radical formation in contrast to the bactericidal effects of ciprofloxacin which is dependent of hydroxyl radical formation. We also found that colistin has increased bactericidal activity on *P. aeruginosa* biofilms during anaerobic condition and that the bactericidal effect of ciprofloxacin on *P. aeruginosa* biofilm is increased by hyperbaric oxygen treatment. *These results represent 'proof of concept'.*

Together with colleagues from DTU we have mathematically modelled the effect of hyperbaric oxygen and ciprofloxacin on biofilm growing *P. aeruginosa* and the penetration and binding of tobramycin to the matrix of *P. aeruginosa* biofilms.

*Our work on biofilm infections has resulted in the first international guidelines for diagnosis and treatment of human biofilm infections Together with our colleagues from WP1, we have described the effect of new peptide antibiotics on colistin-resistant *P. aeruginosa* from cystic fibrosis patients.*

Evidence-based diagnosis and therapy of infections in human and veterinary medicine

Data from about 800 human patients with suspected urinary tract infection shows overuse of antibiotics due to misinterpretation of the diagnostic tests and prescription of antibiotics without microbiological confirmation of the bacterial origin of the symptoms. Our results confirm that prescription of antibiotics based on symptoms only caused 40% overuse of antibiotics, which can be counteracted by using more point-of-care diagnostics. *The results have been cited directly in material leading to National Goals for Antibiotic Usage in Human Medicine.*

Data from 58 companion animal practices in Denmark indicates that the diagnostic validity of current diagnostic modalities for canine UTI is poor, leading to a vast overuse of antibiotics, similar to the situation in people.

Our results have been used to update the national guideline for antibiotic use in clinical practice. National Danish antibiotic use guidelines for companion animals Revision 2018: L.R. Jessen, P.P. Damborg, A. Spohr, B. Schjøth, B. Wiinberg, T.M.Sørensen, G. Houser, J. Willesen, M. Schjærff, T. Eriksen, V.F. Jensen, L. Guardabassi. 2018.

Cost-benefit analyses

The usage of antimicrobials in pig herds using vaccination or not were shown to depend more on the baseline level of use before vaccination was initiated than on the actual vaccination. This is probably due to a higher level of underlying disease on the farm, inadequate biosecurity and management procedures, respectively. Hence, vaccination cannot be recommended as a general advice, but must be based on knowledge of the underlying causal factors and disease patterns in each case.

A theoretical economic study has investigated the incentive mechanisms of relevance for regulating the use of antimicrobials in livestock production and developed an auction-based regulation scheme for obtaining a specified reduction goal at the lowest possible cost for society. Farm-level data from the VetStat database was combined with farm-level economic accounts (FADN) data, and the combined dataset was used to investigate the economic efficiency in agricultural use of antibiotics, and in particular the farm-economic effects of the Danish Yellow Card Scheme.

The work package is characterized by a considerable extent of interdisciplinary collaboration including economists, veterinarians and food scientists. The WP has also had close collaboration with WP6 and international partners, which has enabled incorporation of many different and new perspectives in the analyses.

Antibiotics in social science context – between users and pre-scribers

Only very few research projects and research communities internationally deals with antibiotics from a more societal and broad interdisciplinary perspective. Most research projects focuses on different life science aspects and performs analyses on the use of antibiotics from e.g. a medical or microbiological perspective. The current work has developed and applied new tools including mixed method methodologies involving quantitative descriptive investigation of patterns in antimicrobial use (medical and veterinary), which combined with qualitative interviews with essential actors (e.g. patients, pig farmers, doctors and vets) revealed unexpected conclusions as how we can prevent overuse of antibiotics. In example: patients do generally not expect to get antimicrobial treatment but are more concerned about getting the clear advice. The cultural background (comparing Northern and Southern Europe) do influence the type and format of advice, which may lead to different antibiotic usage patterns and finally a negative societal focus on e.g. pig farmers potentially positive for MRSA leads to stigmatization, which most likely has a counterproductive effect in terms of participation in voluntary initiatives aiming at reducing antibiotics.

2.2 Plans for future activities or embedment related to the project

Please give an account of any plans for continuation or possible embedment of the project. (maximum 1200 keystrokes/½ page).

As evident from the amount of external research funding generated by the consortium members during the project period (~250 Mio DKK) there should be no worry about continuation of the major research activities outlined in the project. However, for some parts, particularly those including social science and humanities, which more than any others have had to develop and apply new tools to the antimicrobial sphere, securing continuation is less obvious.

The current management board have agreed to continue to meet at least twice annually to stimulate continued collaboration across disciplines.

The One Health course “**Antimicrobial resistance: a threat for human and animal health**”, which was developed by a large group of consortium members and aimed at medical and veterinary students at UCPH has now become a compulsory course for master student. This will act as a good platform to ensure continued contact between several participants.

2.3 Publications

Please list the five most important publications derived from the project and explain briefly why these are the most important publications. If relevant, comment also on their interdisciplinary nature.

The following items can be included in your answer (maximum 1200 key-strokes/½ page)

- *To what extent have you been able to co-publish across disciplines within the project?*

A substantial number (>120) of contributions to peer-reviewed journals and books have been published and more will follow. The vast majority of publications are based contributions from different disciplines. Some are based on joint efforts between areas that have a well-established interaction *e.g.* veterinary medicine-molecular biology-pharmaceutical chemistry, whereas others represent more untraditional interactions *e.g.* medicine-economics-psychological sciences. The latter are more elaborate as they require mixing of rather different publication cultures and in some cases appear to results in definitions of new research fields which typically need to identify or develop accompanying disseminations channels.

- *In what way, if any, has the interdisciplinary approach strengthened publications within the team?*

The majority of publications would not have been possible to make if it were not due to an interdisciplinary approach joining specialists across fields.

For those investigations where a more broad-based and untraditional collaboration was made possible by the overall project the team members involved have broken new ground not least from getting first-hand experience with experimental approaches and publication traditions fundamentally different to own experiences. This is particularly true for those parts of the project including participants of WP5 and WP6 that had to join vastly different traditions. Yet, as apparent from the publication list several interdisciplinary contributions were generated on that basis.

- *What are the challenges and opportunities in relation to publication outputs?*

The main challenges include different publication strategies e.g. book chapters vs. journal articles (different areas-different merit) and difficulties at identifying (well-reputed) dissemination channels that fit a broad scope. Mixing vastly different publication cultures requires extra time per publication but also adds very stimulating discussion that would never had happened if it were not for that mix.

Please enclose a full list of all publications produced as a result of the project, including single-author publications (See **Appendix 1**). This list will also be used in the following Leiden bibliometric analysis.

2.4 Prizes, prestigious grants and awards

Please list prizes, prestigious grants and awards if any that project members have received for work related to the project using the outline below.

	<i>Name</i>	<i>Project title</i>	<i>Amount</i>
<i>ESVNU AWARD for best oral abstract (European Society of Veterinary</i>	Tina Møller Sørensen	Evaluation of different sampling methods and criteria for diagnosing canine urinary tract infection by quantitative bacterial culture.	500 Euro
<i>Friederichsen's Memorial Reward</i>	Gloria Cordoba	Diagnostic process in patients with UTI symptoms in Danish Primary Care: Impact on appropriate use of antibiotics and patient's recovery	30.000,- DKK
<i>Best poster presentation prize. Copenhagen Microbiology Center Symposium 2015.</i>	Gry Persson	Outer membrane vesicles as a potential vaccine candidate combined with the putative antigens GtxA-N and FlfA for universal vaccination against <i>Gallibacterium anatis</i>	1000 DKK

2.5 International research collaboration

Please give an account of the current international research collaborations in the project and their interdisciplinary aspects.

As part of the account you are asked to

- *assess the level of visiting researchers, joint publications, visits in foreign universities and projects with foreign universities to date:*

Due to the broad nature of UC-Care and the extensive international research collaboration and the high research output a full account is not possible. All WPs have benefitted from different levels of international collaboration, which is also apparent from the research publications (**Appendix 1**).

- *give an account of invitations to participate in networks and panels as well as contributions to conferences in the fields*
- **WP1:** International research collaborations were established with Prof. Miguel Camara (University of Nottingham, UK), Prof. Roberto Gambari (Ferrara University, Italy), Prof. Christel Bergström (Uppsala University, Sweden), Prof. Roger C. Lévesque (Laval University, Canada), Prof. Hans-Georg Sahl (University of Bonn, Germany), Dr. Stefano Donadio (Ktedogen, Italy), and Dr. Andrew Hesketh (University of Cambridge, UK).
- **WP2:** Close collaboration with Prof. Paul Langford and Janine Bossé (Imperial College, UK), Prof. Andrew Rycroft (Royal Vet. College, UK), Prof. Paul Wigley (University of Liverpool, UK), Assoc. Prof. Tim Johnson (University of Minnesota, USA), Laura Serino (GSK Vaccines, Italy), Marco Soriano (GSK Vaccines, Italy), Koen Degussem (HUVePharma, Belgium).
- **WP3:** We have a cooperation with colleagues in China (Chongqing University, Nanning University and also in Shanghai, where we have a three visiting scientists We have had visitors from Barcelona, Laia Fernández-Barat for three months, from UK, Laura Line, a pre-graduate for one year, a PhD student from University of Sao Paulo, Natalia Candido Cacador for one year, and another one from University of Campinas, Renan Mauch will come on May 1st this year. N. Høiby has also visited University of Campinas in Brazil for a week to give five lectures on biofilm and Cystic Fibrosis research and to present possibilities for cooperation between University of Copenhagen and Rigshospitalet and University of Campinas. N. Høiby has also been invited to the Swiss pharmaceutical company Roche who organised a biofilm session in Basel because they wanted to go into

the biofilm area. Several experts in Europe and from the United States were invited to presentations about the biofilm research including N. Høiby.

- **WP4:** In collaboration with Oslo University, Research Centre for antibiotic Research, and University of Lund, Department of Public Health and Primary Health Care we are involved in a clinical trial (Ibuprofen versus mecillinam for uncomplicated cystitis in adult, non-pregnant women, IMUTI) to investigate the effect of non-antibiotic treatment (non-steroid anti-inflammatory drugs) in patients with non-complicated urinary tract infections. WP4 PI participates as expert in the advisory board for the European project: Antimicrobial Resistance and Causes of Non-prudent Use of Antibiotics in the European Union; ARNA. The project is coordinated from University of Antwerp. WP4 PI participates in the European Centre for Disease Prevention and Control (ECDC) as expert for evaluating the risk from digestive colonization with multidrug-resistant Enterobacteriaceae after international travel and implications for surveillance. WP4 PI participates in the European study initiated by WHO: Understanding knowledge, behaviours and attitudes of antibiotic use in Eastern European and Newly Independent States countries: a qualitative study. Ph.d student Gloria Cordoba has initiated an audit on antibiotic use for respiratory tract infections in South America, involving Argentina, Paraguay, Uruguay and Bolivia. More than 100 GPs from the 4 countries have participated in the study and data have been analysed. Results from the study will be presented at the world congress for General Practice (WONCA-World) in Rio de Janeiro in November 2016.
- **WP5:** Researchers in the work package have also interacted with researchers from Portugal, Switzerland and the US. A stay abroad (US or UK is under planning for one of the PhD students).
- **WP6:** Lindell: Januar – juni 2015: Visiting Graduate Researcher, Center for Language, Interaction and Culture (CLIC), UCLA. Mentor: Prof. Tanya Stivers (incl. presentation of data at CLIC AnthroLingLab, at CA group on Medical Interaction). Lindell: Marts – april 2016: Visiting Phd Fellow, Finnish Centre of Excellence in Intersubjectivity in Interaction

3. Research based educational activities and research training

Please give an account of project-related activities for enhancing the quality of research based education at Bachelor's, Master's and PhD level. As for BA and MA, you may limit your response to activities of a more permanent nature, lasting beyond the end of the project period. Please include the num-

ber of PhD's and postdocs working on the project. (maximum 2400 key-strokes/1 page).

- As an outcome of the UC-CARE cooperation between different research groups a new One Health course entitled “**Antimicrobial resistance: a threat for human and animal health**” bringing together for the first time medical and veterinary students has been organized. The course is presenting the global antimicrobial resistance problem from the One Health perspective. Several PIs of the UC-CARE interdisciplinary project including Niels Høiby, Lars Bjerrum, Jens Peter Nielsen, Anders Miki Bojesen, Lisbeth Rem Jensen and Carsten Strøby Jensen participates in the course, which is coordinated by Oana Ciofu. The course was held for first time in 2017 and will be running twice annually as it is now compulsory for all medical students and a large fraction of the veterinary students at UCPH.
- Conference organization: UC-Care organized the first edition of the International Conference on One Health Antimicrobial Resistance (ICOHAR, Copenhagen September 30 – October 2, see www.icohar.com.) This event brought together over 150 attendees from academia and the public health, medical and veterinary sectors. The second day was entirely dedicated to two roundtable discussions with national (Danish Veterinary and Food Administration and Danish Pig Research Center) and international (European Food Safety Agency and World Health Organization) stakeholders.
- Collaboration in the EU COST Action TD1404 Network for Evaluation of One Health (NEOH): <http://neoh.onehealthglobal.net/> The NEOH network used UC-Care as a case study in the development of a new framework for evaluation of One Health initiatives. The UC-Care consortium and project has been presented multiple times at different meetings in the COST Action network which consists of scientists and stakeholders with many different backgrounds and from many different countries in EU and worldwide. A peer-reviewed paper summarizing the has been submitted on basis of the above:
Léger, A. Stärk, K.D.C., Rushton, J., Nielsen, L.R. One Health evaluation of the University of Copenhagen Research Centre for Control of Antibiotic Resistance (UC-CARE). Frontiers in Veterinary Science, special issue on One Health evaluation. Under review for publication in Frontiers in Veterinary Science, February 2018.
- Workshop on “Evaluation of data and information sharing in One Health initiatives” was held by the NEOH consortium at Faculty of Health and

Medical Sciences in Copenhagen on April 20-21, 2016. (Program available from local organizer Liza Rosenbaum Nielsen, liza@sund.ku.dk)

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- Collaboration within WP5 and between WP5 and WP6 has led to new educational initiatives with more cross-disciplinary teaching including more socioeconomics teaching of veterinary students at master level, and sociology teaching for the veterinary and medical master level students.

PhD students fully or partly financed via the grant (21)	Cyrielle Elyette Fougeroux Mikkel Alanin Hannah Trøstrup Christian Lerche Kim Thomsen Gloria Cordoba Anne Holm Tina Møller Sørensen Lola K.T. Leihart Dagim G. Belay Amanda Kruse	Rikke Prejh Brochmann Mehreen Anjum Rasmus Nielsen Klitgaard Natalia Molchanova Niloofar Yavari Mirko Iubatti Fabio Antenucci Kim Sune Jepsen Johanne Lindell Gry Persson
Post Docs fully or partly financed via the grant (12)	Bimal Jana Zofia Magnoska Kristin Rene Baker Syed Qaswar Ali Shah Susanne E. Pors Egle Kudirkiene	Hengzhuang Wang Mette Kolpen Mads Bank Lars Fynbo Valeria Bortolaia Carmen Espinosa Gongora

4. External funding

Please list the amount of external funding obtained to date with relation to the project using the outline below. If the same grant has two or more grant holders the total amount granted as well as the sub amounts should be listed.

Source	Grant holder	Project title	Period	Total amount granted
WP1: Zoetis grant	Luca Guardabassi	Improved antimicrobial activity of existing antibiotics	2014-16	€300.000
Inovationsfonden	Peter E. Nielsen	Sensitizing Pseudomonas biofilm	2015-18	DKK 1.822.000
DNRF Center of Excellence	Anders Løbner-	Center for Bacterial Stress Response and Persistence (BASP).	2015-21	DKK 50.000.000

	Olesen	Center leader is Kenn Gerdes		PAGE 11 OF 16
Exploratory International Network Grant (ING)	Anders Løbner-Olesen	New molecules & New targets: innovative strategies for antimicrobial development	2015	DKK 241.245
Novo Nordisk Fonden	Peter E. Nielsen	Center for Peptide-Based Antibiotics	2017-2022	DKK 58.000.000
WP2: CPHpig	A.M. Bojesen	Co-funding of two PhDs	2013-16	DKK 1.000.000
SEGES	A.M. Bojesen	Pig experiments	2016	DKK 150.000
HuvePharma	A.M. Bojesen	Vaccine development	2017-19	DKK 2.200.000
WP3: EU-FP7	Niels Høiby and others	IMPACT 261095	2013-17	€6.000.000
NNF challenge	H.M. Nielsen	New knowledge on transporting drugs in the body	2017-22	DKK 60.000.000
WP4: Agria	Tina Møller Sørensen	Flexicult study (RCT)	2015-17	€36.000
Region Hovedstaden	Gloria Cordoba	Bedre behandling af urinvejsinfektioner –almen praksis viser vejen	2015-17	DKK 867.948
Søren Friis legat	Anne Holm	Skru ned for de resistente bakterier	2015-17	DKK 1.200.000
Region Hovedstaden	Gloria Cordoba	Bedre behandling af urinvejsinfektioner -almen praksis viser vejen	2015-17	DKK 102.511
WP5: Cattle Levy Foundation	Liza Rosenbaum / Jørgen Dejgaard	'Robust calves'-research consortium	2018-21	DKK 12.800.000
WP6: DFF Research project 2	Inge Kryger	'Global Challenges, Local Solutions? Rethinking Professional Work in a World of Transnational Jurisdictions	2016-20	6.043.000

Private foundations	J. Lindell		2015-17	PAGE 12 OF 15 DKK 100.000
Grand Total				>247 mio DKK

5. Private and public sector collaboration, innovation and impact

5.1 Private and public sector collaboration

Please give an account of activities in the project related collaboration with businesses, regions, municipalities, museums, NGOs etc. (maximum 1200 keystrokes/½ page).

As part of a PhD project funded by the UC-Care, a PhD student visited the Italian biotechnology company, Naicons Srl., who owns a unique drug discovery engine, based on a vast library of microbial extracts. Following the visit a collaboration agreement was established leading to the identification of deferroxamine as a compound that promotes the viability of hyper-replicating bacterial cells.

Experiences obtained from vaccine development in UC-Care have resulted in a private company, HUVePharma, funded vaccine development project aiming at a commercial vaccine.

Collaboration with the Norwegian company Algipharma and the Danish Company Reaplix Aps, and the Danish company Vivostat, have resulted in projects aiming at new ways to combat biofilm infections.

Insights and expertise gained during the UC-CARE activities have been utilized in the Department of Food and Resource Economics' (IFRO's) research-based commissioned advisory work for the Danish Ministry of Environment and Food. Three tasks related to economic aspects of agricultural antimicrobial use have been undertaken so far

- Review of economic issues in antimicrobial use in livestock production (completed May 2015)
- Economic assessment of alternatives to antibiotics and medical zinc in the handling of diarrhoea in weaner pigs (completed March 2017)
- Economic assessment of strategies to reduce the risk of human cases with MRSA CC398 (completed in June 2017)

Especially the latter has also contributed to 5.3 Societal impact and 5.4 Public outreach.

5.2 Application and commercialisation

Please list to what extent, if any, research results derived from the project have been applied and commercialised, using the following outline. Pipeline agreements may be included:

	<i>Title(s)</i>
<i>Invention disclosures</i>	
<i>Patent applications</i>	UK patent 1704417.3 filed on 20th of March 2017
<i>Patents issued</i>	
<i>License agreements</i>	UK patent 1704417.3 part licensed to a UK and a DK based company, respectively.
<i>Spin-out companies</i>	

5.3 Societal impact

Please give an account of activities and the strategy of the project related collaboration with public bodies and potential influence on politics, practice, legislation etc. (maximum 1200 keystrokes/½ page).

Three UC-Care Professors (L. Bjerrum, J.P. Nielsen, A.M. Bojesen) are members of the Danish National Council for Antibiotics under the Ministry of Health. The Council play an important advisory role for the Ministry and some UC-Care results have been directly referenced in the 2017 national goals for antimicrobial usage in the human medical sector.

Professor A.M. Bojesen is deputy-head of The Council of Improved Hygiene, which is a public body influencing politics on antimicrobial usage at the national level.

The UC-Care activities have resulted in publication of national and international guidelines:

- ESCMID guideline for the diagnosis and treatment of biofilm infections. 2014. N. Høiby, T. Bjarnsholt, C. Moser, GL Bassi, T. Coenye, G. Donelli, L. Hall-Stoodley, V. Holá, C. Imbert, K. Kirketerp-Møller, D. Lebeaux, A. Oliver, A. J. Ullmann and C. Williams for the ESCMID Study Group for Biofilms (ESGB) and consulting external expert Wer-

ner Zimmerli: Clin. Microbiol Infect. 21, Supplementum 1: 1-26; 2015. online: doi.org/10.1016/j.cm.2014.10.024.

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The first international guideline on diagnosis and treatment of biofilm infections

- National Danish antibiotic use guidelines for companion animals Revision 2018: L.R. Jessen, P.P. Damborg, A. Spohr, B. Schjøth, B. Wiinberg, T.M. Sørensen, G. Houser, J. Willesen, M. Schjærff, T. Eriksen, V.F. Jensen, L. Guardabassi. 2018.

5.4 Public outreach

Please give an account of activities related to broader audiences outside of academia and discuss the strategy of the project and what future initiatives might enhance the public outreach. Examples could include lists of newspaper articles or appearances in the media, website activity and popular dissemination (maximum 1200 keystrokes/½ page).

UC-CARE was very well represented with an interactive stand (incl. three live pigs!) at the Euro Science Open Forum (ESOF) 2014 held in Copenhagen (<http://video.ku.dk/ind-i-kroppen>). Several hundreds of visitors stopped by the stand to have a chat about antibiotic resistance or participated in the science slams held several times over the two-day event.

The Co-PI and coordinator has participated in a joint meeting on antibiotic resistant bacteria in general and on MRSA in particular held by the Danish Parliaments committees for Health, and Environment and Food, respectively. November, 2014. Here the complexity of this grand societal challenge was stipulated for a large number of the members of Parliament.

A 2-page UC-Care profile paper was published in the European “Science & Technology” June issue (19), 2016, by Pan European Networks, United Kingdom. Here the scope, main achievements and future perspectives of the centre are summarized.

Several public appearances and contributions have been made by the consortium members:

- Bojesen, A. M., Frees, D. & Nielsen, J. P. (2017). Antibiotikaresistens – debat om fremtidens løsninger. Folkemødet, Svaneke.
- Bojesen, A. M., Frees, D. & Nielsen, J. P. (2017). FRB Talks: Antibiotikaresistens – foredrag og debat om den globale trussel og fremtidens løsninger. Frederiksbergdagene, Frederiksberg C.

- Sørensen, T.M. (2018). Evidensbaseret diagnostik og behandling af urinvejsinfektioner hos hunde – hvor langt er vi nået?. Journalen. DDD – Faggruppe Familiedyr Vol. 2, p. 14-16
- Rafn, C. (2017). Sikker diagnose skal mindske antibiotikaforbrug. Dyr-lægemagasinet for praktiserende dyrlæger Vol. 14 (1), p. 12-14.
- Sørensen, T.M., Jessen, L.R., Bjerrum, L. (2017). Two focus group meetings with lectures and discussions among veterinarians participating in UC-CARE projects.
- Sørensen, T.M. (2013). Evidensbaseret diagnostik og behandling af nedre urinvejsinfektioner hos hund. Dyr-lægemagasinet for praktiserende dyrlæger Vol. 10(6), p.6-7.
- Sørensen, T.M. (2013). Månedens forskningsprojekt. Evidensbaseret diagnostik og behandling af nedre urinvejsinfektioner hos hund. Journalen. DDD – Sektion vedrørende hund, kat og smådyr Vol. 8, p. 20-21.
- Starch, M., Bjerrum, L., Jessen, L.R. (2013). Sundhed på P1: Antibiotika resistens. Radio talk about UC-CARE and antibiotic resistance.
- Jensen J.D. 2017. Markedet for kød fra dyr opdrættet uden antibiotika, presentation at public meeting: Antibiotika og resistens – husdyropdræt uden anvendelse af antibiotika, University of Copenhagen, Jan. 31, 2017
- Lecture at National council of antibiotics (J. Lindell).
- Lindell, J. Invited presentation at the Ministry of Health about Antibiotic campaigns 2018.
- Lindell, J. Article in 'Maanedsskrift for Almen Praksis'.
- Nielsen, S.B. & J. Lindell (2017) "Overvej en ekstra gang hvad du siger til lægen!" i Forskerzonen,
- Fynbo, L. Participation in two multidisciplinary networks centered at the Danish Agriculture & Food Council focusing on bio security and safe and healthy food sources.
- Fynbo, L. Feedback to central veterinarians working with contemporary pig farming.

6. Concluding remarks

Based on the work done in the project and the results achieved, what are your concluding remarks with relation to the investment of your own and the University's resources? (maximum 1200 keystrokes/1/2 page).

The ultimate goal of UC-Care was to create a self-sustainable and durable research programme that would transcend the duration and funding of the current proposal through external funding and academia-industry partnerships. All WPs have been highly active in reaching this goal, which is also apparent from the considerable research output in terms publications (>120), the amount of external funding (>250 mio DKK), embedment of permanent educational initiatives (compulsory One Health course) and memberships in

several permanent or transitory high-level advisory boards ensuring dissemination of knowledge obtained in the project to a broad crowd.

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Based on the above we are confident that the University's decision to support the UC-Care consortium was reasonable and right.

As a closing remark we strongly believe that the initial idea to fund cross-disciplinary projects of this size by University of Copenhagen was clever highly rewarding. If it had not been for the "2016-initiative" UC-Care and probably several others of the excellence centers would never have seen got to be a reality.

These points seems to be shared by the external midterm evaluation panel headed by Dr Klaus Bock

"As I hope to have made clear, the project is very impressive."

"I should close by saying that we would be in better shape globally if more countries were taking this approach and if there was more cross-national cross-disciplinary work going on. Hats off to the University of Copenhagen!"