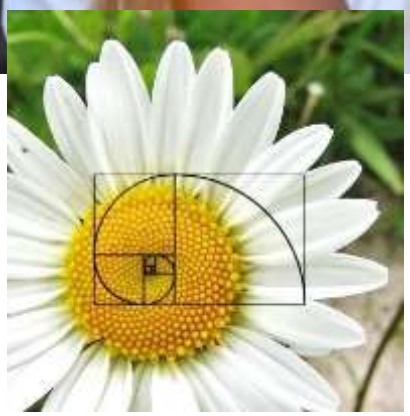
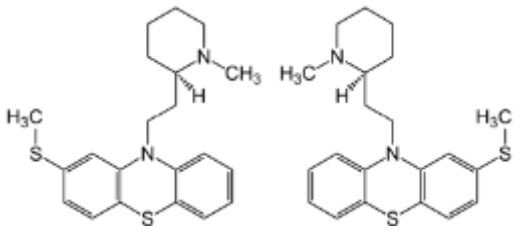
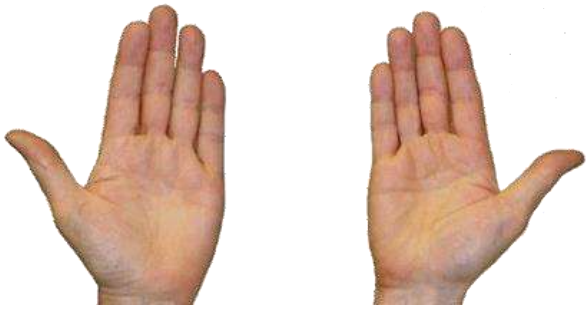
Nye muligheder for behandling af multiresistente infektioner med non-antibiotika







Dagsorden og præsentationer fra

CHRISTIANSBORG 25. JANUAR 2017

Abildgaard Kredsen indbyder til konference

om

Nye muligheder for behandling af multiresistente infektioner med non-antibiotika

Sted : Fællessalen på Christiansborg
Tid : Onsdag den 25. januar 2017 kl. 13.00 – 17.00

På konferencen vil offentligheden for første gang kunne komme i dialog med forskerne bag nye muligheder for at behandle antibiotikaresistente infektioner som f.eks. MRSA, VRE, CPE, ESBL og XDR-TB nu og i fremtiden.

Medarrangør:
Videnskab.dk og EU-projektet "COST Action CM1407"
http://www.cost.eu/COST_Actions/cmst/CM1407

Ordstyrer og moderator: Peter Hyldgård, Videnskab.dk

Yderligere information:
Der vil ved tilmelding blive opkrævet et mindre gebyr. Tilmelding foregår via http://videnskab.dk/nonantibiotics

Evt. spørgsmål kan rettes til:

Flemming Møller
Tlf. 50758424
E-mail: f@nl70.dk

Læs mere om Abildgaard Kredsen på http://www.abildgaardkredsen.dk

Antibiotikaresistens - Dommedag aflyst!

Jens L. Larsen

Danmarks befolkning er gennem pressen blevet udsat for foruroligende dommedagsprofetier baseret på den hjemlige og globale resistensudvikling blandt bakterier.

Den gren af mikrobiologien, der er optaget af avancerede molekylære teknikker har eksponeret offentligheden for diverse skrækscenarier. Disse trækker jævnligt store overskrifter i dagspressen og sætter sundhedsmyndighederne under pres. Forskere med et andet fokus har derimod søgt løsninger på disse problemer. Deres indsigt og viden viser nye effektive behandlingsmuligheder.

For at udbrede kendskabet og styrke grundlaget for beslutningstagere på dette område afholder Abildgaard Kredsen (www.abildgaardkredsen.dk) den 25. januar 2017, kl. 13:00 - 17:00 en international konference på Christiansborg med titlen:

"Nye muligheder for behandling af multiresistente infektioner

med non- antibiotika".

Konferencen er rettet mod politikere og andre beslutningstagere, pressen, forskere og andre med interesse for feltet. Internationale og danske forskere beretter på konferencen om en forskning, der startede i Danmark i 1970'erne, og hvis resultater er med i baggrunden for, at et engelsk og et indisk medicinalfirma nu starter en produktion af non-antibiotika (resistance breakers) til et verdensmarked, der er anslået til 69 milliarder dollars. Har vi mon sovet i timen?

De nye produkter vil udløse et nyt paradigme i behandlingen af resistente infektioner, hvor man direkte kan interferere med de cellepumper, der er ansvarlige for resistensen.

Det er bydende nødvendigt, at pressen informerer befolkningen og politikerne om disse landvindinger og deres potentiale.

Nye muligheder for behandling af multiresistente infektioner med non-antibiotika

Welcome / Velkomst

Jane Heitmann

Venstres sundhedsordfører og dagens vært (DK)

And / Og

Flemming Møller

Fagdyrlæge og tidliger medlem af Folketinget (V) 2008-2011

Nye muligheder for behandling af multiresistente infektioner med non-antibiotika

Moderator / Ordstyrer

Peter Hyldgård

Cand.scient. i biologi

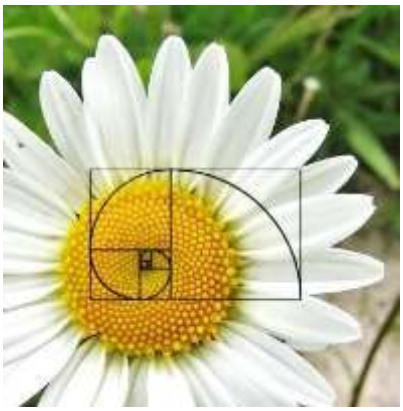
Journalist, redaktør og faglig formidler

Udviklingschef, Videnskab.dk

Program

Subject / Emne	Speaker / Taler
Welcome / Velkomst	Jane Heitmann Venstres sundhedsordfører og dagens vært (DK)
Resistance between professionalism and politics. *Resistens mellem faglighed og politik.*	Flemming Møller (DK)
Investigations and treatment of multidrug-resistant (XMDR) TB with Thioridazine in vitro and in vivo. *Undersøgelser og behandling af multiresistent Mycobacterium tuberculosis med Thioridazine.*	Leonard Amaral (USA/PT/HU)
The historical approach to antibiotics, resistance and nonantibiotics. *Den historiske tilgang til antibiotika, resistens og non-antibiotika (Hvad jeg lærte af Paul Ehrlich).*	Bernd Wiedemann (GE)
Coffee / Kaffe	
Why is non-antibiotics so important in the management of infectious diseases. *Hvorfor non-antibiotika er så vigtige i behandlingen af infektionssygdomme.*	Richard Bax Senior Partner Transcrip and Senior Advisor Helperby Therapeutics (GB)
Reversal and breaking resistance in intestinal bacteria. *Blokering og ophævelse af resistens hos Gram-negative tarmbakterier.*	Rikke Heidemann Olsen (DK)
Breaking resistance development using molecules 'dancing' in Fibronacci patterns. *At bremse resistensudvikling ved hjælp af molekyler der 'danser' i Fibonacci mønstre.*	Stephen J. Fey (GB/DK)
Presentation of a new paradigm to solve resistance problems including MRSA/TB. *Præsentation af et nyt paradigme til at løse mikrobielle resistensproblemer, herunder MRSA og XMDR TB.*	Jette E. Kristiansen (DK)
Debate/Debat	

PRESENTATIONS



Resistens mellem faglighed og politik

Flemming Møller

Født 1950

Nakskov Landevej 70, 4970 Rødby e-mail: f@nl70.dk

Gift med dyrlæge Susanne Møller

Børn: Karen (1978), Søren (1980), Anders (1989)

1980 Dyrlæge

1984 Fagdyrlæge vedr. svin

1987 – 2016: Medejer Maribo Dyrehospital

2008 – 2011: Medlem af Folketinget for Venstre

2009 – 2011: EU ordfører bl.a. medlem af sundhedsudvalget og fødevareudvalget

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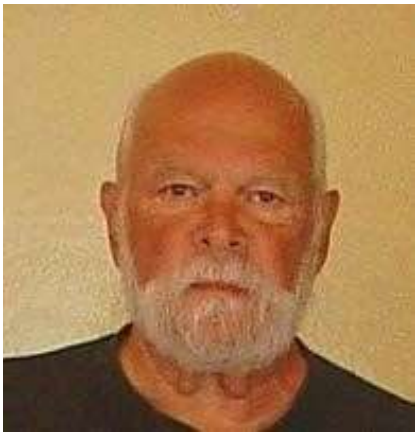
Historisk har Danmark haft en særstatus som et land med meget begrænsede resistensproblemer. Dette gælder både det veterinære og det humane område. Det skyldes, at vi har bygget på et sagligt, fagligt fundament.
Denne særstatus er dog gradvis blevet truet på grund af tættere forbindelser med andre lande. Det har medført en stigende forekomst af antibiotikaresistens i Danmark, der igen har affødt en helt forståelig bekymring, som er kommet til udtryk i den offentlige debat og medført et vedholdende krav om politisk handlekraft. Da de saglige, faglige argumenter kun undtagelsesvis er kommet til udtryk i debatten, har kravene til politikerne i høj grad været meget specifikke holdningsprægede krav. Et eksempel på dette er det meget markante krav om nedsættelse af antibiotikaforbruget i husdyrproduktionen.
Dette krav er i flere omgange blevet tilgodeset gennem begrænsninger af medicinanvendelsen i landbruget. Men fra et sagligt, fagligt perspektiv er der intet der tyder på, at disse ændringer på det veterinære område vil have mærkbar betydning for den resistensudvikling, der har betydning for patienterne i humansektoren.

En af problemstillingerne i dagens emne, hvor vi får klarlagt en række sammenhænge mellem psykofarmaka og antibiotikaresistens, er at få denne viden anvendt, så den kommer patienterne til gode. Interessen hos medicinalindustrien for resistensblokerende midler har ikke været overvældende. Det kan formentlig skyldes, at antibiotikaproduktion generelt ikke er en særlig lukrativ forretning, sammenlignet med behandling af livsstilssygdomme, fordi omsætningen pr. patient er ganske lille. Og derfor bliver interessen for behandling af antibiotikaresistens, som er et endnu mindre marked, naturligt endnu mindre.
Et påtrængende spørgsmål er derfor, om vi skal afvente, at resistensproblemet vokser sig så stort, at produktion af resistensblokerende midler bliver forretningsmæssig rentabelt, eller man politisk skal finde andre løsninger, så denne viden kan komme folkesundheden og dermed alle til gode.

Investigations and treatment of multidrugresistant (XMDR) TB with Thioridazine in vitro and in vivo.

Undersøgelser og behandling af multiresistent Mycobacterium tuberculosis med Thioridazine.

Leonard Amaral, M.D., Ph.D.



Professor Emeritus of the Institute Of Hygiene and Tropical Medicine of Lisbon, Universidade Nova de Lisboa, is a certified clinical pathologist who for the last 20 years has worked and conducted his research in Europe. Despite formal retirement, he continues his research activities at his former institution as an invited distinguished professor and also enjoys a similar appointment at the Institute of Medical Microbiology and Immunobiology and the Institute of Pharmacology of the University of Szeged, Szeged, Hungary.

AREAS OF CURRENT MAIN CONTRIBUTIONS:
Development of therapy by which the resistance of MDR/XDR Mtb is by-passed and the non-killing macrophage is transformed into a killer of MDR/XDR Mtb.
Therapy of MDR/XDR TB with an inexpensive drug that is beyond patent protection, has no serious toxicity and has been now shown to cure XDR TB.
Development of new methods for the characterisation, evaluation and assessment of efflux pumps that render bacteria and cancer cells resistant to therapy.
Demonstration of biophysical/biochem mechanisms by which efflux pumps render bacteria multi-drug resistant.
Development of new theories for therapy of cancer based upon the 2nd law of thermodynamics.
Development of a new chemistry system based upon the use of lasers for modification of bioactive compounds.

PUBLICATION RECORD: over 300 scientific articles in Peer Review International Journals:
Publications in Bacteriology, Immunology, Hematology, Clinical Pathology, Chemical Pathology, Endocrinology, Cancer, Human Embryology, Methods for Clinical Laboratories. Currently, serves in 14 Editorial Boards of International Journals in Pharmacology, Microbiology and Cancer.

RESEARCH ACTIVITY:
Development of drugs that are active (kill) against intracellular MDRTB and XDRTB.
Development of methods that assess and evaluate efflux pump activity of MDR bacteria.
Mechanisms by which efflux pumps are genetically controlled and regulated.
Development of agents that inhibit and or regulate efflux pumps.
Control of permeability of MDR bacteria to antibiotics.
Development of drugs that inhibit ABC transporters of mdr cancer cells.
Collaboration with 38 European Scientists from 33 countries via the Cost Action Programmes of the Eur Comm/Eur Sci FND-Cost Action B16 and BM0701 (ATENS).

Research supported by the Foundation of Science and Technology of Portugal
Workshops supported by the European Science Foundation
Interactive and cooperative projects supported by treaties between Portugal and participating EU countries
Leader in clinical trials for therapy of MDR/XDR TB infections.

This presentation is a review that covers 3 decades of research and presents the evidence that supports the use of thioridazine (TZ) for the therapy of a pulmonary tuberculosis infection regardless of its antibiotic resistance status. The evidence consists of *in vitro* and *ex vivo* assays that demonstrate the activity of TZ against all encountered *Mycobacterium tuberculosis* (Mtb) regardless of its antibiotic resistance phenotype, *in vivo* evidence that consists of successful therapies of the mouse infected with multi-drug resistant strains of Mtb and successful therapies of human subjects infected with extensively drug resistant (XDR) Mtb. The mechanisms of action by which TZ brings about successful therapeutic outcomes are presented in detail. The proposed use of TZ as an adjuvant has been named by the World Health Organisation as one of 5 best drugs for therapy of problematic antibiotic resistant TB infections such as extensively drug resistant XDR TB. Moreover, because the mechanism of action by which TZ enhances the killing activity of non-killing macrophages involves the activation of the hydrolytic system of the phagolysosome which kills the intracellular pathogen, the antibiotic resistance phenotype of the pathogen is irrelevant and does not affect the killing effectiveness. The activation of the killing machinery by TZ creates a new concept for therapy of intracellular bacterial infections that survive within their phagolysosomal prisons and are in general beyond access to conventional antibiotics.

Presentation: *See presentation*

See also link: http://memphys.dk/amaral-video

The historical approach to antibiotics, resistance, and nonantibiotics.

Prof. Dr. rer nat Bernd Wiedemann

11th July 1939	Born in Plön/Germany
1959 – 1966	Training in natural sciences, medical microbiology and hygiene at the Universities Tübingen, Karlsruhe and Kiel
1966	PhD, University Kiel
1966– 1967	Research assistent at Hygiene-Institut, Kiel
1967– 1972	Research assistent at Hygiene-Institut, Frankfurt/M.
1970	Reader for medical microbiology, University Frankfurt
1972	Professor of medical microbiology, University Frankfurt
1972 – 1973	Research Fellow at the Medical School, Dept. of Bacteriology, Bristol with Prof. Richmond
1974 - 2004	Head of Pharmaceutical Microbiology, University Bonn
1976 –2000	Chairman of „Ausschuß Mikrobiologie“ of the German Pharmacopoeae
1976 – 2000	Member of the German Pharmacopoeae commission since 1995
	Chairman of the committee Medical Microbiology and Immunology in
	DIN-Standards Medicine
Since 1976	Member of the DIN committee “Sensitivity Test of Antibiotics” 1988 – 1992 President of the "Paul-Ehrlich-Society for Chemotherapy"
1999 - 2005	Chairman of the GENARS-project of the Paul-Ehrlich-Gesellschaft für Chemotherapie (PEG), der Deutschen Gesellschaft für Hygiene und Mikrobiologie (DGHM) und der Deutschen Gesellschaft für Infektiologie (DGI)
1993 – 2003	Member of EUCAST steering committee
2003 - 2009	Member of EUCAST General commettee
July 2004	retired
December	Recept of the Garrod Medal
2004	Honorary member of the British Society ot Antimicrobial Chemotherapy
Since 2004	Consultant in the field of Resistance of bacteria to antibiotics, specifically ß-lactamaseinduction, quinolone resistance (epidemiology, pharmacodynamics, molecular biology). total of 300 papers published
Since 2012	Member of the NAK (National Antibiotic Testing Committee)

Early last century, Paul Ehrlich was the first scientist to study the development of resistance in microbes towards antimicrobial drugs in detail. In addition, he was the first to realise that antimicrobial drugs need to bind to a receptor to achieve activity. Following this idea he looked for “Zauberkugeln”, “magic bullets”, which selectively hit the parasite without damaging the host organism. He found Salvarsan as the first effective chemotherapeutic drug for the treatment of Syphilis. Until today these considerations established the modern understanding of antimictobial activity and resistance.

However, Paul Ehrlich did not know about plasmids, transposons, and integrons, those genetic elements, which enable bacteria to transfer resistance from cell to cell, and to form the basis of multi resistance. Due to these genetic elements and many different biochemical mechanisms of resistance we have to manage multi resistant mycobacteria or outbreaks of multi resistant Pseudomonas, Enterobacteriaceae, or Staphylococci species in hospitals. With today’s methods and techniques, we are able to follow the emergence of resistance in “statu nascendi”, what would enable us to kill resistant bacteria before they are able to spread. However, we do not have the resources to do it in the clinical setting.

Let us remember Paul Ehrlichs words: learn to aim chemically, find magic bullets with selective toxicity, and aim to “therapia magna sterilisans”. With Methylenblue Paul Ehrlich did not only use a dye, he also realised this as a neurotropic drug, which in addition showed antimicrobial activity. J. Kristiansen 1990 pointed out this context and followed this concept to nowadays strategy of the use of nonantibiotics to reverse resistance.

Presentation: *See presentation*

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tranScrip

WHY ARE NON-ANTIBIOTICS SO IMPORTANT IN THE MANAGEMENT OF INFECTIOUS DISEASES?

DR RICHARD BAX

TranScrip Partners, Senior Advisor Helperby Therapeutics

November 2016

Richard trained in medicine in London and after seven years in clinical medicine joined Glaxo Research in 1977. Since then, he has worked in various senior positions in the pharmaceutical industry and was Vice President for Global AntiInfective Clinical Research for SmithKline Beecham from 1991 to 1999. Richard led the team that developed Augmentin BD and Famciclovir / Penciclovir.

Richard was Chief Scientist from 2000 to 2003 at Biosyn Inc., a HIV company based in Philadelphia. Richard became Vice President of Chiron Biopharma in Europe in January 2004 until the Novartis take over in July 2006 where Richard led the development of daptomycin resulting in European registration in November 2005.

Richard was Vice President of ViroPharma Europe from 2007 to 2009 and led the development of maribavir in Europe.

Richard is now a Senior Partner of TranScrip based near London and works with small, medium and large companies and academics on drug development.

Richard has sat on the advisory boards of a multitude of antibiotic companies. Richard has been a non-executive Director of 4 companies.

Richard has held various academic and clinical roles. He was honorary Registrar at Northwick Park Hospital, Senior Lecturer and Honorary Clinical Assistant in the Urinary Tract Infection Clinic at the Royal Free Hospital and currently is a visiting Senior Research Fellow of Kings College London.

He has served on advisory boards of the European Union, WHO, IFPMA, EFPIA, ESCMID, and the BSAC and was an advisor to the Office of Aids (NIH) in 2003.
Richard served on the committee of the ECMID Study Group for Clostridium difficile (2010 – 2016). Richard was a founder member of the Faculty of Pharmaceutical Medicine in London and is a Fellow of the Royal Colleges of Physicians of London and Edinburgh.

Richard has over 110 publications in peer reviewed journals, 9 book chapters and he has lectured on antibiotic prescribing use, drug development, phase I, II, III and IV studies and translational medicine in Europe, America, Asia and Africa.

In 2000 Bax, Mullan and Verhoef wrote, “In the next 10 years we will witness the development of completely new antibiotics”. In 2007 Levy wrote, “To restore efficacy to earlier antibiotics and to maintain the success of new antibiotics, we need to use antibiotics in a way which assures an ecological balance that favours the predominance of susceptible bacterial flora”.

The current antibiotic pipeline consists of 33 compounds in development Phase 1 and beyond. Eighteen are aimed at MDR Gram negative bacteria of which 6 are in Phase 1, 6 are in Phase 2 and 6 are in Phase 3. All but one are from known classes of antibiotics! The present antibiotic pipeline is precarious, with gaps in the spectrum for carbapenem resistant bacteria.

Alternatives to antibiotics are defined as non -compound approaches that is products other than classical antibiotics that target bacteria or approaches that target the host. These include probiotics, phage, vaccines, host defence, innate defence, peptides, immunodulation, immune suppression and others. The CARB-X initiative set up this year by NIH, BARDA, The Wellcome Trust and others is proposing a fund of over $6 billion over 14 years which is expecting around 5 new entries of which 2 are truly novel.

These are conservative predictions but it is clear that the future antibiotic portfolio will not be able to manage the predicted increases in antimicrobial resistance! That is why it is important to progress as soon

as possible increased investment across a range of opportunities in order to support the R&D and the availability of non-antibiotics with the potential to in part also to reduce the increase in resistance to standard antibiotics

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Presentation: *See presentation*

Antidepressive midler – Et våben i kampen mod antibiotika resistente bakterier?

Rikke Heidemann Olsen

Adjunkt ved Institut for Veterinær Sygdomsbiologi, Københavns Universitet

Personal Born 1982

data: William Boothsvej 19, 2650 Hvidovre E-mail: cava@sund.ku.dk; Phone: 20729044

Married to Martin Olsen (CEO, Fysiozone)

Children: Albert (2008), Anna (2013)

Key research areas:

- **Opportunistic bacterial *pathogens (human and animal)***
- ***Bacterial zoonosis***
- ***Antimicrobial resistance***
- ***Bacterial and drugs interactions***
- ***Food safety***

Education:

2008	Cand.med.vet
2012	Ph.D
2014	Higher educational training (”adjunkt pædagogikum”)

Occupational experience:

2002-2005	Student assistent at Dyrlægeklinikken V/Liselotte Aarsø
2003-2007	Student assistant at the cancer research company TopoTarget
2007-2008	Scientific assistant at Professor Magne Bisgaard’s group
2008-2012	PhD Student, Department of Veterinary Disease Biology
2013-2016	Assistant professor in Preventive Veterinary Microbiology

Maternity leaves from Dec. 2008- aug. 2009 + Dec.2012- nov.2013) ***Position of trust:***

2003-2004	Student representative at the Institute for Basal Animal Science
2004-2006	Student representative at the Institute for Disease
2011 -	Appointed member of Young Investigators Network (YIN) 2016 Head of working group for "Non-antibiotics"

Grants

2015	Dkr. **2.7 mio**	DFF Post doc grant " CURE – curing of plasmids as a novel line of attack".
2015	Dkr. **500.000**	Poultry Levy Board (shared with DTU) " Highly Pathogenic E.coli"
2015	Dkr. **15.000**	Houghton trust travel and educational grant
2015	Dkr. **490.000**	Poultry Levy Board (shared with DTU) " Persistence of E. coli in broiler production"

Supervision:

BSc	17 students (all completed). Main supervisor
MSc	1 student (completed), co-supervisor
PhD	2 student (2014 -), co-supervisor

Publications (obs surname was "Gregersen" before 2012, hereafter "Olsen"):

Peer-review	19 (hereof 14 as first author)
Journalistic	4
Book contributions	1

Conference contributions

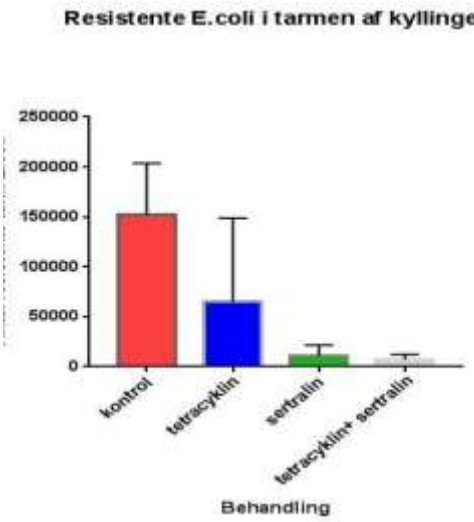
Oral presentations	21 (hereof 17 as presenting author, 2 as invited key-notes speaker
Posters	3

Most recent:

16. Olsen,R.H., Thøfner, I., Pors, S., Christensen, H., Bisgaard, M., Christensen, JP. Draft Genome Sequences of Three *Escherichia coli* Strains with Different *In Vivo* Pathogenicities in an Avian (Ascending) Infection Model of the Oviduct Genome Announc. 2015 May-Jun; 3(3): e00399-15.
17. Dolka B, Boyen F Butaye P, Heidemann Olsen R, Naundrup Thøfner IC, Christensen JP. Draft Genome Sequences of Two Commensal Enterococcus cecorum Strains Isolated from Chickens in Belgium. Genome Announc. 2015 Sep 24;3(5). pii: e01108-15. doi: 10.1128/genomeA.01108-15.
18. Dolka B , Boyen F, Butaye P, Heidemann Olsen R, Naundrup Thøfner IC, Christensen JP. Draft Genome Sequences of Two Commensal Enterococcus cecorum Strains Isolated from Chickens in Belgium. Genome Announc. 2015 Sep 24;3(5). pii: e01108-15. doi: 10.1128/genomeA.01108-15.
19. Journal of Food Protection "Antimicrobial Resistance and Resistance Genes in Aerobic Bacteria Isolated from Pork at Slaughterhouse" by Lili Li, Rikke 028X.JFP-15-455. Li L, Olsen RH, Ye L, Wang W, Shi L, Yan H, Meng H.Olsen, Lei Ye, He Yan, Qing Nie, Lei Shi, and Hecheng Meng. J Food Prot. 2016 Apr;79(4):589-97. doi: 10.4315/0362-

Opdagelsen af penicillinet har været en af den medicinske histories største succeser for den human og veterinære sundhed. Penicillinets "opdager" Alexander Flemming advarede dog allerede den gang om bakteriers evne til at blive modstandsdygtige overfor antibiotika ved lang tids eksponering. Denne sandhed er i det sidste årti blevet mere og mere klart, eftersom forekomsten af multi-resistente bakterier (bakterier, modstandsdygtige overfor mange forskellige slags typer af antibiotika) er steget dramatisk inden for både den human og veterinær medicin. Desværre har udvikling af nye typer af antibiotika langt fra kunnet følge med behovet herfor. Derfor er der kommet fornyet interesse i de såkaldte "non-antibiotika", dvs. lægemidler, der bruges mod ikke-infektiøse sygdomme, men samtidig besidder egenskaber, der påvirker bakterier. I 2015 blev af det frie forskningsråd bevilliget omkring 3 millioner til

forskning i disse såkaldte ”non-antibiotika”. Vores indledende resultater viser at Sertraline, et antidepressivt lægemiddel, atter gøre antibiotika resistente *Esherichia coli* (*E. coli*) bakterier modtagelige overfor det vigtige antibiotikum tetracycline. Sertraline påvirker især bakteriens energi omsætning, så den vokser langt dårligere, og samtidig hæmmer Sertraline de såkaldte "efflux-pumper" som de antibiotika resistente bakterier anvender til at pumpe antibiotika ud af bakteriecellen. Den allernyeste forskning (endnu upubliceret) viser at denne antibiotika-egenskab af Sertraline er bibeholdt under behandling af kyllinger, inficeret med en antibiotika resistent *E. coli*.



In English

The discovery of penicillin has been one of the greatest successes for human and veterinary health. The "father" of penicillin antibiotics,
Alexander Flemming concurrent with the discovery of antibiotics, came with the warning that prolonged exposure of bacteria to
antibiotics could create an antibiotic-resistant phenotype. This statement has unfortunately become more and more evident, as the prevalence of multiresistant bacteria (bacteria, resistant to a number of different classes of antibiotics) has increased dramatically in the last two decades. The development of novel classes of antibiotics has seriously fallen behind the need for them. As a consequence, there has arisen an interest in “non-antibiotics”. These are medical compounds, which are used to treat non-infectious conditions, but which can also sensitise bacteria to antibiotics. In 2015, the council of independent research granted 3 million Kroner to a research project regarding non-antibiotics.
Our preliminary results show that Sertraline, an anti-depressive drug, can reverse antimicrobial resistance in *Escherichia coli (E. coli),* making it possible to treat these clinically important bacteria with tetracycline antibiotics again. Sertraline affects the energy metabolism of E. coli so that they grow slower. It also inhibits the efflux pumps which antibiotic resistant bacteria use to pump antibiotics out of the bacterial cell. Our most recent research shows that the antibiotic-like properties of Sertraline also can be documented in animals experimentally infected with antibiotic resistant *E. coli*.

Powerpoint: Rikke Heidemann Olsens præsentation kommer her på et senere tidspunkt

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Breaking resistance development using molecules ‘dancing’ in Fibronacci patterns

At bremse resistensudvikling ved hjælp af molekyler der ‘danser’ i Fibonacci mønstre

Stephen J. Fey[1], Himanshu Khandelia[2] and Jette E. Kristiansen[2]

CURRICULUM VITAE

Name	***Position Title***	***Birth date***	
STEPHEN JOHN FEY	*ASSOCIATE PROFESSOR* **tenured permanent position**	***23.10.1953***	**Non-**

CEO CelVivo IVS

Personal data

Home: Middelfartvej 469, DK-5491 Blommenslyst. Married, with two grown up children, Jennifer and Adrian

Scientific Education

King's College, London University, Department of Biophysics, BSc, Cell and Molecular Biology	1975
King's College, London University, PhD, Biophysics	1980
Technical University of Danmark, Radioisotope Techniques (Competence-giving diploma)	2001

Business and Leadership Education

Change-Track: Goal-oriented leadership for top management (Karl Barslev)	2008
Lean Leadership using the RACI matrix in a business environment (Maja Wiberg)	2010
Managing Projects in a Controlled Environment (Prince2™): Foundation and Practitioner Certified	2010

Employment

Biostructural Chemistry Division, Chemistry Institute, Aarhus University	1980-84
Institute of Medical Microbiology & Institute of Human Genetics, Aarhus University(Group Leader)	1984-96
Centre for Proteome Analysis, International Science Park Odense, University of Southern Denmark (SDU), Odense (Founder and Associate professorship)	1996-06
DrugMode A/S (Founding Scientist and CTO)	2006-07
DrugMode A/S (CEO) responsible for a yearly budget of ca. DKK 25 million	2007-11
Department of Biochemistry and Molecular Biology, SDU (Associate professorship)	2011-to date
Cofounder and CEO of CelVivo IVS cvr 35671099	2014-to date

Honorary Professorship

Third Military Medical University and West China Hospital, Chongqing, People's Republic of China (Professor in Medical Proteomics)	2003

Teaching

Supervisor, co-supervisor or mentor for 6 bachelor, 8 MSc and 9 PhD students

Examiner for 7 Ph.D. candidates (National and International)

Lecturer at SDU in courses: (currently FF501/NAT 507, BMB 206 BMB 504 and NAT 806)

Hundreds of lectures in Local, National and International Fora

Proteins for Diagnosis, Beyond 2000, International TV Series	1991

Lecture tours

Invited speaker in 3 lecture tours or chains of symposia (all sponsored by Amersham Pharmacia Biotech) European

Proteome Project Tour (Copenhagen, Stockholm, Köln, Hamburg, Paris, London, Madrid	1997
European Proteome Project Tour (Stockholm, London, Berlin, Cologne, Paris and Madrid	1999
“50 Years of DNA” (Co-sponsored by the the Ministery of Science, Technology and Medicine India: New Delhi, Pune, Bangalore, Hyderabad, Chenni and Calcutta)	2003

Focus areas

Proteomics, 3D cell culture, diabetes (diagnosis and treatment), toxicology, human cellular physiology, plant medicines, equipment design, commercialisation, collaboration with industry.

International Projects (examples)

Project leader, Co-ordinator or Prime Contractor for:-

"Experimental pilot study for a European cooperation in gene function search in Saccharomyces cerevisiae", EEC contract under the BRIDGE program (DKK 5.6m)	
"Proteome Analysis Group in Europe: Saccharomyces cerevisiae (PAGES)",	1993-96
EU contract under the Biotechnology Program (DKK 31m)	1997-00
"Center for Experimental BioInformatics (CEBI)" Danish National Research Foundation (DKK 34m)	1998-03
"The Danish Biotechnology Instrument Centre: Proteome Analysis (DABIC)", (DKK 12.4m)	2000-04
"Genomics and Proteomics - New Methods in Pollution Research (GENIPOL)", EU contract under the 5th Frame Program (DKK 17m)	2001-05
NATO International Summer School (co-organsier), Chengdu, China	2003
Early Diagnosis and Treatment of Diabetes (MC2 Biotek) (DKK 250m)	2004 - to date
“Liver functionality of DrugMode’s ProtoTissue™ during a 21 day period” (Roche)	2009
“PPAR agonist in vitro study using ProtoTissue™ (Roche)	2009
“Early Markers for Diabetes Identification of markers in human subjects” (Medical Research Council of South Africa) (DKK 0.865m)	2012-14
“Investigating the lipo-protective effect of PPAG on insulin producing beta cells” MC2 Therapeutics	2016-17

International Network

Collaboration with numerous research groups in academia and industry in South Africa, China, UK, Belgium, Italy, Switzerland, Japan, South Korea and USA.

Entrusted Activities

Expert Study required by the EEC Commission: "2DGE and the yeast genome project"	1991-92
International reviewer for the Major National Research Facilities Program, Australia	1995
External evaluator for a PhD degree at Macquarie University, Australia (Marc Wilkins)	1995
External evaluator for 2 PhD degrees at Sydney University, Australia (S. Cordwell & V.Wasinger)	1996 & 99
External expert for the EC Commission “Health and infectious diseases”	2004 &07
Member of the SDU delegation visiting the Fraunhofer Gesellschaft in Munich	2004
Member of TCM Denmark and the Fyn Region Delegation to visit P.R. China	
Participant in “Future Needs for Research Infrastructures in BioMedical Sciences” organised by the EC Commission	2004
External evaluator for a PhD degree at Nelson Mandela Metropolitan University,	2005
Port Elizabeth, South Africa (Wayne Chadwick)	2006
External expert for the EC Commission “Innovative Medicines Initiative”	2008 & 09
External reviewer for National Research Foundation, South Africa	2011-2012
External expert for the EC Commission “Health 2013”	
External evaluator for a PhD degree at University of Zululand, KwaDlangezwa,	2012
South Africa (Sithandiwe E. Mazibuko)	2014
Senior scientific advisor to MC2Biotek	2006–to date
Member of EU Cost action 1407 (Chemistry of Natural Products)	2014–to date

Honour

Associateship of King's College Londin, UK (AKC)	1975
Hafnia-Haand i Haand Foundation's Award for Outstanding Research (DKK 165,000)	1985
Pedersholm Prize: Contribution to International Cancer Research (DKK 100,000)	1988
Top-Danmark Prize: To Establish a Pilot Laboratory for New Diagnostic Methods (DKK 500,000)	1990

Fyens Stiftstidende's Research Prize 2000 (DKK 50,000)	2000
EU Robotics Entrepreneurship – First Prize	2012

Peer Reviewer

Reviewed manuscripts for: Journal of Proteomics, Journal of Molecular Biology, Expert opinions on Drug Discovery, Toxicology Research, Electrophoresis, Journal of Biological Engineering, Journal of Physiology and Biochemistry, Plant, Bioinformatics, Biomaterials & Yeast.

Funding

SJF has raised more than DKK 175 million from Research Councils, Private Institututions, Investors and companies as his groups share of funding to support his research.

Publications and Patents

SJF has 115 scientific publications in peer reviewed journals. One more is in press. He is inventor in 34 patent families (which has given rise to 102 published documents). Most patents have been used either to start companies (PicoSep, DrugMode & CelVivo) or sold to existing companies (MC2 Therapeutics, Nordic Marine).

Bibliometry

h-index: 35 and 3,455 citations calculated at the Web of Science (https://apps.webofknowledge.com/) ORCID ID: 0000-0001-6463-9477

TCEL, Department of Biochemistry and Molecular Biology and MEMPHYS, Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, Odense, Denmark. sjf@bmb.sdu.dk

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Presentation: *See presentation*

Video: *See video*

Himanshu Khandelia

MEMPHYS, Center for Biomembrane Physics
University of Southern Denmark (SDU)
Campusvej 55, 5230 Odense M, Denmark

DATE OF BIRTH 28-12-1977

CURRENT POSITION Associate Professor, University of Southern Denmark

EDUCATION

Ph.D., Chemical Engineering, 2001-2006 (GPA:3.77/4.0) University of Minnesota, Minneapolis.
Advisor: Dr.Yiannis N. Kaznessis **Thesis:** Computer Simulations of Antimicrobial Peptides

5-year Integrated M.Tech., Biochemical Engineering and Biotechnology
19962001(GPA:8.94/10.0),
Indian Institute of Technology (IIT),New Delhi (Class Rank:1)

SCIENTIFIC CAREER AND POSITIONS

2006-2009: Postdoc, MEMPHYS, Center for Biomembrane Physics, University of Southern Denmark(SDU) w.Ole G Mouritsen
2009-2010: Research Assistant Professor (SDU)
2010-2012: Assistant Professor (SDU)
2013-current: Associate Professor (SDU)

AWARDS AND EXTERNAL FUNDING

DENMARK:
2011 Lundbeckfonden Young Group Leader award for DKK 10 million (~ Euro 1.35 million)
2014 Novo Nordisk postdoctoral grant
2011-2016 Danish e-Infrastructure Cooperation (DeIC) computing grants. 2014---2015 International Network Programe (INP) grant with RIKEN, Japan

EUROPE (FP7):
Associated partner on the FP7 EUROMEMBRANES network: "OXPL" (2010---2012).
FP7 PRACE computing grants amounting to ~ 10 million core hours.

INTERNATIONAL:
2010: Samsung Korea awarded $100,000 for work on Biomimetic Membranes in 2010.
Director's Doctoral Fellowship at the University of Minnesota in 2005, awarded to the top 5% PHD students.

SHORT RESUME OF SCIENTIFIC INTEREST

We employ and develop computational methods fundamental molecular scale biomolecular phenomena, with specific focus on simulations of membranes, and membrane- associated biological processes, including

transport across membrane proteins and interaction of membranes with membrane-active molecules.
Some key research areas are the mechanisms of ion selectivity in ion pumps, the biogenesis of lipid droplets, and development of new methods to simulate proton transport in proteins. Much of my research is done in close collaboration with experimental groups.

PROJECT MANAGEMENT and MANAGERIAL EXPERIENCE

Besides smaller postdoctoral projects, I am currently managing one large DKK 10 million project. I have also managed the large FP7 PRACE grant with two international partners. I have completed a 2-day Project Management course at SDU, and plan to attend the advanced course next year.

SELECTED RESEARCH ACHIEVEMENTS

Method Development: We implemented algorithms that accelerate biomolecular simulations by a factor of two (10.1021/ct500100f). We developed accurate methods to calculate mechanical properties of lipid membranes (10.1063/1.4826462). We are currently working on methods to improve the stress and pressure calculations in simulations, and to simulate proton transport efficiently.

Ion Pumps: Our simulations combined with electrophysiology discovered a new ion pathway in the Na+ K+ ATPase, which has the potential to change textbook definitions on transport cycle (10.1038/nature09309). We have made novel insights into the molecular mechanisms of diseases causing mutations in (10.1021/bi40142g)and regulation (10.1074/jbc.M112.340406) of ion pumps.

Lipid Droplets: Our large-scale simulations explained how a large amount of oil is accommodated in cancer cell membranes and for the first time, showed how lipid droplets can be formed in the Endoplasmic Reticulum membrane (10.1371/journal.pone.0012811).

Radioactive Soil Bioremediation: In collaboration with plant biologists in Japan, we have developed compounds that help remove radioactive Cesium from soil after the Fukushima disaster (10.1038/srep08842).

Oxidized Phospholipids: We were the first to demonstrate the reorientation of lipid tails in oxidized lipids (10.1016/j.bpj.2009.01.007) and the possibility of lipid oxidation driven phase separation in biomembranes, in collaboration with biophysicists in Prague (10.1039/C3SM52310A).

EDITORIAL CONTRIBUTIONS

Editor, Nature Scientific Reports. Referee for several journals for the Nature Group, ACS, RSC, EMBO and Elsevier Journals.

SUPERVISION AND ACADEMIC TEACHING

One PhD and two Master students have graduated under my supervision. I am currently supervising two otherPhD students. I have supervis ed 4 postdocs, and am currently supervising 2 more.
I have designed and developed a new Masters/PhD level course in Biomolecular Simulations (KE824). The course is aligned with SDU's policy of encouraging research in the computational sciences. The course has been offered three times and has received positive feedback. I have completed the "Pegadogicum" training on academic teaching. I also teach Physical Chemistry to second year Bachelor's students.

POSITIONS OF TRUST

Member, e-Science Board at SDU.
Referee for funding organizations in France, Netherlands and FP7 PRACE. Referee for ESF scientific proposals

Gaven ingen vil pakke op/The gift no one will open

Jette E. Kristiansen; M.D., D.Sc.

Senior Consultant and Researcher: Specialist in Clinical Microbiology

Address Sundgade 54, 6320 Egernsund;

Mai: malthe@dadlnet.dk, Jette-e-k@mail.dk

Born 19th September 1943 in Aarhus, Denmark

Academic qualifications

2006-to date Senior Researcher at Memphys, Southern Danish University in Odense, Denmark
Memphys · Campusvej 55 · DK-5230 Odense M · Tel. +45 6550 3506 · www.sdu.dk **2004-2007**
Clinical associated professor KMA, OUH, SDU, Odense.

2006 Educated in special infections in elder patients at University of Harvard, Boston USA.

1999 Educated and examined in Tropical and Travel medicine at Bernard Nocht Institute in Hamburg, Germany.

1996 Educated in Hygiene and Epidemiology at the Bronx-Lebanon Hospital Center, Albert Einstein College of Medicine at the Departments of Professor Victor Lorian MD and the Laboratory Department of Prof. Leonard Amaral MD. (I have visited the Departments more times from 1988 - 1996).

1990 Dr. Science at University of Copenhagen (KU), Denmark with the thesis: "The Antimicrobial Activity of Psychotherapeutic Drugs and Stereo isomeric Analogues". (The highest academic recognition that can be obtained in Denmark)

1988 Scientific visit in the autumn 1988 at NIH, USA (HIV investigations with Phenothiazines and Thioxanthenes on HIV virus). Atlanta and Bronx-Lebanon Hospital Center.

1988-2013 Scientific visits (one to two times) each year to prof. Jóseph Molnár, Department of Medical Microbiology and Immunobiology, University of Szeged, Hungary.

1985 Specialist in Clinical Microbiology (MD). Educated at Staten's Serum Institute in Copenhagen, Denmark.

1977 Educated as Family Doctor (1971-1977).

Employment

1971-1994 Reservelæge (MD) and 1. Reservelæge at Roskilde Amtssygehus, Staten's Serums Institute, County of Copenhagen and County of Frederiksborg; Adjunct at the University of Copenhagen, Denmark

1994-2008 Consultant (Overlæge dr.med.) in Clinical Microbiology and responsible for education at the Clinical Microbiological Department at Sønderborg Hospital the County of Sønderjylland **2008 -2014**
From 2008 Chief for the International Vaccination Clinic, Aabenraa, Denmark.

Membership of International Societies etc.

1990-2016 Member of Paul Ehrlich Gesellschaft (PEG) and initiator to the working group"nonantibiotics" as a part of the PEG`s research area.

1990-2017 Initiator and General Secretary for "The International Society of Non-antibiotics" (ISN). **Google**: "ISN non-antibiotics".

1993-2010 Member of American Society of Microbiology (ASM) and SHEA

1995-2017 I am Representative for ISN in relation to "The International Society of Chemotherapy" (ISC). **1998-2017** Initiated and established "The International Non-antibiotic Research Group (INRG)" Denmark.

2006-2013 Member of the executive committee "Federation of European Societies for Chemotherapy and Infections" (FESCI).

2000-2012 Initiator and Danish representative (MC member) for the EU-projects COST B16 OG COST BM 0701"Atens". The COST-projects have in the scientific research areas "nonantibiotic","reversal of resistance" and"mikrobielle efflux pumpes". 40 international research institutions and universities have participated.

2015- Danish representative (MC) member for EU-project COST CM 1407

Publications and abstracts

I have published more than 120 articles and abstracts in internationally recognized journals. 83 of these can be found on PubMed. /more can be found on Google/"Kristiansen JE".
I have participated in countless conferences around the world from 1980, in particular via International Society of Chemotherapy and FESCI (the European Arm of ISC) and. I have initiated sessions and held lectures on my own subject: Antimicrobial activity of compounds not developed as antibiotics.
Since my research field was never included on an equal footing as antibiotics in any organisation, I have not continued my membership or continued to register my work since the mid 1990's but I have inspired established researchers I meet and young people to follow up in my research field.
Since then I have continued to develop my research area in my free-time and holidays and have been associated with Memphys SDU since 2005/2006 up to date.

Selected review-articles

Kristiansen JE.: Er Chlorpromazin og andre phenothiaziner også antibiotika? Ugeskr Læger. 1981, Jul 20; 143(30):1900-1904. Danish.

Kristiansen JE, Amaral L.: The potential management of resistant infections with non-antibiotics. J Antimicrob Chemother. 1997, Sep; 40 (3):319-27. Review. Free Article

Kristiansen JE, Hendricks O, Delvin T, Butterworth TS, Aagaard L, Christensen JB, Flores VC, Keyzer H.: Reversal of resistance in microorganisms by help of non-antibiotics. J Antimicrob Chemother. 2007, Jun; 59(6):1271-9. Epub 2007 Apr 2. Free article.

Keyzer H, Fey J. S, Thornton B, Kristiansen JE, 2015: Molar ratios of therapeutic water-soluble phenothiazine . waterinsoluble phospholipid adducts reveal a Fibonacci correlation and a putative link for structure-activity relationship. RSC Adv. 2015, 5, 20865-20877. (View Article Online).

Kristiansen JE, Dastidar SG, Palchoudhuri S, Roy DS, Das S, Hendricks O, Christensen JB. Phenothiazines as a solution for multidrug resistant tuberculosis: From the origin to present. Int Microbiol. 2015 Mar;18(1):1-12. doi: 10.2436/20.1501.01.229. Review. PMID: 26415662

Tortoli E, Richter E, Borroni E, Cabibbe AM, Capitolo E, Cittaro D, Engel R, Hendricks O, Hillemann D, Kristiansen JE, Mariottini A, Schubert S, Cirillo DM. Mycobacterium alsense sp. nov., a scotochromogenic slow grower isolated from clinical respiratory specimens. Int J Syst Evol Microbiol. 2016 Jan;66(1):450-6. doi: 10.1099/ijsem.0.000744. PMID: 26545358

Selected publications 2012:

Samantaa, A, Chattopadhyayb, D, Sinhaa, C, Janaa, AD, Chosha S, Banerjeea, AMA, Hendricks,O, Christensen, JB & Kristiansen, JE: 2012 "Evaluation of in vivo and in vitro Antimicrobial Activities of a Selective Serotonin Reuptake Inhibitor Sertraline Hydrochloride " Anti-infective Agents in Medical Chemistry, vol 10, 95-104.

Smarandache A, Kristiansen JE, Christensen, JB & Pascu, M-L: 2012 "Optical Studies of the Spectral Properties of Phenothiazines "Letters in Drug design & Discovery, vol 9, s.352-360.

Veje CT, Willatzen M, Hendricks, O, Pagés, J-M, Kristiansen, JE: 2012 "Populations Dynamics Approach for the Study of Synergetic Coupling between Antibiotic and Helper Compounds" Computational Molecular Bioscience, vol.2 No.1, 2012, pp 1-6. Doi:10.4236/cmb.2012.21001.

Wainwright M, Amaral L, Kristiansen JE: 2012 Review Article "The Evolution of Antimycobacterial Agents from Non - Antibiotics. " Open Journal of Pharmacology, 2012, 2-1. (Please look at the attached).

Publications in 2013:

Simons SO, Kristiansen JE, Hajos G, van der Laan T, Molnár J, Boeree MJ, van Ingen J, Christensen JB, Viveiros M, Riedl Z, Amaral L, van Soolingen D. Activity of the efflux pump inhibitor SILA 421 against drug-resistant tuberculosis. Int J. Antimicrob Agents. 2013, Feb 12. doi:pii: S09248579(13)00024-1.

Dastidar SD, Kristiansen JE, Molnar J and Amaral L: Role of Phenothiazines and Structurally Similar Compounds of Plant Origin in the Fight against Infections by Drug Resistant Bacteria. "Open Access" Antibiotics 2013,2, 58-71. ISSN 2079-6382.

Christensen JB, Hendricks O, Chaki S, Mukherjee S, Das A, Pal TK, Dastidar SG, Kristiansen JE. A comparative analysis of in vitro and in vivo efficacies of the Enatiomers Thioridazine and its racemate. Plos One 8(3): e57493. doi:10.1371/journal.pone.0057493

Prizes and accolades:

Essex Prize for Clinical Microbiology 1988: awarded for her exceptional contribution to clinical microbiology.

The Thorvald Madsen prize: Statens Serum Instituts prize for the most recognised researcher in 1990. Several

Scholarships to promote international research in Southern Jutland including the Nissen Foundation in Tønder and the County Hospital of Southern Jutland.

Special invited speaker at the Topic meeting in 2002 in London at the Commonwealth House: Research "The antimicrobial actions of non-antibiotics" in a perspective of the questions stated by Paul Ehrlich to the future!

Symposium: The 4. June 2012 at Memphys, SDU: Progress in Studies of Drug resistance. Arranged by Ole G. Mouritsen and Jette E. Kristiansen.

Symposium: The 19. September 2013 at Memphys, SDU: Progress in the Basic and Clinical studies (II). This symposium was a celebration of my 35 year scientific in the footstep of Paul Ehrlich and 70 years Birthday. Arranged by Ole G. Mourtisen.

Other activities

Part owner of NoaSic ApS

Patent applications: Enantiomers of thioridazine and derivatives thereof for reversing drug-resistance. DK PA 2003 01690 and WO 2005/046694

Jette Elisabeth Kristiansen
25. Januar 2017

I 1891 beskrev nobelprismodtageren Paul Ehrlich (1854-1915), at han sammen med kollegaen Paul Guttmann havde helbredt 2 patienter for malariainfektion. De havde for første gang i den medicinske historie anvendt et syntetisk lægemiddel "Methylenblåt". Beskrivelsen i tidskriftet afsluttes med et spørgsmål til fremtiden:

"Vil det være muligt at gøre malariaparasitten følsom igen, hvis den er blevet resistent over for kinin (et naturprodukt) ved at anvende "Methylenblåt".

Jeg har nu brugt 40 år af mit liv til netop at besvare dette spørgsmål stillet af Paul Ehrlich`s for så mange år siden. Mit svar er et rungende: Ja!!

Jeg har måttet udvide Paul Ehrlich's spørgsmål, og jeg har besvaret det ved at anvende de moderne syntetiske lægemidler, som anvendes som nervemedicin verden over, og hvor mange af disse lægemidler netop har den samme/beslægtede kemiske kerne, som findes i "Methylenblåt". Også disse nye syntetiske lægemidler kan anvendes til at gøre højresistente mikroorganismer følsomme for antibiotika igen. Jeg og

min forskergruppe har ligeledes påvist, at de bakterier, som særligt angriber vores nervesystem, også er de mest følsomme over for den nervemedicin, vi har undersøgt. En yderligere udvidelse blandt de kemiske forbindelser, vi anvender til at påvirke vores nervesystem, og som ikke er direkte beslægtede med den i Methylenblåts fundne kemiske struktur, kan på samme måde gøre højresistente mikroorganismer følsomme igen.
Jeg og min gruppe har nu i de senere år også vist, at vi kan rense den moderne nervemedicin op og derved slippe uden om virkningen/nedsætte virkningen på hjernen og alligevel bevare muligheden for at gøre højresistente mikroorganismer følsomme igen (såsom resistent TB, de resistente stafylokokker og vancomycinresistente enterokokker)
Yderligere er det således, at de moderne lægemidler, vi udvikler i disse år til at påvirke dyr og menneskers nervesystem, samtidig er antimikrobielle (kan dræbe bakterier, parasitter og vira). Denne synsvinkel (iagttagelsen af det mulige slægtskab mellem nerveceller og mikroorganismer), som jeg nu har beskæftiget mig med i mere end 40 år, har vist sig at være anvendelig til at løse mange af de resistensproblemer, vi frygter i dag. Det giver os samtidig en mulighed for, at vi ikke behøver at blive overhalet af mikroorganismerne, hvis vi forstår at anvende de kombinationer af lægemidler, som vores videnskabelige resultater påpeger med hensyn til at udvikle de nye antibiotika/ kemoterapeutika sammen med ”Helper compounds” også kaldet non antibiotika Det, jeg her beskriver, er ikke en trossag!! Det er naturvidenskab. Og de naturvidenskabelige metoder er anvendt i denne forskning.

”Kære Paul Ehrlich.
Ja, vi kan reversere resistens, således som De har bedt os om at besvare i Deres spørgsmål fra 1891. Med venlig hilsen og i taknemlighed for Deres helt fantastiske arbejde, som har flyttet så mange fastgroede synsvinkler og har hjulpet så mange mennesker, og alligevel er det næsten umuligt, her 100 år efter det stillede spørgsmål er besvaret, at få den generelle opinion interesseret i den af Dem allerede påpegede mulighed i 1891.

Jette Elisabeth Kristiansen.”
(Publiceret Fyens 24.11 2015)

Billede fra Åbnings Festen af Statens Serum Institut i 1902

Første store Serumfest.

Seruminstitutet blev i Thorvald Madsens 38-årige ansættelsestid ikke blot et internationalt uddannelsessted, men også fra starten et hus, hvor man gerne festede.

Ovenstående billede er taget allerede ved indvielsen af Seruminstitutet i 1902 i Thorvald Madsens privatbolig – det senere Wassermannlaboratorium.

Navnelisten viser, at Thorvald Madsen fra starten havde fortrinlige internationale forbindelser. Her er deltagerne med de ovennævnte numre: 1. Prof. ved Landbohøjskolen G. Sand. 2. Dr. Th. Madsen. 3. Dr. Julius Morgenroth. 4. Direktør O. Malm (Norge). 5. Prof. Johs. Bock. 6. Dr. Wm. Bulloch (London). 7a. Dr. G. Dean (London). 7. Prof. Paul Ehrlich. 8. Krigsminister V. H. O. Madsen. 9. Fru Ellen Salomonsen. 10. Prof. Carl Weigert (Frankfurt a. M.). 11. Prof. Axel Holst (Norge). 12. Prof. Johs. Fibiger. 13. Dr. Niels Muus. 14. Prof. Knud Faber. 15. Prof. C. O. Jensen. 16. Overlæge H. P. Lie (Bergen). 17. Prof. Vald. Henriques. 18. Overlæge Ustvedt (Norge). 19. Prof. Bernhard Bang. 20. Overlæge Armauer Hansen (Bergen). 21. Prof. Sims Woodhead (Cambridge). 22. Prof. Svante Arrhenius (Stockholm). 23. Dr. (senere Overlæge) Axel Jørgensen. 24. Dr. Edv. Selander (Stockholm). 25. Prof. C. J. Salomonsen. 26. Dr. (senere Overlæge) Fr. Vermehren. 27. Overlæge Aaser (Kristiania). 28. Dr. Vilh. Jensen. 29. Dr. (senere Overlæge) Fr. Vogelius. 30. Prof. J. Forssman (Lund). 31. Prof. Lassar (Berlin). – Seruminstitutets arkiv.

The close connections between Paul Ehrlich, Carl Julius Salomonsen and Thorvald Madsen and the National and International microbiologists can be seen in the above picture. Note that there was excellent collaboration between the microbiologists working in human and veterinary medicine. This close relationship is described in detail: Letters from the Nobel laureate Paul Ehrlich to the Director for the State see: **https://www.ncbi.nlm.nih.gov/pubmed/15685791** This can also be found in German at "Briefe des nobelpreisträgers Paul Ehrlich an Thorvald Madsen, direktor am dänischen staatlichen serum-instiut (Statens Serum Institut)"

Kristiansen J.E., Hendricks O. and Permin, H. 2007: Chemotherapie Journal. 5, 16, s. 143-151

Presentation: *See presentation*

Das Geschenk, das niemand auspacken will

Jette Elisabeth Kristiansen, Senior Wissenschaftler bei SDU, Dr. med. Spezialist in der klinischen Mikrobiologie.

Im Jahre 1891 beschrieb der Nobelpreisträger Paul Ehrlich (1854-1915), das er und seine Kollege Paul Guttmann zwei Patienten für Malariainfektion geheilt hatten. Sie hatten zum ersten Mal in der medizinischen Geschichte eine synthetische Droge "Methylenblau " verwendet. Die Beschreibung in der Zeitschrift endet mit einer Frage für die Zukunft:

"Wird es möglich sein, die Malaria-Parasiten mit " Methylenblau " wieder empfindlich zu machen, wenn sie von Chinin (ein Naturprodukt) resistent geworden sind?“

Ich habe jetzt 40 Jahre meines Lebens damit verbracht gerade diese Frage, die vor so vielen Jahren von Paul Ehrlich gestellt wurde, zu beantworten. Meine Antwort ist ein klares Ja !!

Ich hatte die Paul-Ehrlich-Frage zu erweitern, und ich beantwortete sie durch die Verwendung von moderne synthetische Drogen, die als Beruhigungsmittel überall in der Welt verwendet werden.

Viele dieser Medikamente haben den gleichen oder verwandten chemischen Kern, wie "Methylenblau".

Auch diese neuen synthetischen Drogen können, um hochresistente Mikroorganismen wieder empfindlich auf Antibiotika zu machen, verwendet werden.

Ich, und meine Forschungsgruppe, haben auch dokumentiert, dass die Bakterien, die speziell unser Nervensystem angreifen, auch auf die Nervenmedizin, die wir untersucht haben, am empfindlichsten sind.

Eine weitere Ergänzung der chemischen Verbindungen, die wir um unser
Nervensystem zu beeinflussen verwenden und nicht direkt mit der chemischen Struktur des Methylenblau ähnlich sind, können wieder hochresistente Mikroorganismen empfindlich machen.

Ich und meine Gruppe haben nun in den letzten Jahren auch gezeigt, dass wir die modernen Psychopharmaka chemisch reinigen können, und dadurch die Wirkungen auf das Gehirn vermeiden / reduzieren und dennoch die Fähigkeit behalten, hochresistente Mikroorganismen wieder empfindlich zu machen (sowie Tuberkulose, resistente Staphylokokken und Vancomycinresistente Enterokokken).

Außerdem können moderne Medikamente, die wir in diesen Jahren entwickeln um tierische und menschliche Nervensysteme zu beeinflussen, gleichzeitig eine antimikrobielle Wirkung haben (können Bakterien, Parasiten und Viren töten).

Aus dieser Sicht (Beobachtung der möglichen Beziehung zwischen Nervenzellen und Mikroorganismen), womit ich seit über 40 Jahren beteiligt bin, hat diese Lösung viele der Resistenzprobleme, die wir heute fürchten, sich als nützlich erwiesen. Es gibt uns auch eine Möglichkeit von den Mikroorganismen nicht überholt zu werden, wenn wir verstehen, wie wir die Kombinationen von Medikamenten zu verwenden haben, die unsere wissenschaftlichen Erkenntnisse im Hinblick auf die Entwicklung neuer Antibiotika / Chemotherapeutika zusammen mit "Helper Compounds" auch Non-Antibiotika genannt werden.

Was ich hier beschreibe, ist nicht eine Frage des Glaubens!! Es ist Naturwissenschaft. Und die wissenschaftlichen Methoden sind in dieser Studie verwendet.

"Lieber Paul Ehrlich.

Ja wir können Ihrer Frage von 1891, die Sie uns zu beantworten gebeten haben, mit einem Ja bestätigen. Der Resistenz können wir umlenken (reversieren)“.

Mit freundlichen Grüßen und in Dankbarkeit für Ihre ganz fantastische Arbeit, die so viele tief verwurzelte Standpunkte bewegt hat und so vielen Menschen geholfen hat. Hier, 100 Jahre nachdem die Frage beantwortet ist, ist es doch fast unmöglich die allgemeine Meinung an die Möglichkeit, die Sie schon in 1891 angegeben haben, interessiert zu machen.

Jette Elisabeth Kristiansen

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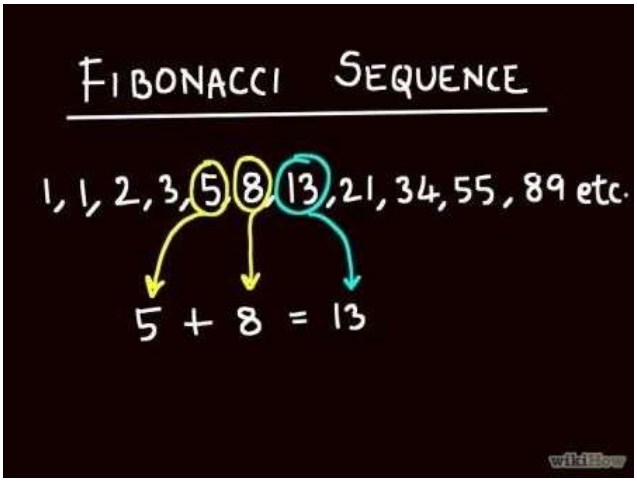
In 1891 the Nobel Prize winner Paul Ehrlich (1854-1915) described, that he and his colleague Paul Guttmann had cured two patients of a malaria infection. For the first time in the medical history, they had used a synthetic compound "Methylene Blue" as a pharmaceutical drug. The publication concluded with a question to the future:
"Will it be possible to make the malaria parasite sensitive again using Methylene Blue, if it has become resistant to quinine (a herbal drug)?"
I have now spent about 40 years of my life just to answer the question asked by Paul Ehrlich`s so many years ago.
My answer is a resounding: Yes!!
I had to extend the Paul Ehrlich's question and I have answered it by investigating modern synthetic drugs used all over the world as sedatives and/or psychopharmaceuticals. Many of these modern drugs also have the same or a related chemical core that exists in Methylene Blue. Unexpectedly these new synthetic drugs may be used to make highly resistant microorganisms sensitive to antibiotics again both *in vitro* and *in vivo*.
My research has also shown that the bacteria that specifically attack the nervous system in animals and humans, are the most sensitive to the nerve medicine, we have examined.
Exploration among the chemicals we use to affect our nervous system, and which are not directly chemically related to “Methylene Blue”, has revealed that they can equally well make highly resistant microorganisms sensitive again.
My group and I have in recent years also shown that we can purify modern tranquilizers and psychopharmaceuticals and thereby reduce their effect on the brain and yet retain the capacity to make highly resistant microorganisms sensitive to antimicrobials (including examples like TB- resistant staphylococci and vancomycin-resistant enterococci). These modern drugs are able to kill bacteria, parasites and viruses.
This point of view (the apparent ‘link’ between nerve cells and microorganisms), has guided my work for more than 40 years and it has proven to be useful for solving many of the resistance problems, we fear today. It has also provided us with the opportunity not to succumb to microorganisms. If we use the combinations of drugs that our scientific findings have demonstrated to be effective, in other words use antibiotics/chemotherapeutics together with "non-antibiotic” helper compounds, it is possible to reverse the development of resistance. What I am describing here, is not a matter of faith!! It is science. Scientific methods have been used throughout in our research.

"Dear Paul Ehrlich.
Yes, we can reverse the resistance, as you have asked us to answer in your question in 1891. Best regards and we extend our gratitude for your fantastic work that has moved so many entrenched points of view and has helped so many seriously infected people over all the years. Even now in 2015, it is almost impossible, more than 100 years after the question was raised and now answered, to get the public opinion interested in these fantastic possibilities, you have already pointed out in 1891. "

Sincerely

Jette Elisabeth Kristiansen.



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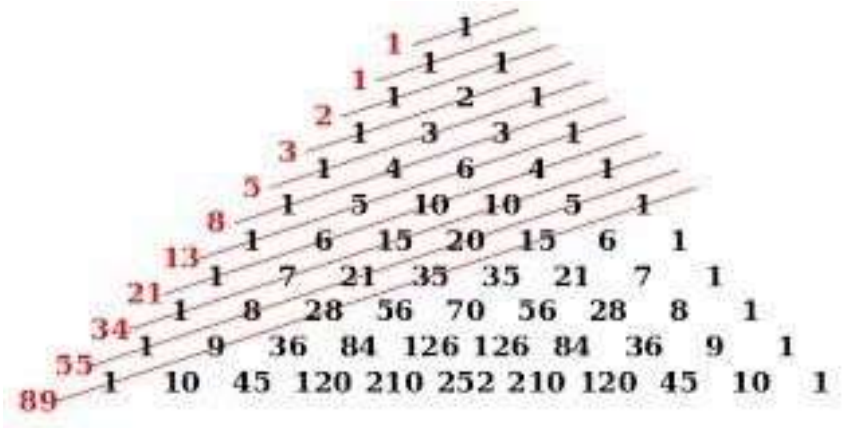
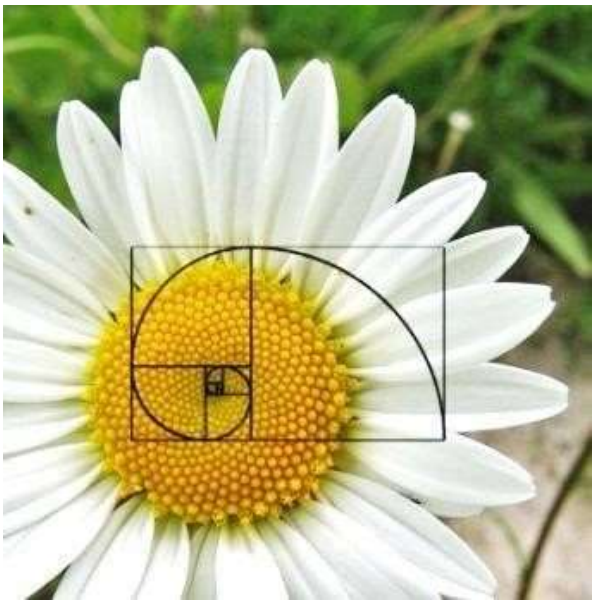


Fibonacci https://en.wikipedia.org/wiki/Fibonacci



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SDU

The "Reality Interaction Model" – described on the principles of J.M. Keynes