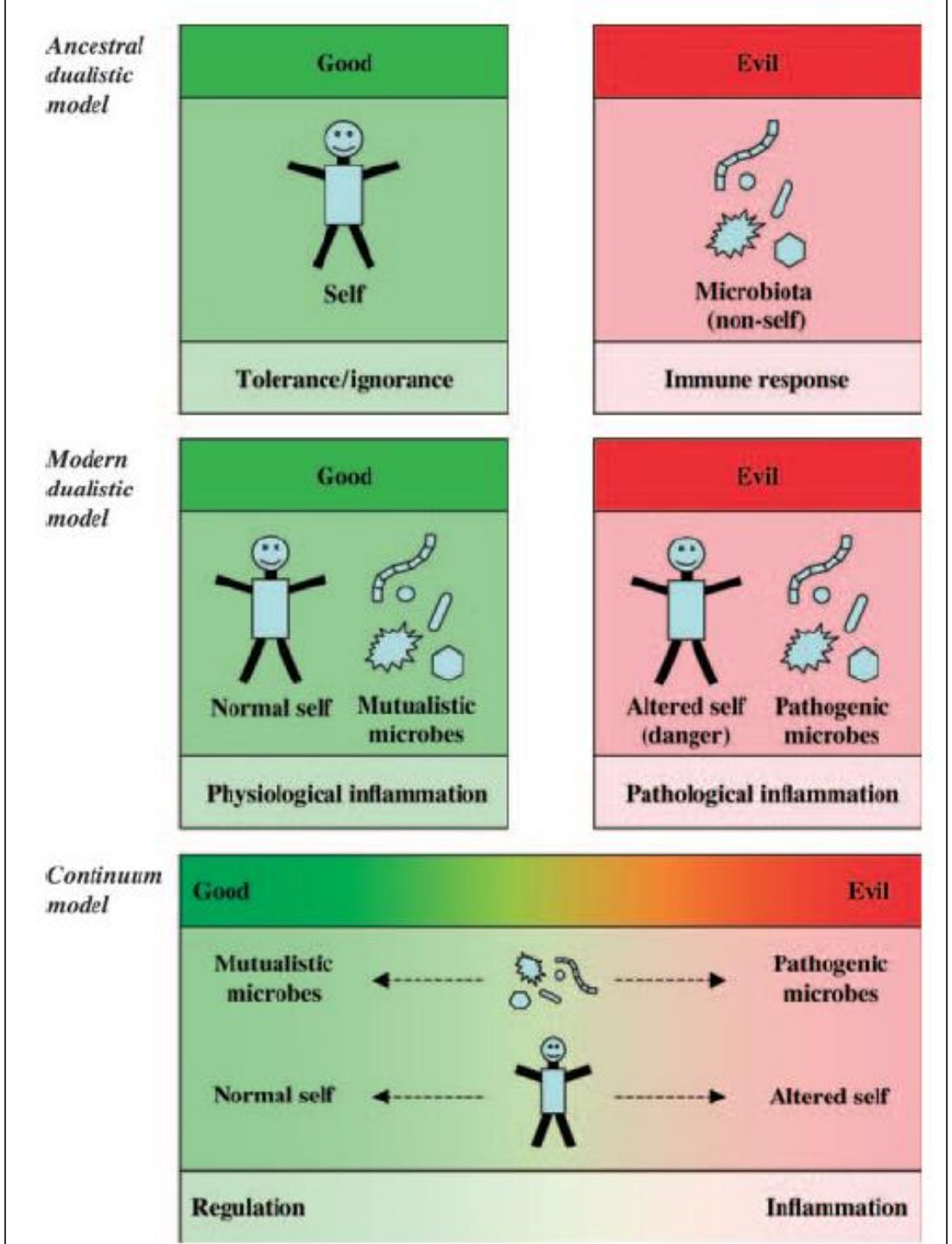
LEBEN IN SYMBIOSE

Daniel Reheis
2020



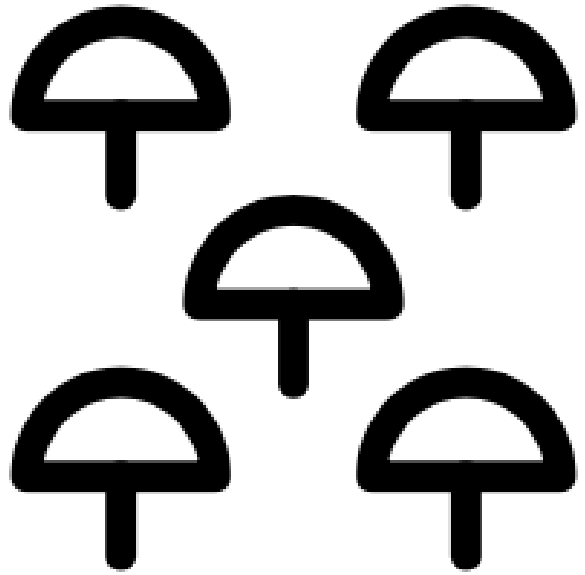
Dr. Jekyll and Mr. Hide

Das Immunsystem wird "selfish" wenn pathologische Mikrobien den Superorganismus dominieren

Eberl. VOLUME 3 NUMBER 5 | SEPTEMBER 2010 | www.nature.com/mi

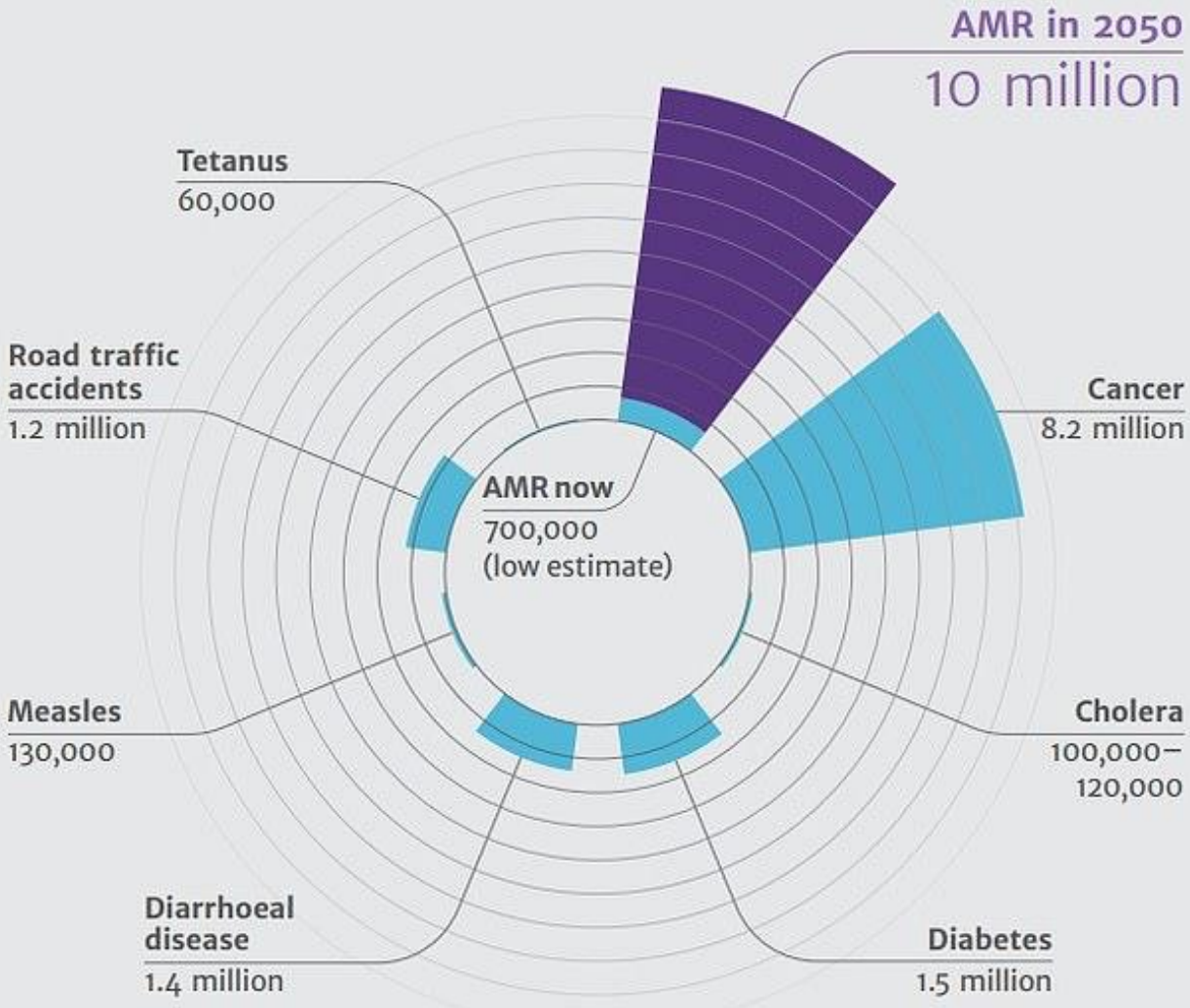
Bakterien

Viren



Pilze

Deaths attributable to AMR every year
compared to other major causes of death

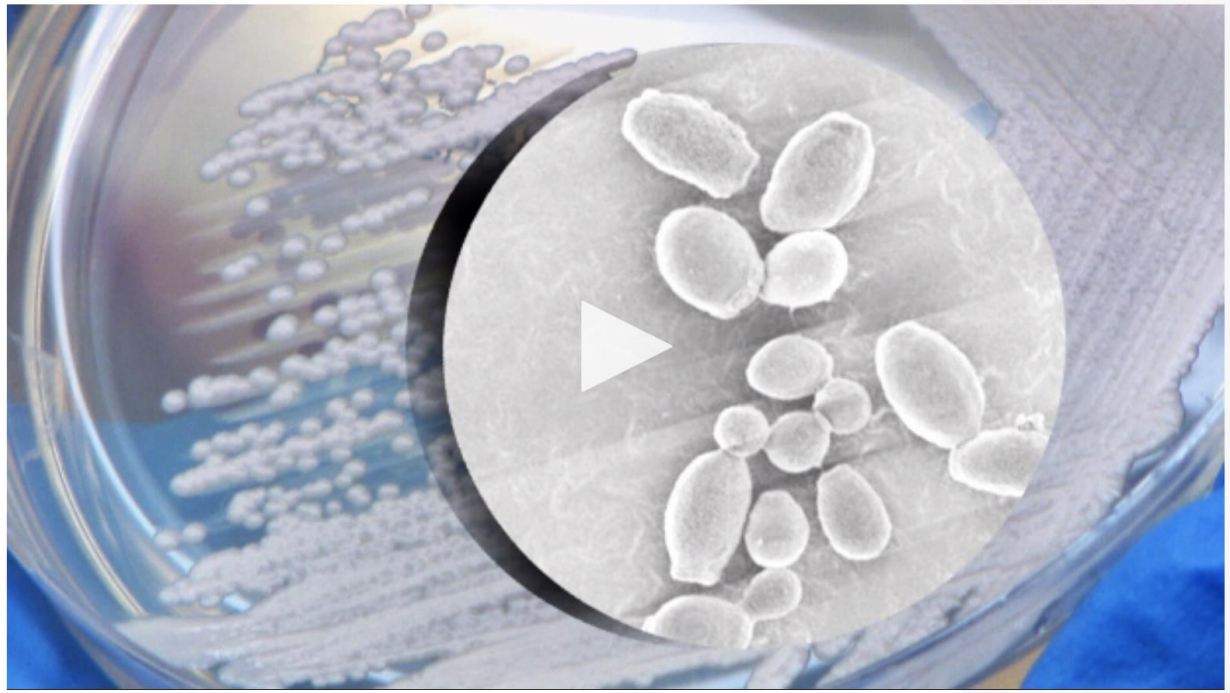


HEALTH

Potentially deadly drug-resistant 'fungal superbug' emerging in Canada

Jackie Dunham
CTVNews.ca staff, with a report from CTV's medical specialist Avis Favaro

Published Monday, May 20, 2019 10:00PM EDT



CTV National News: New fatal fungus

A new fatal fungus dubbed 'C. auris' is rapidly spreading and could be a threat to the public. Avis Favaro explains.

Doctors in Canada are being warned about the emergence of an extremely contagious pathogen described as a “fungal superbug” that is resistant to most medications and can be deadly for patients who are already sick.

REVIEW

Virulence 4:2, 119–128; February 15, 2013; © 2013 Landes Bioscience

Candida albicans pathogenicity mechanisms

François L. Mayer,[1] Duncan Wilson[1] and Bernhard Hube[1,2,3,*]

[1]Department of Microbial Pathogenicity Mechanisms; Hans-Knoell-Institute; Jena, Germany; [2]Center for Sepsis Control and Care; Universitätsklinikum; Jena, Germany; [3]Friedrich Schiller University; Jena, Germany

Keywords: *Candida albicans*, pathogenicity, virulence factors, fitness attributes, candidiasis

Abbreviations: AMP, antimicrobial peptide; Hsp, heat shock protein; sHsp, small Hsp; RHE, reconstituted human oral epithelium; RNS, reactive nitrogen species; ROS, reactive oxygen species

The polymorphic fungus *Candida albicans* is a member of the normal human microbiome. In most individuals, *C. albicans* resides as a lifelong, harmless commensal. Under certain circumstances, however, *C. albicans* can cause infections that

C. albicans and to a lesser extent other *Candida* species are present in the oral cavity of up to 75% of the population.[6] In healthy individuals this colonization generally remains benign. However, mildly immunocompromised individuals can frequently suffer

MRSA und ESBL (Extended spectrum ß-lactamase) bildende Bakterien

- Geflügel 30%
- Schweinefleisch 25%
- Rindfleisch 20%

- Beim Zubereiten aufpassen: Alle Messer, Schneidbretter usw. mit heißem Wasser waschen. Eventuell einmalhandschuhe tragen

ANTIBIOTIC RESISTANCE

Will Kill More People Than Cancer and Diabetes Combined By 2050

How Resistance Develops and Spreads

Fertilizing with antibiotic resistant manure

80%

of all antibiotics are given to livestock, mostly to speed their growth and prevent diseases

Manure encourages the proliferation of antibiotic resistant bacteria when applied as a fertilizer in agriculture

Consumption

of livestock and grain treated with multi-use antibiotics significantly increases the spread of resistance in bacteria.

50%

of all antibiotics given to humans are prescribed unnecessarily or used inappropriately

Journal of Oral Microbiology

co-action PUBLISHING

REVIEW ARTICLE

Can oral infection be a risk factor for Alzheimer's disease?

Ingar Olsen[1]* and Sim K. Singhrao[2]

[1]Department of Oral Biology, Faculty of Dentistry, University of Oslo, Oslo, Norway; [2]Oral & Dental Sciences Research Group, College of Clinical and Biomedical Sciences, University of Central Lancashire, Preston, UK

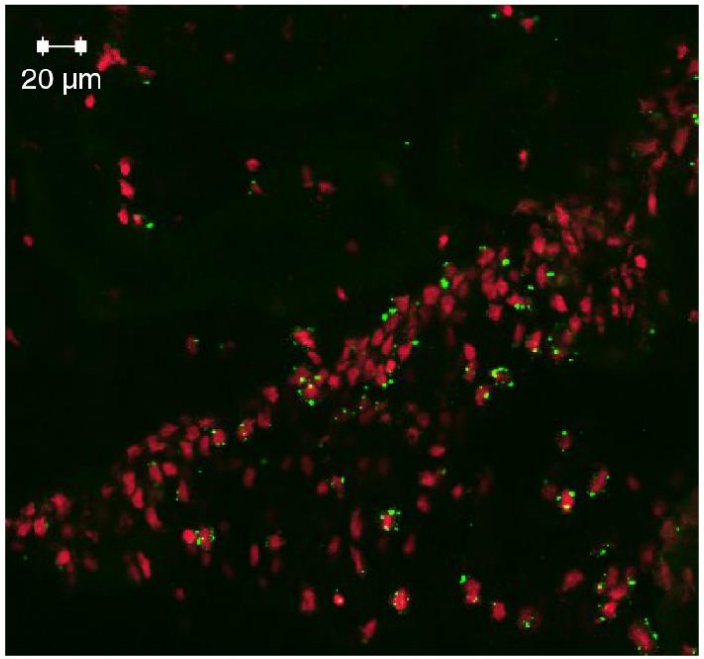


Fig. 2. Immunofluorescence labeling (green dots) of hippocampal CA neurons opsonized by iC3b following mono-infection with *P. gingivalis* at 24 weeks of *APOε* gene knockout ($ApoE^{-/-}$) mice. This is indirect evidence of an oral infection having affected the host's brain.

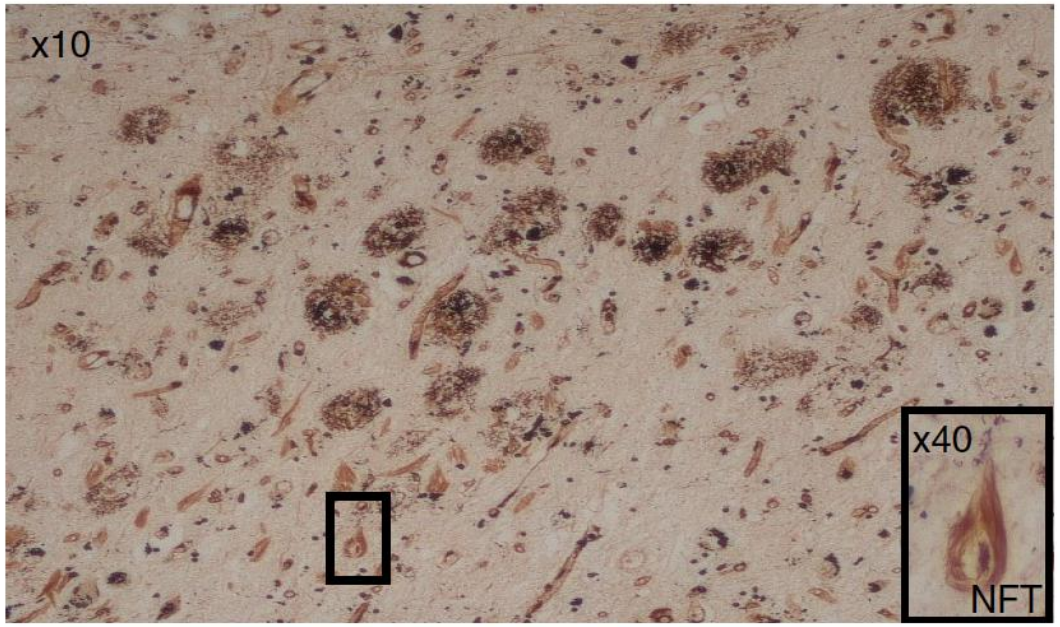


Fig. 1. The pathological hallmarks of AD, numerous extracellular amyloid-Aβ plaques and intra-neuronal neurofibrillary tangles (NFTs). Although there are several NFTs, only one is picked out in boxes at 10 × and 40 × objective lens magnification.

Urquhart *et al. BMC Medicine* (2015) 13:13
DOI 10.1186/s12916-015-0267-x

BMC Medicine

RESEARCH ARTICLE Open Access

Could low grade bacterial infection contribute to low back pain? A systematic review

Donna M Urquhart[1*], Yiliang Zheng[1], Allen C Cheng[1], Jeffrey V Rosenfeld[2,3], Patrick Chan[2,3], Susan Liew[2,4], Sultana Monira Hussain[1] and Flavia M Cicuttini[1]

Table 6 Methods used for bacteria identification and to minimize contamination and prevalence, and type of bacteria identified

Studies and design	Biopsy: Method, site and no. of specimens	Methods to minimize contamination	Duration of culturing biopsy material	Bacteria identification methods	Culture-positive samples (n, %)	Organisms identified in positive cultures (%)	Subsequently made generic analysis of *P. acnes* species	Quality score
Albert [2] Cross-sectional	Open Disc material Five specimens	All scalpels flamed before use as extra precaution	7 days with subsequent 1 day of subculture	Culture, PCR	28/61 (46%)	***P. acnes*: 86%** Gram-positive cocci: 14% Coagulase-negative (CN) staphylococci: 7%	Analytical profile index biochemical analysis using Rapid ID 32A kit (bioMerieux) and PCR amplification of 16S rDNA	78
Stirling [14] Cross-sectional	Open Disc material Not stated	Stringent aseptic precautions taken to minimise risk of contamination	7 days	Culture, serology	19/36 (53%)	***P. acnes*: 84%** CN staphylococci: 11% Corynebacterium propinquum: 5%	Microscopy of Gram-stained smears of tissue samples	78
Stirling [17] Cross-sectional	Open Disc material Not stated	Not stated	7 days	Culture, serology	76/207 (37%)	***P. acnes*: 64%** CN staphylococci: 14% Propionibacteria: 10.5%	Microscopy of Gram-stained smears of tissue samples	56
Agarwal [16] Cross-sectional	Open Disc material Not stated	Disc material retained in a closed sterile sample cup	5 days	Culture	10/52 (19.2%)	***P. acnes*: 70%** Peptostreptococci: 10% Staphylococci aureus: 10% CN staphylococci: 10%	Not stated	78
Arndt [9] Cross-sectional	Open Disc material 1 in 1st 25 disk replacements; 3 in following 58	Disc structures stored in sterile syringes filled with physiological saline solution, care was taken to avoid contamination during conditioning process of biopsy	Blood agar, Drigalski agar: 24 h Polyvitex chocolate agar: 4 days Blood agar supplemented with hemin: 5 days Peptone glucose yeast broth: 10 days Bactec Peds Plue bottle with fructooligosaccharide nutritional supplement: 7 days	Culture	40/83 (48.2%)	***P. acnes*: 45%** CN staphylococci: 40% CN bacilli: 7.5%	Not stated	67
Coscia [11] Cross-sectional	Open Disc material Not stated	Specimens were obtained sterilely immediately at the time of surgical excision	Cultured using extended duration incubation techniques (repeated subcultures up to several weeks duration)	Culture	16/30 (53.3%)	Staphylococcus: 36% ***P. acnes*: 18%**	Not stated	78
	Open		2 weeks	Culture	2/30 (6.7%)	CN staphylococci: 100%	Not stated	67

Table 6 Methods used for bacteria identification and to minimize contamination and prevalence, and type of bacteria identified *(Continued)*

Ben-Galim [10] Cross-sectional	Disc material Four pieces (disc material dissected into four pieces)	Samples are processed and cultured intraoperatively under stringent, sterile operating theatre conditions, culture mediums were warmed to room temperature before each operation						
Fritzell [12] Cross-sectional	Open Disc material Two – one from annulus fibrosus and one from nucleus pulposus	Samples taken openly (no needle), all operations except for one were performed through a microscope with use of bipolar diathermy, assuring a very 'dry' operation field	Not applicable	PCR	(PCR) 2/10 (20%)	(PCR) Bacillus cereus: 50% Citrobacterbraaki/freundi: 50%	Not stated	67
Carricajo [13] Cross-sectional	Open Disc material, muscle, ligamentum flavum Three – muscle, ligamentum flavum, herniated intervertebral discs	Obtained under aseptic conditions	One horse-blood agar, two chocolate PolyVitex agar: 10 days One Schaedler medium: 20 days	Culture	12/54 (22%)	***P. acnes*: 17%** Anaerobic streptococci: 8%	Not stated	67
Wedderkopp [15] Cross-sectional	Needle Vertebral body One – at site of Modic Type 1 change	Obtained with sterile technique	2 weeks	Culture	2/24 (8.3%)	Staph epidermidis: 50% CN staphylococci: 50%	Not stated	67

Table 4 Outcome measures at baseline and 1-year follow-up

	Antibiotic baseline $n = 90$	Antibiotic 1-year follow-up $n = 77$	Placebo baseline $n = 72$	Placebo 1-year follow-up $n = 67$	*P* value for difference between placebo and antibiotic groups at 1-year follow-up
Had low back pain	100 %	67.5 %	100 %	94.0 %	0.0001
Had constant pain	75.3 %	19.5 %	73.1 %	67.2 %	0.0001
Had disturbed sleep at night due to pain	74.0 %	29.9 %	76.1 %	61.2 %	0.001
Had pain during the Valsalva maneuver	75.3 %	41.6 %	71.6 %	56.7 %	0.05
Had pain during active flexion of the lumbar spine	96.1 %	49.4 %	100 %	83.6 %	0.0001
Had pain during active extension of the lumbar spine	87.0 %	51.9 %	86.6 %	74.6 %	0.005
Positive cranial compression test	36.4 %	19.5 %	35.8 %	34.3 %	0.044
Had pain during springing test	92.2 %	55.8 %	94.0 %	77.6 %	0.006
Consulted a doctor the follow-up year due to back pain		23.4 %		41.8 %	0.002
Compliance consuming 95–100 % of all tablets		94.8 %		94.0 %	NS
Observed volume volume 1, minute size	16	29	31	24	0.05
Observed volume volume 2–4, moderate/large size	126	113	99	96	0.07


Corona
Extra

BMC Immunology

BioMed Central

Research article

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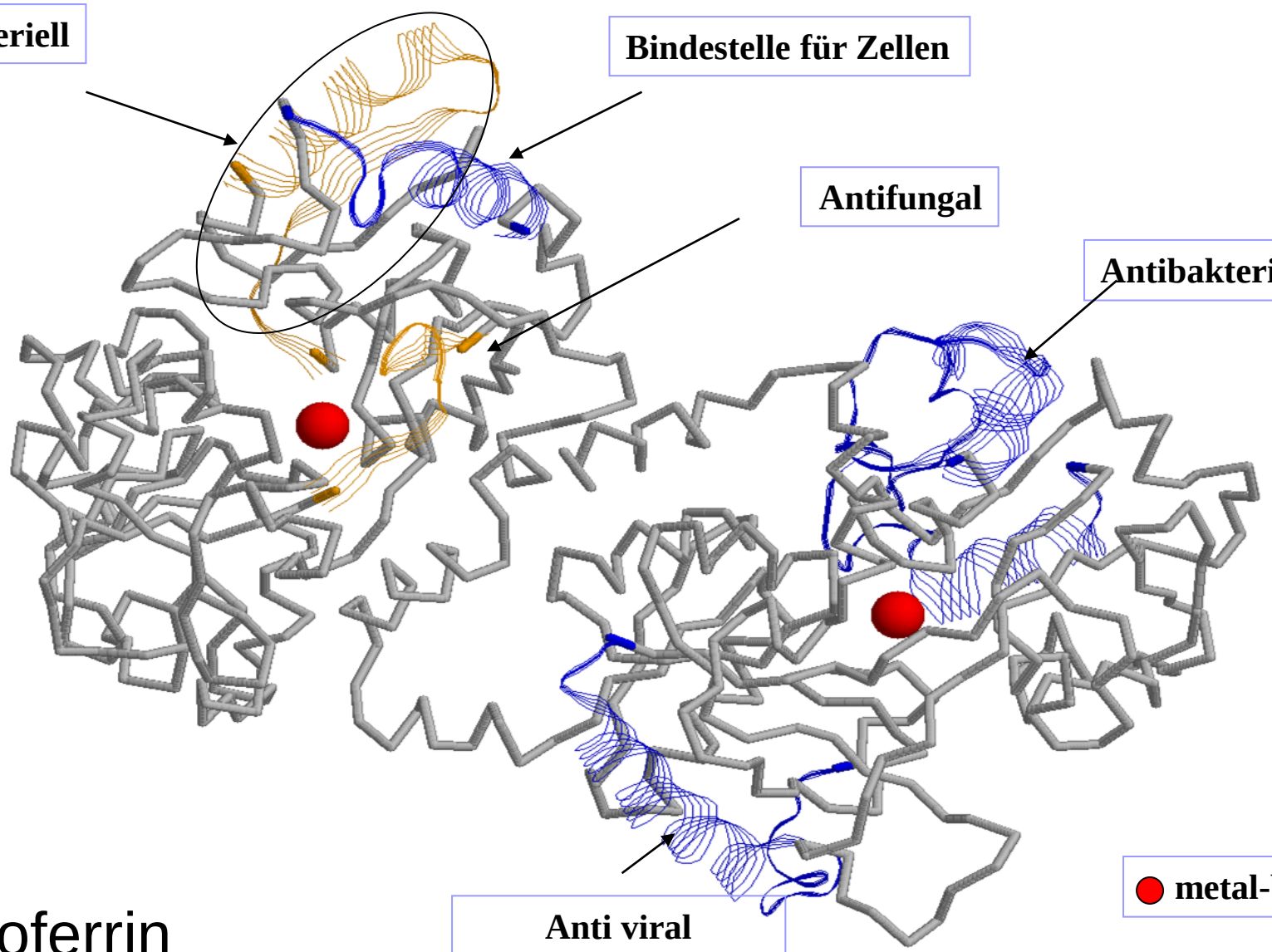
Expression profile of immune response genes in patients with Severe Acute Respiratory Syndrome

Renji Reghunathan[†1], Manikandan Jayapal[†1], Li-Yang Hsu[2], Hiok-Hee Chng[3], Dessmon Tai[4], Bernard P Leung[1] and Alirio J Melendez*[1]

Table 1: Immune-response related genes which were found to be significantly up-regulated in PBMCs of SARS patients. Level of expression is expressed in Fold change (average of fold changes of ten patients, S1-S10) as compared to that of control samples from normal human subjects (C1-C4).

Gen Bank ID	Description	Gene name	Fold change (S1-S10)
NM_002343.1	Lactotransferrin	LTF	149.63
M33326.1	Carcinoembryonic antigen-related cell adhesion molecule 8	CEACAM8	97.29
NM_005564.1	Lipocalin 2	LCN2	80.40
NM_004660.2	S100 calcium binding protein A9	S100A9	65.39
NM_001725.1	Bactericidal permeability-increasing protein	BPI	49.94
NM_005091.1	Peptidoglycan recognition protein	PGLYRP	47.86
NM_001925.1	Defensin alpha 4	DEFA4	46.88
U19970.1	Antimicrobial LPS-binding protein CAP18	CAMP	43.36
NM_005980.1	S100 calcium-binding protein P	S100P	39.52
NM_005143.1	Haptoglobin	HP	34.78
NM_004084.2	Defensin alpha 1	DEFA1	29.51
NM_006865.1	Leukocyte immunoglobulin-like receptor, subfamily A, member 3	LILRA3	19.43

Das Schweizer Taschenmesser

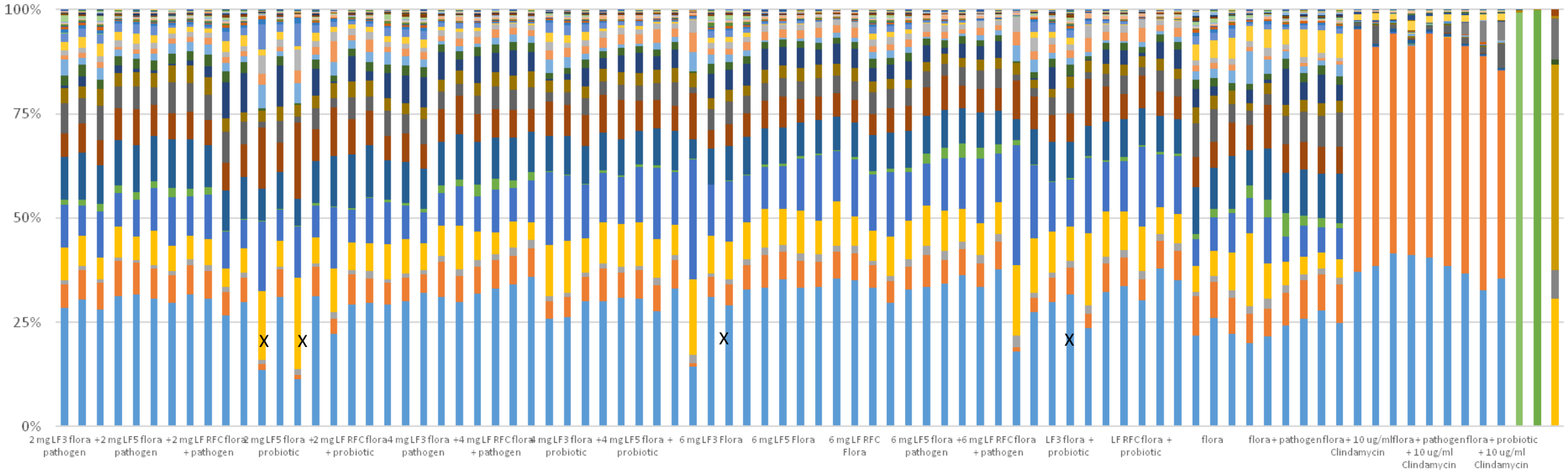


Lactoferrin

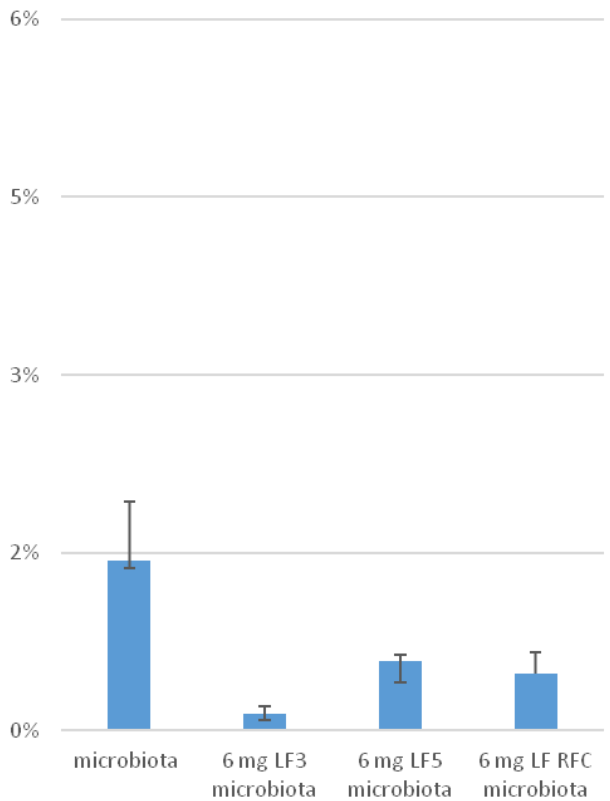
The first study on Lactoferrin and the Human gut flora

This first large-scale investigation compared the action of Lactoferrin NFQ on human gut flora. We compared our Lactoferrin with top quality Lactoferrin from the company Friesland Campina, one of the largest dairies in Europe. They were interested to find out if our Lactoferrin NFQ really was more effective than that which Friesland Campina produced, potentially with a view to deciding whether to switch to our patented technology. The testing delivered a very clear result.

Different lactoferrins and several concentrations were tested on the human gut flora plus a control group and an antibiotic group.

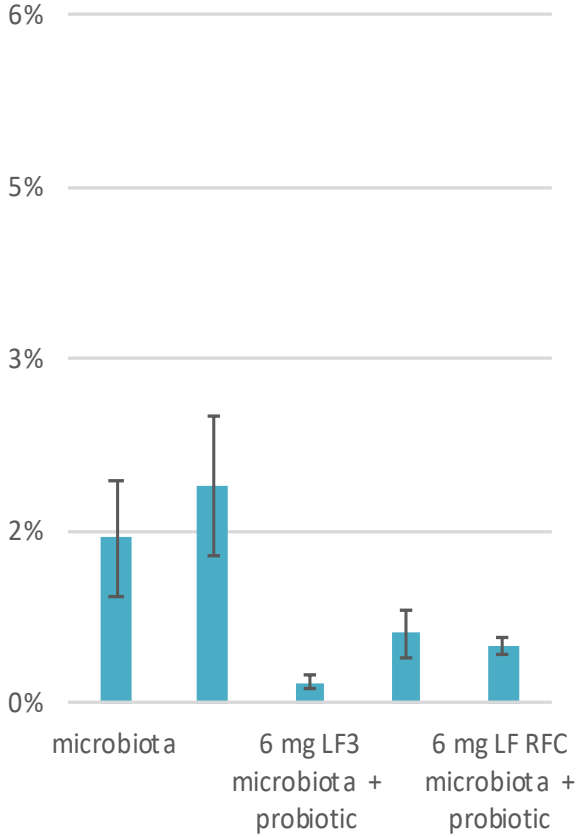


X --- indicates sample that is deviating in the triplicate and therefore not used in further analysis.
Note: By pointing the bar-colors in each lane with cursor, the genus affiliation is indicated

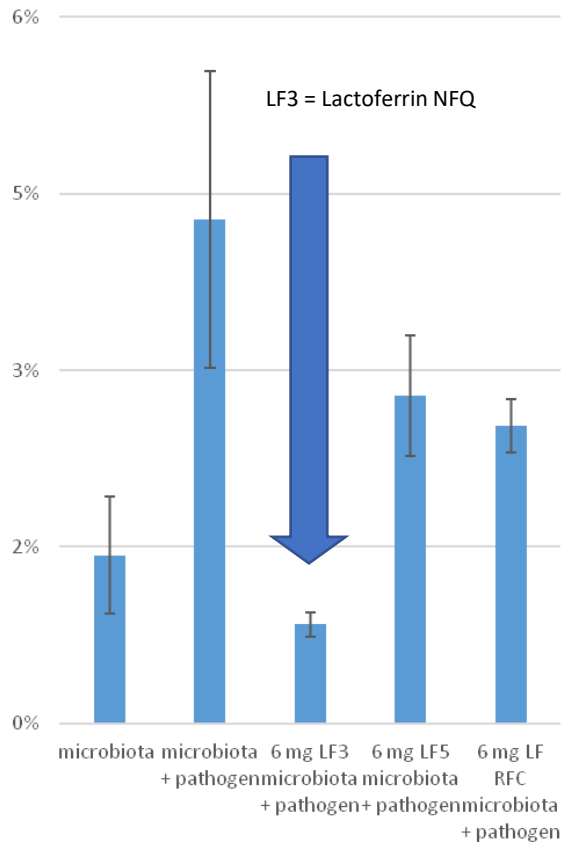


A

Pathogenic loading with Clostridia



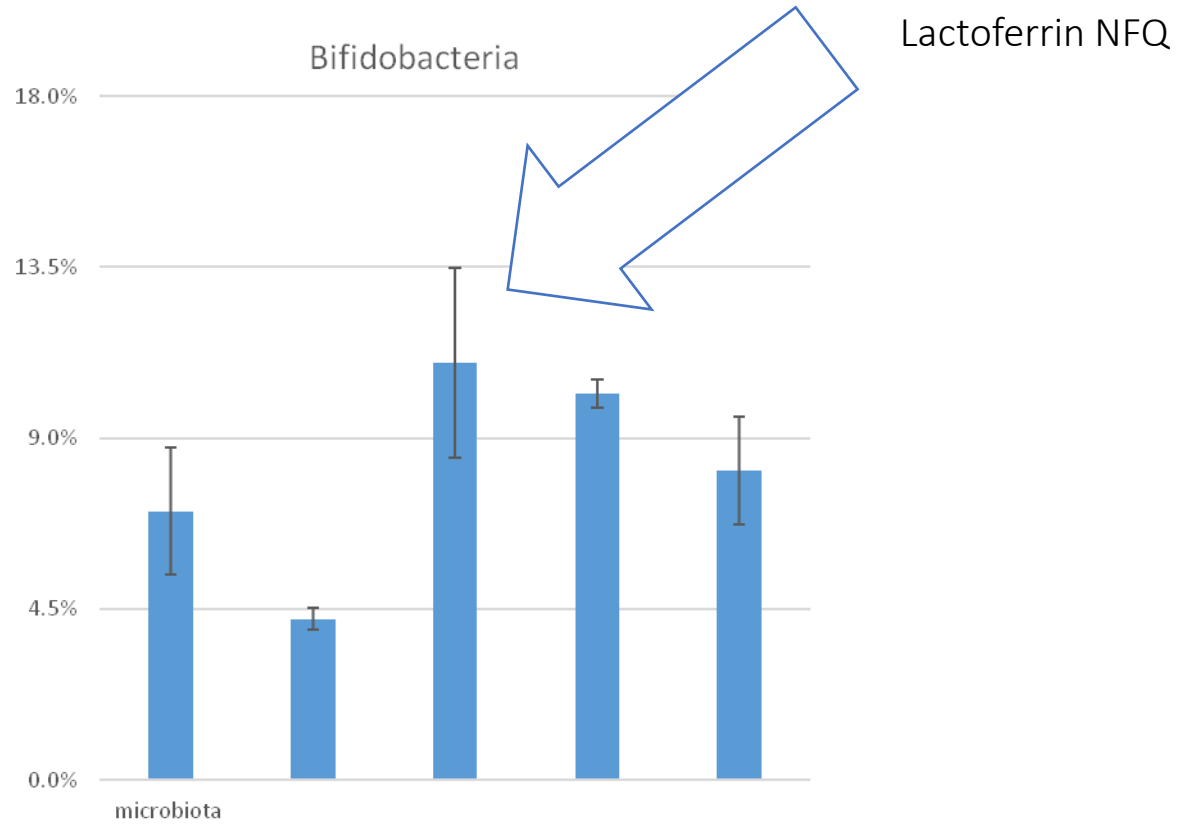
B



C

Effect of 4mg/ml Lactoferrin on *Bifidobacterium* (representative probiotic)

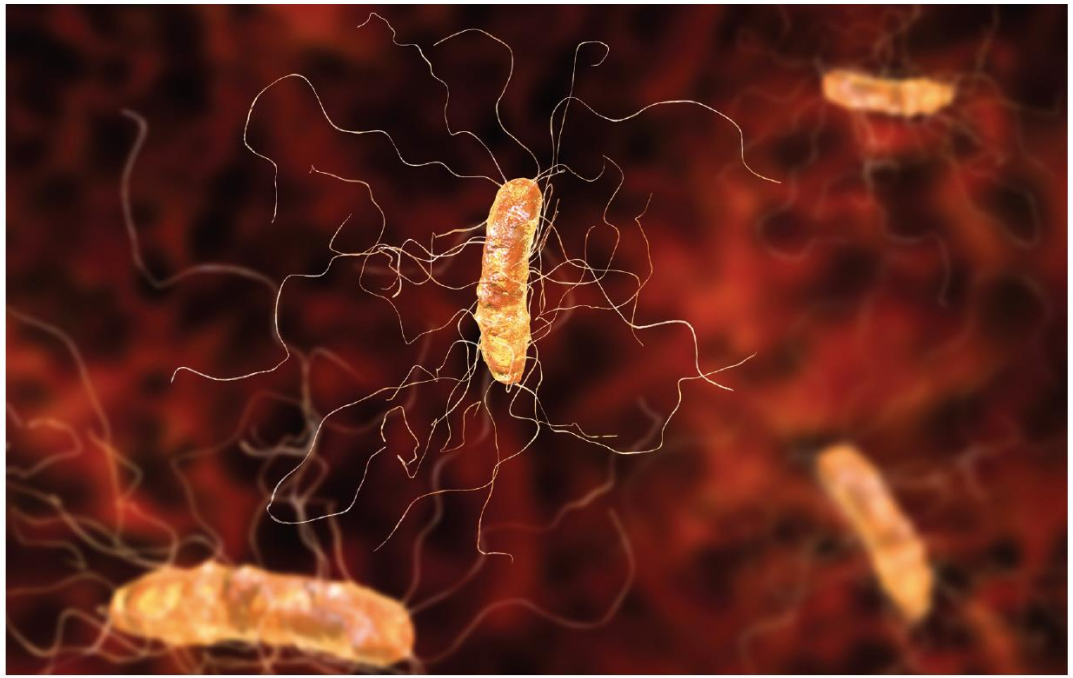
Extraordinary finding:
In the Lactoferrin CLN environment, *Clostridia* species were clearly reduced, whilst *Bifidobacteria* as representative of symbiotic bacteria, grew faster than in the control group.



A major challenge for this project will be the identification of solutions specifically targeting pathogenic Clostridia without harming the commensal or even beneficial Clostridia which are also present in the GI-tract.

PARTNERING OPPORTUNITY

SEARCH FOR NATURAL SOLUTIONS FOR CONTROLLING PATHOGENIC CLOSTRIDIA



J Infect Chemother xxx (2014) 1–6

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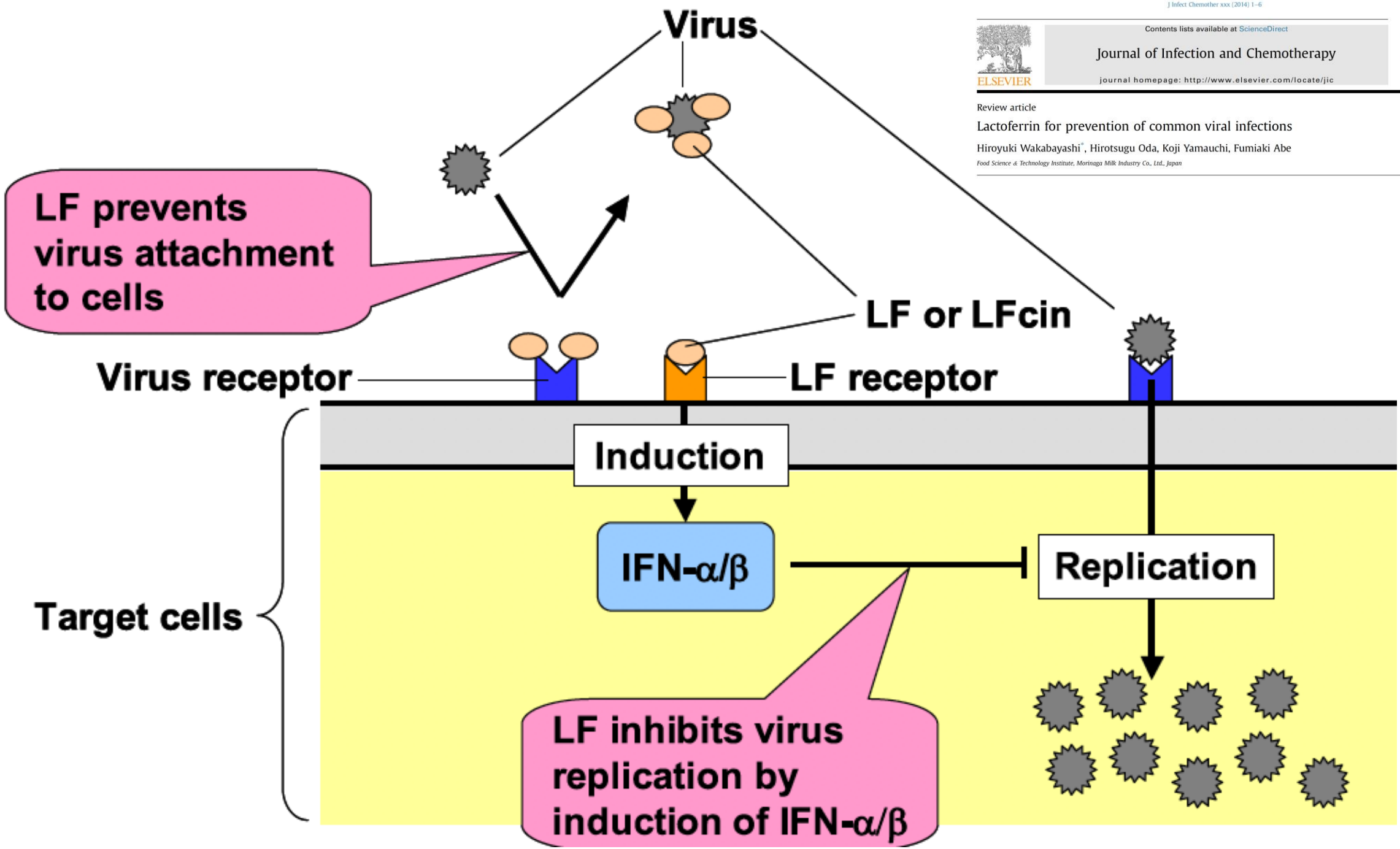
Review article

Lactoferrin for prevention of common viral infections

Hiroyuki Wakabayashi*, Hirotsugu Oda, Koji Yamauchi, Fumiaki Abe

Food Science & Technology Institute, Morinaga Milk Industry Co., Ltd., Japan



Effects of orally administered lactoferrin on common viral infections.

Disease virus[a]	Lactoferrin species[b]	Dose, duration[c]	Subject, number	Method	Effect	Reference
Common cold						
ND	bLF	600 mg LF/body/d or no administration, 3 m	Human (adult woman), 398	Questionnaire survey	Reduction of common cold-like symptoms	[17]
ND	bLF and Ig-rich whey protein	400 mg LF + 200 mg Ig/body/d or placebo, 3 m	Human (adult), 105	Double blind randomized placebo-controlled trial	Reduction of cold incidence	[18]
RSV	bLF	2 to 10 mg LF/body/d or PBS, 7 d	Mice, 58	Intranasal virus infection	No difference in viral loads or disease severity	[19]
Influenza						
Influenza virus A (H1N1)	bLF	62.5 mg/body/d, 6 d	Mice, 40	Intranasal virus infection	Reduction of lung consolidation score and infiltrated leukocytes	[20]
Viral gastroenteritis						
Rotavirus	bLF	100 mg LF/body/d or no administration, 3 m	Human (children), 234	Non-randomized controlled study	Amelioration of severity of rotaviral gastroenteritis	[30]
Rotavirus and other pathogens	hLF	50 to 80 mL solution with 1 g/L hLF and lysozyme/kg or control solution, 48 h	Human (children) 140	Randomized, double-blind controlled trial	Decrease in duration and volume of diarrhea, but no difference in rotaviral incidence	[31]
Norovirus	bLF	400 mg LF/body/d or no administration, 4 m	Human (children), 91	Randomized controlled study	Reduction of noroviral gastroenteritis incidence	[32]
Norovirus and other pathogens	bLF	500 mg LF twice/d or placebo, 6 m	Human (children) 555	Randomized, double-blind controlled trial	Reduction of diarrhea longitudinal prevalence, but no difference in noroviral incidence	[33]
Norovirus	bLF	100 mg LF/body/d at 1−7 times per w, one winter season	Human, 461	Questionnaire survey	Lower incidence of noroviral gastroenteritis in frequently consuming groups	[34]
Summer cold						
EV71	pLF	Milk of wild type or pLF-transgenic mice, 3 w	Mice (neonate), 30	Intraperitoneal virus infection	Increase in survival rate and body weight	[45]
EV71 and rotavirus	bLF	70 to 85 mg LF/body/d or no administration, 15 m	Human (children), 172	Randomized, single blind trial	No difference in incidence of enterovirus or rotavirus infection	[46]
Herpes						
HSV-1	bLF	1.5% bLF solution in drinking water, 20 d	Mice, 30	Cutaneous viral infection	Prevention of body weight loss and increase in cytokine responses	[56]

[a] ND indicates that virus species were not determined.
[b] Lactoferrin species are abbreviated as follows: bovine lactoferrin (bLF), human lactoferrin (hLF), and porcine lactoferrin (pLF).
[c] Duration is abbreviated as follows: hours (h), days (d), weeks (w), and months (m).

Table 1
In vitro effects of lactoferrin against viruses causing common infections.

Disease virus	Lactoferrin species[a]	Effective dose (IC50)	Cell type	Effect	Reference
Common cold					
Respiratory syncytial virus (RSV)	hLF	10–100 μg/ml	Human epidermoid carcinoma (HEp-2)	Inhibition of virus growth	[9]
RSV	hLF	100–1000 μg/ml	HEp-2	Inhibition of virus growth	[10]
RSV	hLF	100 μg/ml	HEp-2	Reduction of virus entry into cells	[11]
Parainfluenza virus type 2 (PIV-2)	bLF		Rhesus monkey kidney ($LLCMK_2$)	Inhibition of virus entry into cells	[12]
Influenza					
Influenza A virus (H3N2)	bLF	0.89 μM	Madin–Darby canine kidney (MDCK)	Inhibition of cytopathic effect	[13]
Influenza A virus (H3N2)	Native bLF	0.625 μM	MDCK	Inhibition of cytopathic effect	[14]
	Apo-bLF	1.56 μM			
Influenza A virus (H1N1, H3N2)	bLF	25–250 pM	MDCK	Inhibition of virus replication	[15]
	bLF C-lobe	10–50 pM			
Avian influenza A virus (H5N1)	bLF	40–80 μg/ml	MDCK	Antiviral activity	[16]
	Esterified bLF	<20 μg/ml			
Viral gastroenteritis					
Rotavirus	Apo-bLF	29–58 μg/ml	Human colon adenocarcinoma (HT-29)	Inhibition of cytopathic effect	[25]
	Fe^{3+}-bLF	29–58 μg/ml			
Rotavirus	Apo-bLF	50 μg/ml	HT-29	Inhibition of cytopathic effect	[26]
	Desialylated bLF	12 μg/ml			
Feline calicivirus (FCV, norovirus surrogate)	bLF	1000 μg/ml	Crandell-Reese feline kidney (CRFK)	Inhibition of cytopathic effect	[27]
	LFcin B	50–200 μg/ml			
Murine norovirus (MNV)	bLF	5–15 μg/well	Murine macrophage (Raw264.7)	Inhibition of cytotoxic damage	[28]
Summer cold					
Adenovirus	bLF	80 μg/ml	HEp-2	Inhibition of cytopathic effect	[35]
	hLF	560 μg/ml			
Adenovirus	bLF	0.78 μM	HEp-2	Inhibition of cytopathic effect	[36]
	hLF	6.25 μM			
	LFcin B	6.25 μM			
Adenovirus	bLF			Interaction with viral III and IIIa structural proteins	[37]
Adenovirus	hLF	100 μg/ml	Human corneal epithelial (HCE)	Promotion of virus binding and infection of cells	[38]
Poliovirus (PV)	bLF	650 μg/ml	African green monkey kidney (Vero)	Inhibition of cytopathic effect	[39]
	hLF	370 μg/ml			
Enterovirus 71 (EV71)	bLF	11–25 μg/ml	Human embryonal	Inhibition of cytopathic effect	[40]

EV71	bLF	34.5 μg/ml	RD and human neuroblastoma (SK-N-SH)	Inhibition of infection	[41]
Coxsackievirus A16	bLF	9.3 μg/ml	Vero	Inhibition of cytopathic effect	[40]
Echovirus 5	bLF	1000 μg/ml	Human colorectal adenocarcinoma (Caco-2)	Inhibition of virus replication	[42]
	Digested bLF	1000 μg/ml			
Echovirus 6	bLF	12.5 μM	Green monkey kidney (GMK)	Inhibition of viral infection	[43]
	bLF N-lobe	12.5 μM			
	LFcin B	12.5 μM			
Echovirus 6	bLF			Interaction with viral capsid proteins	[44]
Echovirus 9	bLF	>250 μg/ml	Vero	Inhibition of cytopathic effect	[40]
Herpes					
Herpes simplex virus-1 (HSV-1)	hLF	500 μg/ml	Human embryo lung (HEL)	Inhibition of viral infection	[47]
HSV-1	hLF	1.41 μM	Vero	Inhibition of cytopathic effect	[48]
	bLF	0.12 μM			
HSV-1	Apo-bLF	28 μg/ml	Vero	Reduction of infection	[49]
	Fe^{3+}-bLF	12 μg/ml			
HSV-2	Apo-bLF	31 μg/ml	Vero	Reduction of infection	[49]
	Fe^{3+}-bLF	5 μg/ml			
HSV-1	bLF	10 μg/ml	Vero	Inhibition of cytopathic effect	[50]
	bLF1-280	25 μg/ml			
	bLF345-689	320 μg/ml			
HSV-1	bLF	10 μg/ml	Vero	Inhibition of viral antigen synthesis	[51]
	bLF N-lobe	30 μg/ml			
	bLF C-lobe	860 μg/ml			
HSV-1	bLF	252 μg/ml	Vero	Inhibition of viral replication	[52]
	bLF with glycyrrhizic acid	15 μg/ml			
HSV-1, HSV-2	bLF		Vero	Inhibition of viral cell-to-cell spread	[53]
	hLF				
	LFcin B				
	LFcin H				
HSV-1	bLF		Vero	Inhibition of intracellular virus trafficking	[54]
	LFcin B				
HSV-2	bLF	1000 μg/ml	GMK	Inhibition of viral infection	[55]
	LFcin B	100 μg/ml			

Lactoferrin species are abbreviated as follows: human lactoferrin (hLF), bovine lactoferrin (bLF), lactoferricin B (LFcin B), and lactoferricin H (LFcin H).

Inhibition of SARS Pseudovirus Cell Entry by Lactoferrin Binding to Heparan Sulfate Proteoglycans

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State Key Laboratory of Medical Molecular Biology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Peking Union Medical College, Tsinghua University, Beijing, People's Republic of China

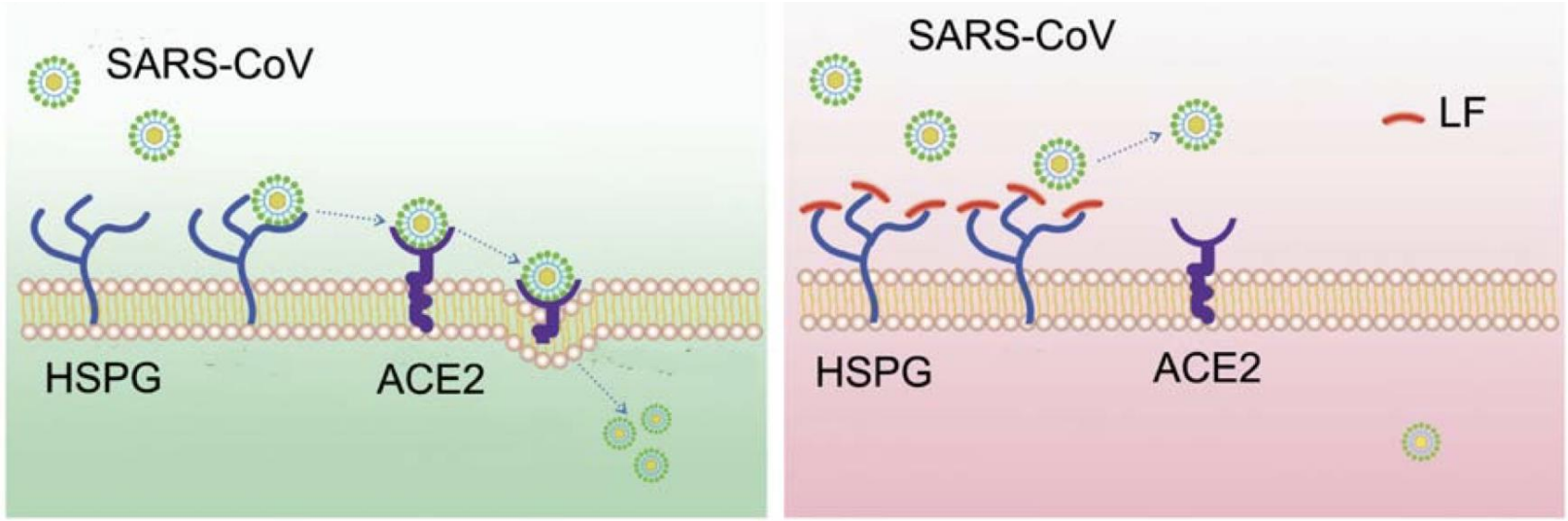

Figure 9. A model of SARS-CoV cell entry and the protective role of Lactoferrin in SARS-CoV infection. (**A**) HSPGs play an important role in the process of SARS-CoV cell entry. The anchoring sites provided by HSPGs permit initial contact between SARS-CoV and host cells and the concentration of virus particles on cell surface. SARS-CoV rolls onto the cell membrane by binding to HSPGs and scans for specific entry receptors, which leads to subsequent cell entry. (**B**) LF blocks the infection of SARS-CoV by binding to HSPGs. LF expression may be up-regulated when SARS-CoV infects the human body. LF locates to cell-surface HSPGs and prevents the preliminary interaction between the virus and host cells and the subsequent internalization process.
doi:10.1371/journal.pone.0023710.g009

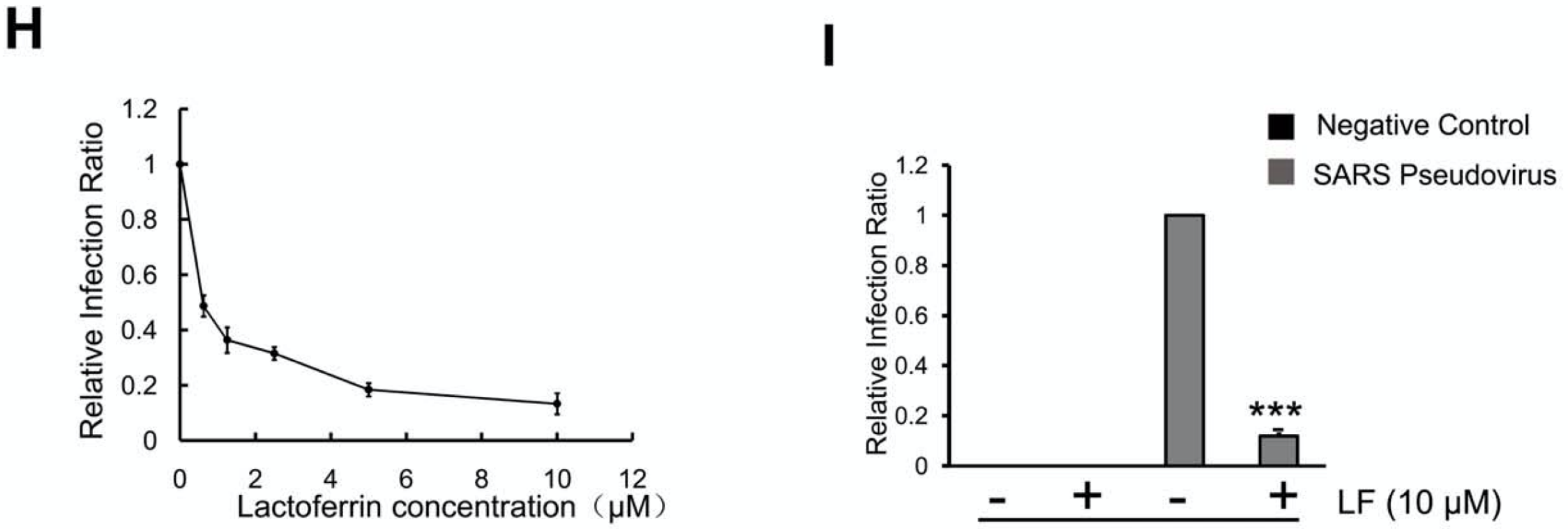

Figure 1. Lactoferrin inhibits SARS pseudovirus infection of HEK293E/ACE2-Myc cells. (**A–D**) Fluorescence microscopy illustrates that the number of SARS pseudovirus-infected GFP-expressing HEK293E/ACE2-Myc cells decreases in the presence of LF. HEK293E/ACE2-Myc cells were treated with LF for 1 h at 37°C at the concentration of 1 μM (B), 3 μM (C) or 10 μM (D). BSA (10 μM) was used as control (A). The LF-pretreated cells were treated with SARS pseudovirus as described in Methods. (**E and F**) Western blotting reveals that LF markedly reduces GFP expression in HEK293E/ACE2-Myc cells incubated with SARS pseudovirus. Statistical analysis of the relative band density ratio of GFP to actin was performed using a *t*-test. Error bars represent the SD of three independent experiments. **$P<0.01$ and *$P<0.05$. (**G and H**) Flow cytometry demonstrates that LF is able to inhibit the infection of HEK293E/ACE2-Myc cells by SARS pseudovirus. The concentration of LF was 0.625 μM, 1.25 μM, 2.5 μM, 5 μM or 10 μM. BSA (10 μM) served as control. The percentage of GFP expressing cells in the total population was calculated by flow cytometry. The relative viral infection ratio was measured by comparing the percentage of GFP expressing cells in each group with that of the BSA control. Error bars represent the SD of three independent experiments. (**I**) No GFP expression can be detected in the cells treated with viral particles without spike protein. The percentage of GFP expressing cells in the total population was calculated by flow cytometry as described above. Error bars represent the SD of three independent experiments.

doi:10.1371/journal.pone.0023710.g001

JOURNAL OF
GENERAL VIROLOGY

SHORT COMMUNICATION

Carvalho *et al.*, *Journal of General Virology* 2017;98:1749–1754

DOI 10.1099/jgv.0.000849

Bovine lactoferrin activity against Chikungunya and Zika viruses

Carlos A. M. Carvalho,[1,*] Samir M. M. Casseb,[1] Rafael B. Gonçalves,[2] Eliana V. P. Silva,[1] Andre M. O. Gomes[3] and Pedro F. C. Vasconcelos[1]

Abstract

Chikungunya (CHIKV) and Zika (ZIKV) viruses are arboviruses which have recently broken their sylvatic isolation and gone on to spread rampantly among humans in some urban areas of the world, especially in Latin America. Given the lack of effective interventions against such viruses, the aim of this work was to evaluate the antiviral potential of bovine lactoferrin (bLf) in their infections. Through viability, plaque, immunofluorescence and nucleic acid quantification assays, our data show that bLf exerts a dose-dependent strong inhibitory effect on the infection of Vero cells by the aforementioned arboviruses, reducing their infection efficiency by up to nearly 80 %, with no expressive cytotoxicity, and that such antiviral activity occurs at the levels of input and output of virus particles. These findings reveal that bLf antimicrobial properties are extendable to CHIKV and ZIKV, underlining a generic inhibition mechanism that can be explored to develop a potential strategy against their infections.

JOURNAL OF
GENERAL VIROLOGY

SHORT COMMUNICATION

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DOI 10.1099/jgv.0.000849

MICROBIOLOGY SOCIETY

Bovine lactoferrin activity against Chikungunya and Zika viruses

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a dose-dependent strong inhibitory effect
infection efficiency by up to nearly 80 %, w
input and output of virus particles. These

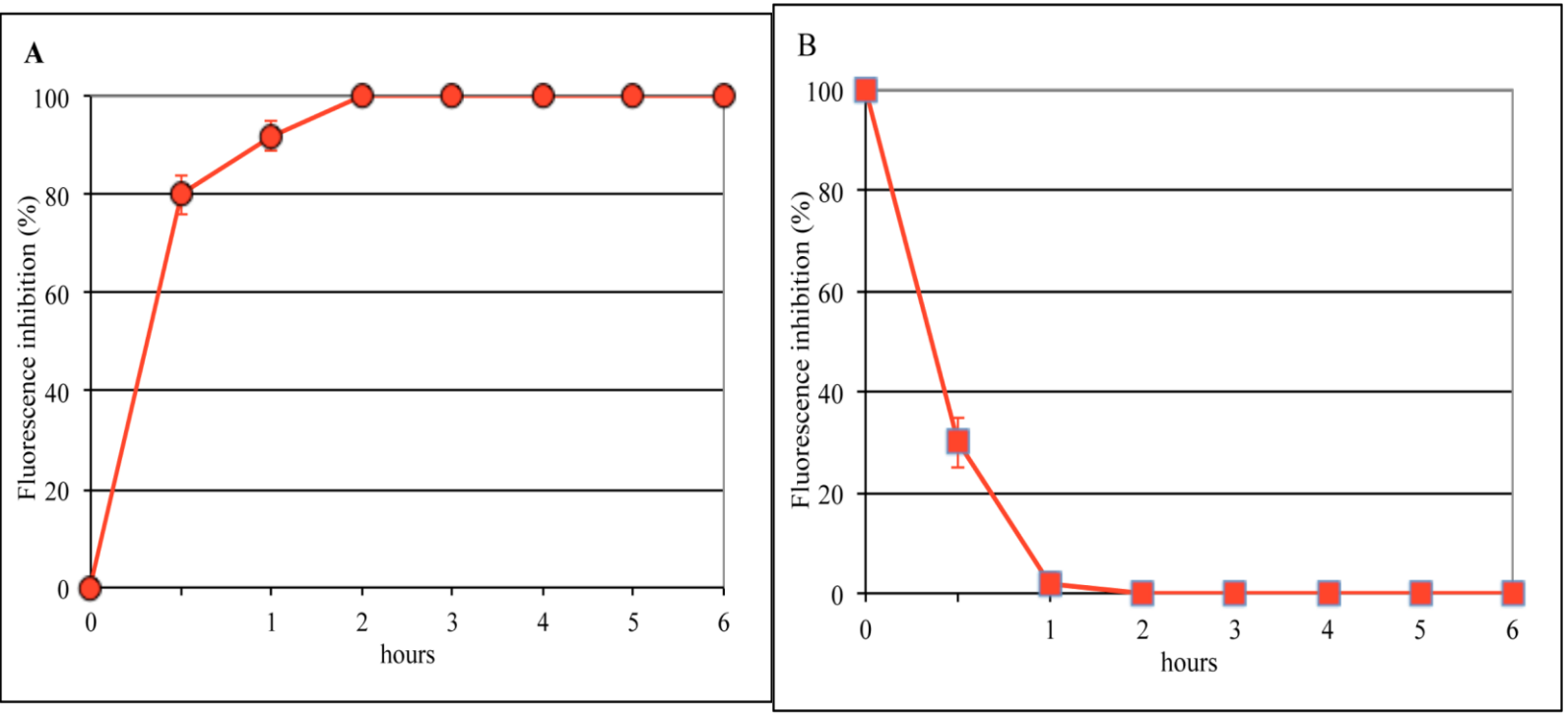
viruses

MDPI

Article

Bovine Lactoferrin Prevents Influenza A Virus Infection by Interfering with the Fusogenic Function of Viral Hemagglutinin

Fabiana Superti [1,*], Mariangela Agamennone [2], Agostina Pietrantoni [1,3] and Maria Grazia Ammendolia [1]



Dependence of 12.5 µM bLf time of addition on infection by the A/RomaISS/2/08 H1N1 strain. BLf was incubated with the cells directly after the virus-binding step and left for different periods of time (**A**), or, after virus adsorption, infected cells were kept at 37 °C for various periods of time before bLf addition (**B**). Six hours after viral infection, the synthesis of viral antigens was assessed by indirect immunofluorescence.

Anti Viral drugs and Lactoferrin

Lactoferrin shows synergistic effects in combination with anti-viral drugs like Zidovudin (HIV-1), Cidofovir (Cytomegalovirus), Acyclovir (Herpes simplex Type 1 and 2) as well as Interferon and Ribavirin (Hepatitis C-Virus).

- Gonzalez-Chavez S. A.,Arevalo-Gallegos S., Rascon-Cruz Q.: Lactoferrin: structure, function and applications. International journal of antimicrobial agents. 2009; 33.
- Jenssen H., Hancock R. E.: Antimicrobial properties of lactoferrin. Biochimie. 2009; 91.
- Zuccotti G. V.,Vigano A., Borelli M., et al.: Modulation of innate and adaptive immunity by lactoferrin in human immunodeficiency virus (HIV)-infected, antiretroviral therapy-na.ve children. International Journal of Antimicrobial Agents. 2007; 29.

Contents lists available at ScienceDirect

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Microbiology: bacteriology, mycology, parasitology, virology/Microbiologie : bactériologie, mycologie, parasitologie, virologie

Potential lactoferrin activity against pathogenic viruses

Elrashdy M. Redwan [a,b,*], Vladimir N. Uversky [a,c,d], Esmail M. El-Fakharany [b], Hussein Al-Mehdar [a]

Lactoferrin has a unique immunomodulatory action on adaptive cellular functions, on both T and B lymphocytes and other immune cells, by promoting the maturation of Tcell precursors into competent helper cells and the differentiation of immature B-cells into efficient antigenpresenting cells (APCs). LF causes a Th1 polarization in diseases in which the ability to control infection or tumor relies on a strong Th1 response. Th1 cells stimulate and activate macrophages, resulting in intracellular killing events that eliminate intracellular pathogens, often through the production of reactive oxygen intermediates. A well-studied phenomenon is the ability of LF to modulate and directly change the balance between the Th1 and Th2 immune responses, often defined by the T-cell cytokines IFN-g and IL-4/IL-5, respectively. The oral consumption of LF by chronically viremic HCV patients not only promotes the inflammatory cascade and recruits and activates APCs, but also potentiates the production of Th1 cytokines in the peripheral blood, specifically IL-18. The ingestion of lactoferrin professionally stimulates the gut-associated immune response through the expression of IL-18 and type I IFNs, in addition to increasing the activity of dg T-cells and natural killer lymphocytes

Further specific inhibitory functions of Lactoferrin on viruses

- Ability to bind to and block viral receptors such as glycosaminoglycans, especially heparan sulfate (HS). Thus, the binding of LF to HS avoids the first contact between host cell and virus, preventing viral infection
- Increase the phagocytic activity of macrophages in infections by vesicular stomatitis virus infections
- Inhibitory action on HIV-1 reverse transcriptase and HIV-1 integrase (Huang, N. Liu, Inhibition of HBV infection by bovine lactoferrin and iron-, zinc-saturated lactoferrin, Med. Microbiol. Immunol.)
- LF increases the TH1 lymphocyte production of cytokines, including IFN-γ, IL- 12, and IL- 18, which act to protect the host against infection (Lactoferrin for prevention of common viral infections, J. Infect. Chemother.)

Lactoferrin in combination

RESEARCH ARTICLE Open Access

Antiviral effects of nisin, lysozyme, lactoferrin and their mixtures against bovine viral diarrhoea virus

Joanna Małaczewska*, Edyta Kaczorek-Łukowska, Roman Wójcik and Andrzej Krzysztof Siwicki

Results: The highest efficacy among the single treatments was achieved by bovine lactoferrin, which was effective both at the early stages of viral infection and during its entire course, although the effect weakened over time. Nisin and lysozyme were effective at later stages of infection, and the intensity of their effect did not diminish with time. Nisin+lactoferrin and lysozyme+lactoferrin combinations demonstrated stronger antiviral effects than did the single substances. The nisin+lactoferrin mixture present during the whole period of infection produced the strongest anti-BVDV effect in our entire research on both the extracellular viral titre (titre reduction up to 2.875 log ≈ 99.9%) and the intracellular viral RNA level (reduction up to 89%), and this effect intensified over the incubation time.

Journal of Medical Microbiology (2005), **54**, 717–723 **DOI** 10.1099/jmm.0.46018-0

Effects of orally administered bovine lactoferrin and lactoperoxidase on influenza virus infection in mice

Kouichirou Shin,[1,2] Hiroyuki Wakabayashi,[1,2] Koji Yamauchi,[1] Susumu Teraguchi,[1] Yoshitaka Tamura,[1] Masahiko Kurokawa[2]† and Kimiyasu Shiraki[2]

In conclusion, the present study demonstrated for the first time the beneficial effects of orally administered LF and LPO in influenza-virus-infected mice. LF and LPO were shown to

Welches Lactoferrin?

Journal of Engineering and Applied Sciences Technology

SCIENTIFIC Research and Community

Research Article

Open Access

Lactoferrin Production from Bovine Milk or Cheese Whey

Léo De Valck[1] and Jean-Paul Perraudin[2]*

[1]Mirakal, 2 avenue Léon Champagne, 1480 Tubize, Belgium

[2]Taradon Laboratory, 4 Allée de la Recherche, 1070 Bruxelles, Belgium

ABSTRACT

Today, the industrial scale production of lactoferrin is carried out in one step by extraction from bovine milk or whey. As the role of lactoferrin in the milk is to protect the liquid against the bacterial contamination binding the lipopolysaccharides (LPS) of those bacteria, it is not surprising that the lactoferrin extracted from milk is covered by bacterial LPS, losing the most part of its biological activities. It is absolutely crucial that the production of Lactoferrin consists to a two steps process. The first step consists to extract from milk or from whey a solution that we called lactenin which contains different molecules including lactoferrin, lactoperoxidase, angiogenin and some other minor components. The second step consists to purify the lactoferrin from the other components including the LPS. Only under such conditions, we could recuperate a high level pure molecule with all its biological activities as it is not done actually.

Journal of Engineering and Applied Sciences Technology

SCIENTIFIC Research and Community

Research Article

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It is absolutely crucial that the production of Lactoferrin consists to a two steps process. The second step consists to purify the lactoferrin from the other components including the LPS.

din[2*]

elles, Belgium

Today, the industrial scale production of lactoferrin is carried out in one step by extraction from bovine milk or whey. As the role of lactoferrin in the milk is to protect the liquid against the bacterial contamination binding the lipopolysaccharides (LPS) of those bacteria, it is not surprising that the lactoferrin extracted from milk is covered by bacterial LPS, losing the most part of its biological activities. It is absolutely crucial that the production of Lactoferrin consists to a two steps process. The first step consists to extract from milk or from whey a solution that we called lactenin which contains different molecules including lactoferrin, lactoperoxidase, angiogenin and some other minor components. The second step consists to purify the lactoferrin from the other components including the LPS. Only under such conditions, we could recuperate a high level pure molecule with all its biological activities as it is not done actually.

Heat treatment

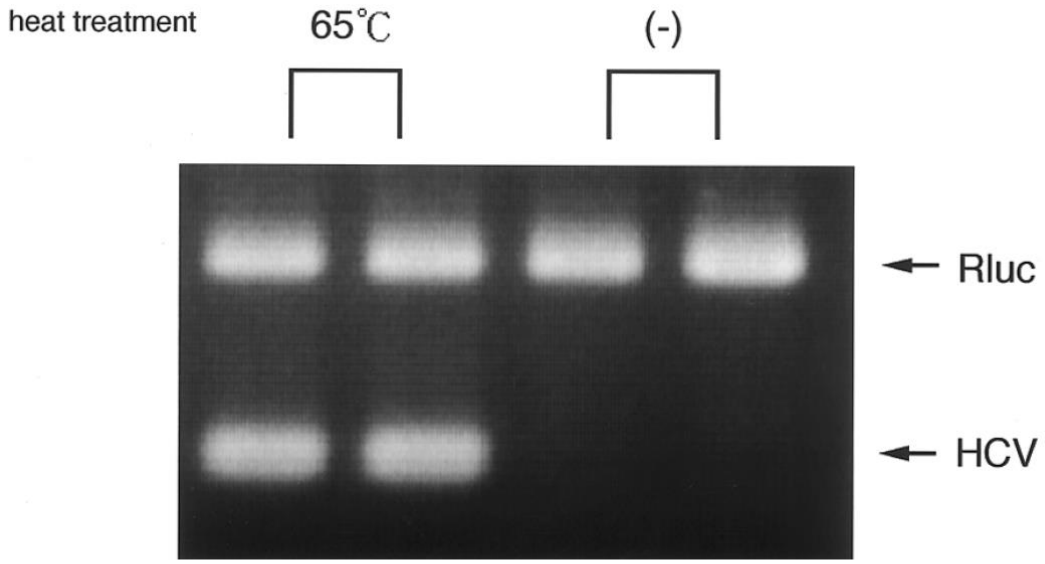


Fig. 2. Heat inactivation of bLF. bLF (1.0 mg/ml) treated for 60 min at 65°C was used for the standard assay of anti-HCV activity. HCV RNA and Rluc RNA were detected as described in (A) of Fig. 1.

ELSEVIER

Virus Research 66 (2000) 51–63

Virus Research

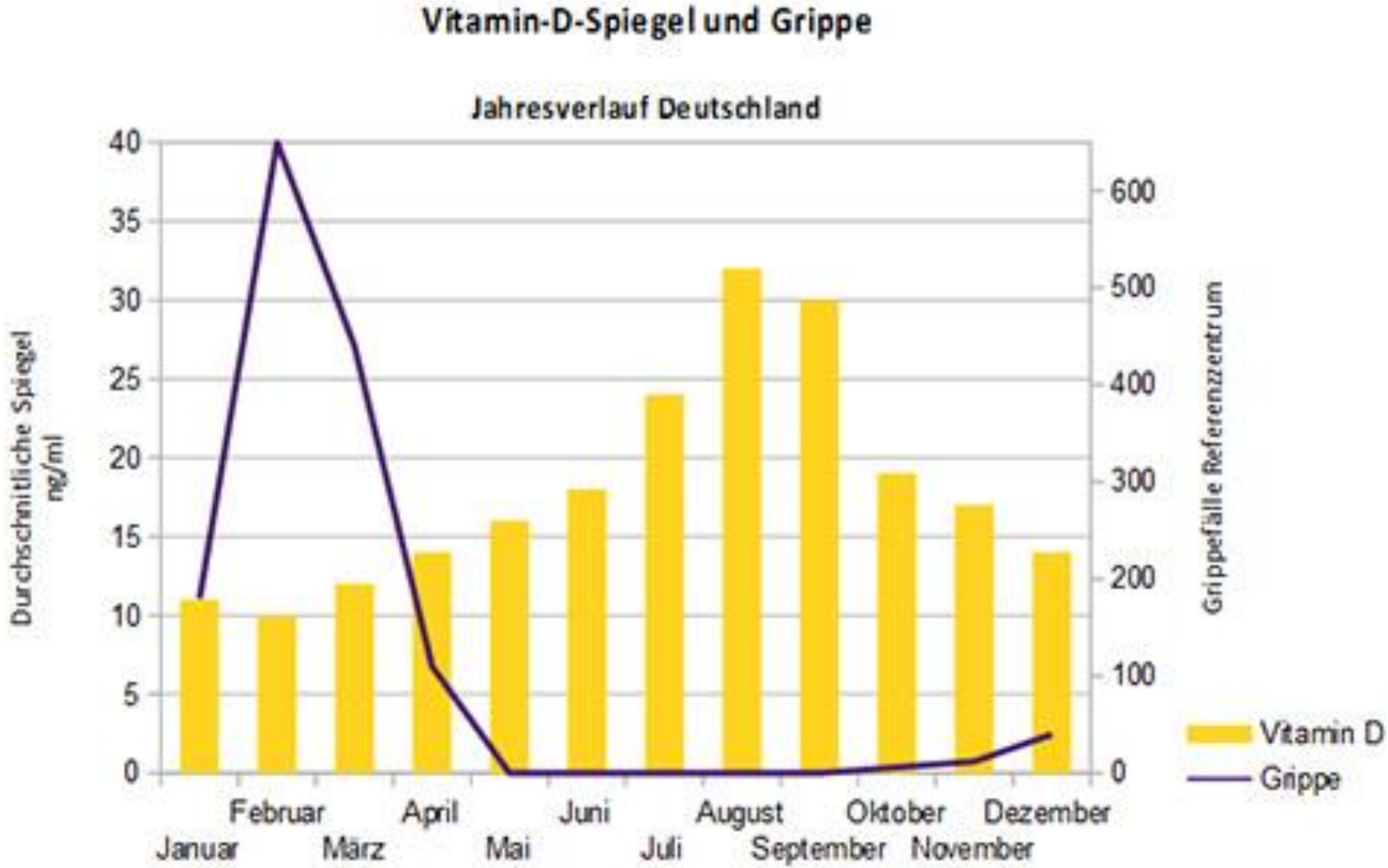
www.elsevier.com/locate/virusres

Characterization of antiviral activity of lactoferrin against hepatitis C virus infection in human cultured cells

Masanori Ikeda [a,b], Akito Nozaki [a], Kazuo Sugiyama [a], Torahiko Tanaka [a], Atsushi Naganuma [a], Katsuaki Tanaka [b], Hisahiko Sekihara [b], Kunitada Shimotohno [c], Masaki Saito [a], Nobuyuki Kato [a,*,1]

[a] *Virology and Glycobiology Division, National Cancer Center Research Institute, 5-1-1, Tsukiji, Chuo-ku, Tokyo 104-0045, Japan*

- Nahrungsvielfalt
- Fermentierte Nahrung
- L-Lysin 100 mg
- 1200mg NAC
- 2 Kapseln Echinacea (Sonnenhut)
- Gemischtes Pilzpulver- oder Kapseln Reishi, Maitake, Shiitake, Cordyceps, Agaricus
- So viele Kräuter wie möglich oder eine Kapsel Oreganoöl
- 400mg Lactoferrin, akut: mindestens 1g
- Zink 30mg
- Cistus incanus (Zistrose)
- Vitamin D3 3000 IE Oktober bis Mai, Akut 10.000 IE über eine Woche
- Propolis
- Bewegung (nicht zu lange sitzen)


Vitamin-D-Spiegel und Grippe
Jahresverlauf Deutschland
Durchschnittliche Spiegel ng/ml
Grippefälle Referenzzentrum
40
35
30
25
20
15
10
5
0
600
500
400
300
200
100
0
Januar
Februar
März
April
Mai
Juni
Juli
August
September
Oktober
November
Dezember
Vitamin D
Grippe

Journal of Functional Foods

Volume 55, April 2019, Pages 48-56

Lactoferrin stimulates the expression of vitamin D receptor in vitamin D deficient mice

Jingxuan Wang [a], Yixuan Li [b], Liang Zhao [a, b], Fazheng Ren [a, b], Huiyuan Guo [a, b]

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https://doi.org/10.1016/j.jff.2019.02.012

Published in final edited form as:
J Med Food. 2007 September ; 10(3): 423–434.

Enhancement of Innate and Adaptive Immune Functions by Multiple *Echinacea* Species

Zili Zhai[1,2], **Yi Liu**[3], **Lankun Wu**[4], **David S. Senchina**[5,6], **Eve S. Wurtele**[4], **Patricia A. Murphy**[3], **Marian L. Kohut**[5,6], and **Joan E. Cunnick**[1,2,5,6]

1*Department of Animal Science, Iowa State University, Ames, Iowa*

eCAM 2005;2(3)285–299
doi:10.1093/ecam/neh107

Review

The Pharmacological Potential of Mushrooms

Ulrike Lindequist, Timo H. J. Niedermeyer and Wolf-Dieter Jülich

Institute of Pharmacy, Ernst-Moritz-Arndt-University, Friedrich-Ludwig-Jahn-Strasse 17,
17487 Greifswald, Germany

This review describes pharmacologically active compounds from mushrooms. Compounds and complex substances with antimicrobial, antiviral, antitumor, antiallergic, immunomodulating, anti-inflammatory, antiatherogenic, hypoglycemic, hepatoprotective and central activities are covered, focusing on the review of recent literature. The production of mushrooms or mushroom compounds is discussed briefly.

Keywords: antiatherogenic – antimicrobial – antitumor – basidiomycetes – bioactive compounds

Table 1. Immunomodulating drugs from mushrooms (selected)

Mushroom scientific name	Mushroom common names	Immunomodulator	Structure of immunomodulator(s)	Selected references
A. brasiliensis	Royal sun Agaricus, Himematsutake	FIo-a-β	(1→6)-β-D-glucan, heteropolysaccharides, polysaccharide–protein complex	(144,145)
		FA-2-b-Md	RNA–protein complex (MW 6200 daltons)	
C. volvatus		H-3-B	(1→3)-β-D-glucan	(146)
F. velutipes	Winter mushroom, Enokitake	Flammulin	Protein	(147)
G. lucidum	Reishi, Ling Zhi	GLP(AI), Ganopoly, Ganoderans	β-D-glucans, heteropolysaccharides, Glykoproteins	(148)
		Protein LZ 8		
G. frondosa	Maitake, Hen-of-the-Woods	MD-fraction	(1→6)-β-D-glucan with (1→3)-β-D side chains	(46,47)
		Grifolan	(1→3)-β-D-glucan with (1→6)-β-D side chains	(149)
H. caput-medusae Syn. *H. erinaceus*	Lion's Mane, Monkey's Head, Yamabushitake		Glucoxylan; Heteroxyloglucan, Glucoxylan–protein complex; Galactoxyloglucan–protein complex	(40)
L. edodes	Shiitake, Golden Oak mushroom	Lentinan, KS-2	(1→3)-β-D-glucan with (1→6)-β-D-glucosyl branches	(39,150)
		LEM	Complex mixture of polysaccharides and lignin	
Lentinus strigellus			Polysaccharides	(151)
P. linteus			Polysaccharides	(87,152)
S. commune		Schizophyllan, Sonifilan, SPG	(1→3)-β-D-glucan with (1→6)-β-D-glucosyl branches	(5,49)

Journal of Traditional and Complementary Medicine 6 (2016) 424–430

Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: http://www.elsevier.com/locate/jtcme

Original article

Enhancement of the Th1-phenotype immune system by the intake of Oyster mushroom (Tamogitake) extract in a double-blind, placebo-controlled study

Aiko Tanaka, Mie Nishimura, Yuji Sato, Hiroki Sato, Jun Nishihira*

Department of Medical Management and Informatics, Hokkaido Information University, Hokkaido, Japan

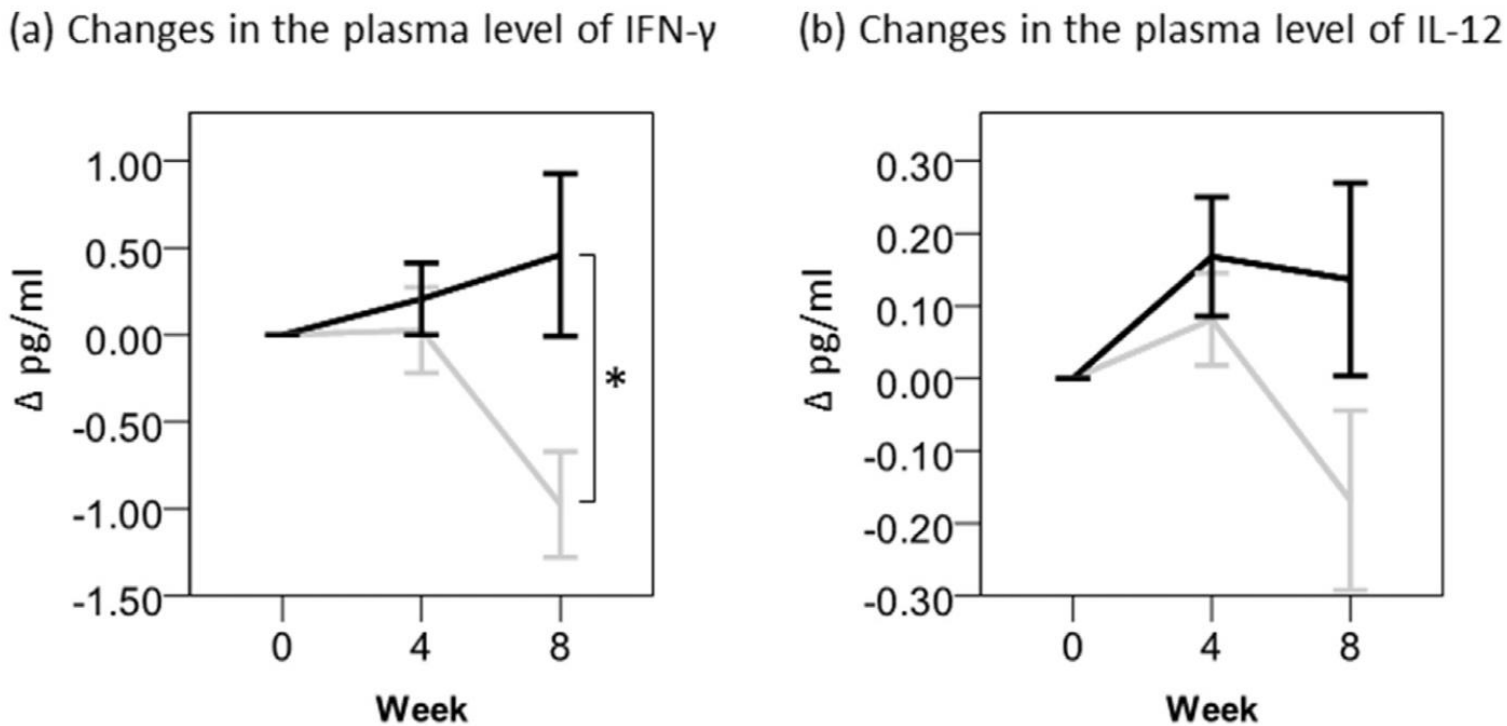

Fig. 2. Changes in the plasma levels of IFN-γ and IL-12. Values are means ± standard errors (SEs). Black bar, Oyster mushroom; Gray bar, placebo. Blood samples were collected at weeks 0, 4 and 8. The plasma levels of IFN-γ and IL-12 were measured as described in "Materials and Methods." The statistical analysis was carried out by SPSS. *Statistically significant, *P* value less than 0.05.

biomedicines

MDPI

Article

Beyond the Biological Effect of a Chemically Characterized Poplar Propolis: Antibacterial and Antiviral Activity and Comparison with Flurbiprofen in Cytokines Release by LPS-Stimulated Human Mononuclear Cells

Paolo Governa [1], Maria Grazia Cusi [2], Vittoria Borgonetti [3], José Mauricio Sforcin [4], Chiara Terrosi [2], Giulia Baini [5], Elisabetta Miraldi [5] and Marco Biagi [5,*]

Antiviral Activity of Propolis Against A/PR/8 H1N1 Influenza Virus

Table 5. Anti-neuraminidase activity of PP and oseltamivir.

Sample	IC_{50} (µg/mL)
oseltamivir	5.88 ± 0.89
PP	35.29 ± 4.08

N-acetyl-L-cysteine (NAC) inhibits virus replication and expression of pro-inflammatory molecules in A549 cells infected with highly pathogenic H5N1 influenza A virus

Janina Geiler, Martin Michaelis, Patrizia Naczk, Anke Leutz, Klaus Langer, Hans-Wilhelm Doerr, Jindrich Cinatl

Janina Geiler, Martin Michaelis, Patrizia Naczk, Anke Leutz, Klaus Langer, et al.. N-acetyl-L-cysteine (NAC) inhibits virus replication and expression of pro-inflammatory molecules in A549 cells infected with highly pathogenic H5N1 influenza A virus. Biochemical Pharmacology, Elsevier, 2009, 79 (3), pp.413. 10.1016/j.bcp.2009.08.025 . hal-00538093

Journal of Ethnopharmacology
Volume 257, 15 July 2020, 112316

The old pharmaceutical oleoresin labdanum of *Cistus creticus* L. exerts pronounced *in vitro* anti-dengue virus activity

Kenny Kuchta [a, b], Nguyen Huu Tung [c], Tomoe Ohta [c], Takuhiro Uto [c], Muhareva Raekiansyah [d], Kristina Grötzinger [e], Hans Rausch [f], Yukihiro Shoyama [c], Hans Wilhelm Rauwald [e], Kouichi Morita [d]

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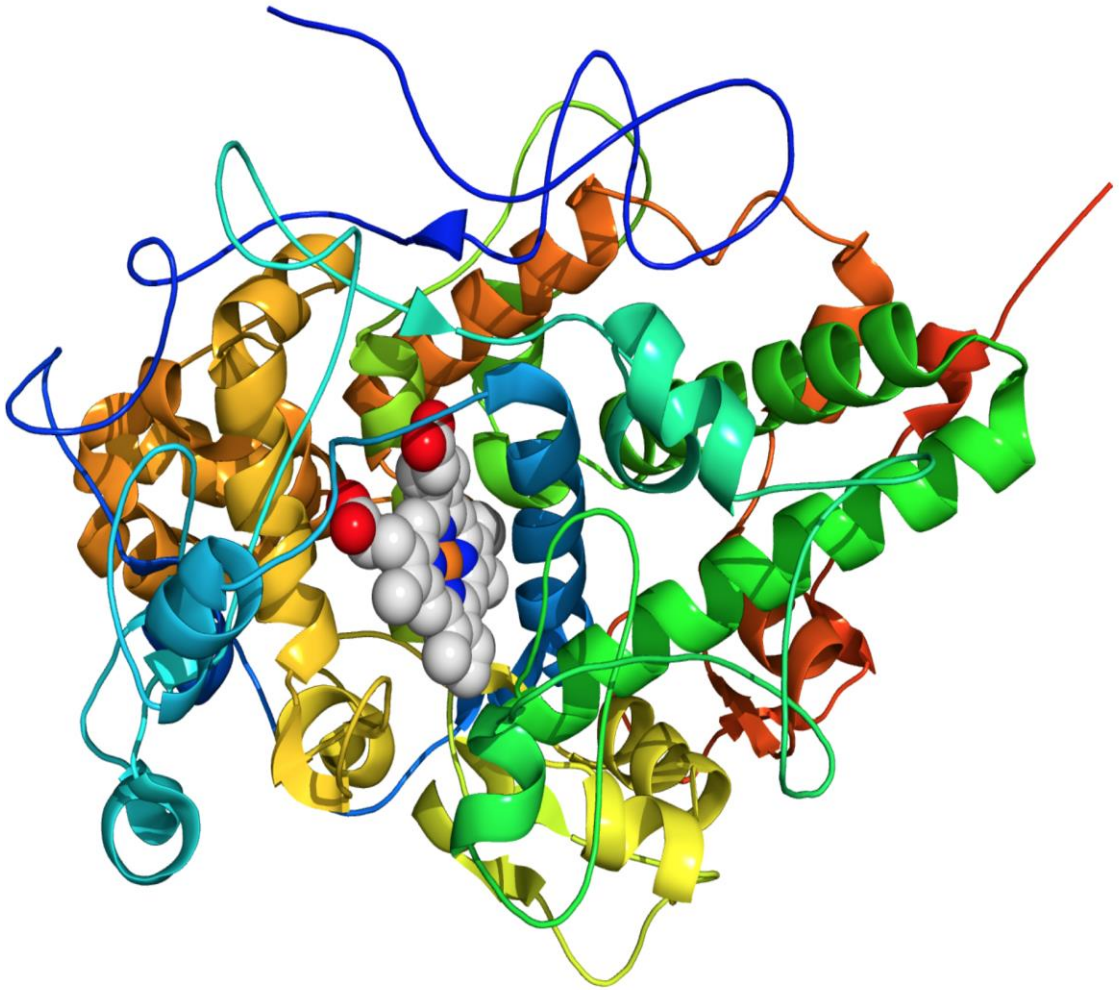
https://doi.org/10.1016/j.jep.2019.112316



https://de.wikipedia.org/wiki/Lactoperoxidase#/media/File:Lactoperoxidase_2R5L.png

Lactoperoxidase

Reaction products of Lactoperoxidase are antimicrobial, antiviral, antiyeast, anti fungi agents

Applications

- Food preservation
- Pre-Harvest crops (Research program with Gembloux University)
- We are also currently working on oral care products

Manual production
⇒In the tank, insert LP-A, substrates and water
⇒Mix
⇒Remove LP-A
⇒Pulverize

		KSCN+KI	KSCN	KI
FUNGI & YEAST	*Colletotrichum lindemuthanium*	++++		
	Fusarium avenaceum	+++		
	Septoria tritici	+		
	Verticillium dahliae	++++		
	Phytophthora infestans	+++		
	Pythium ultimum	++++		
	Colletotrichum musae	++++	0	0
	Pencillium italicum	++++	0	++++
	Penicillium digitatum	++++	+	++++
	Botrytis cinerea	++++		
	Penicillium expansum	++++		
	Plasmopora viticola	++++		
	Candida albicans	++++		

BACTERIA	*Erwinia carotova atroseptica*	++++	+	+
	Pseudomonas syringae pv syringae	++++	+	0
	Erwinia carotova carotova	++++	+	0
	Erwynia amylovora	++++	+	0
	Pseudomonas syringae pv. tomato	++++	+++	+
	Clavibacter michiganensis subsp. michiganensis	++++	++++	+++
	Escherichia coli	++++	0	0
	Xylella fastidiosa subsp. fastidiosa	++++		
	Xylella fastidiosa subsp. multiplex	++++		
	Xylella fastidiosa subsp. Pauca Salento-1	++++		

% of inhibition:

++++:79-100

+++:60-78

++:41-59

+:]0-40

0: no inhibition

/: not tested

Mehltau (mildew)

Control

Treatment 1
Dilution 1/50 of the AS

Treatment 2
Dilution 1/20 of the AS

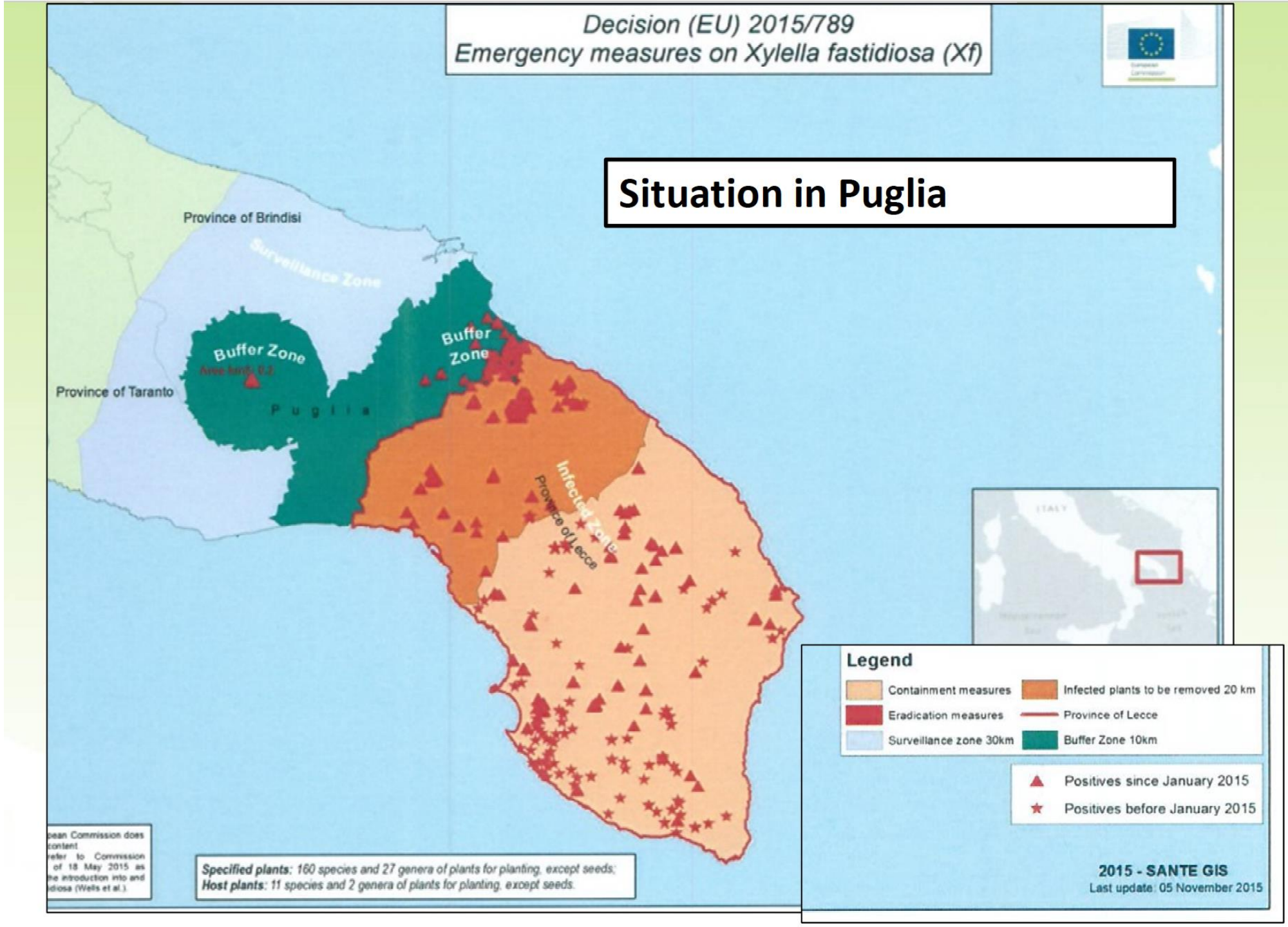
Treatment 3
Dilution 1/5 of the AS

Phytophtora infestans

Témoin

Ions

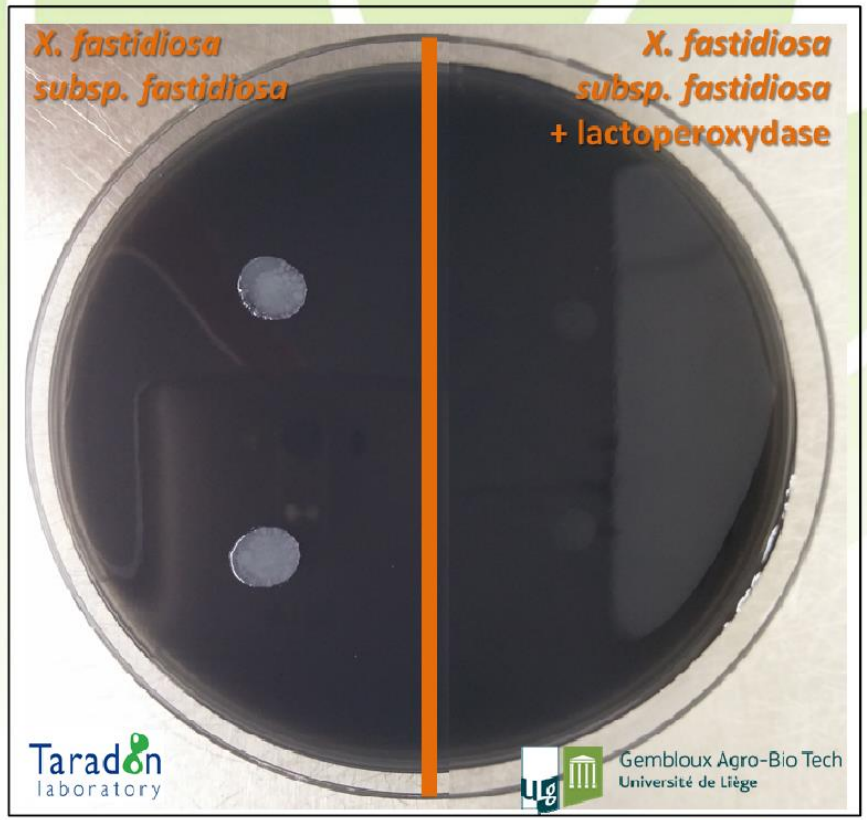
Fongicide


Decision (EU) 2015/789
Emergency measures on Xylella fastidiosa (Xf)
Situation in Puglia
Province of Brindisi
Surveillance Zone
Buffer Zone
Buffer Zone
Province of Taranto
Puglia
Infected Zone
Province of Lecce
Specified plants: 160 species and 27 genera of plants for planting, except seeds;
Host plants: 11 species and 2 genera of plants for planting, except seeds.
Legend
Containment measures
Infected plants to be removed 20 km
Eradication measures
Province of Lecce
Surveillance zone 30km
Buffer Zone 10km
Positives since January 2015
Positives before January 2015
2015 - SANTE GIS
Last update: 05 November 2015

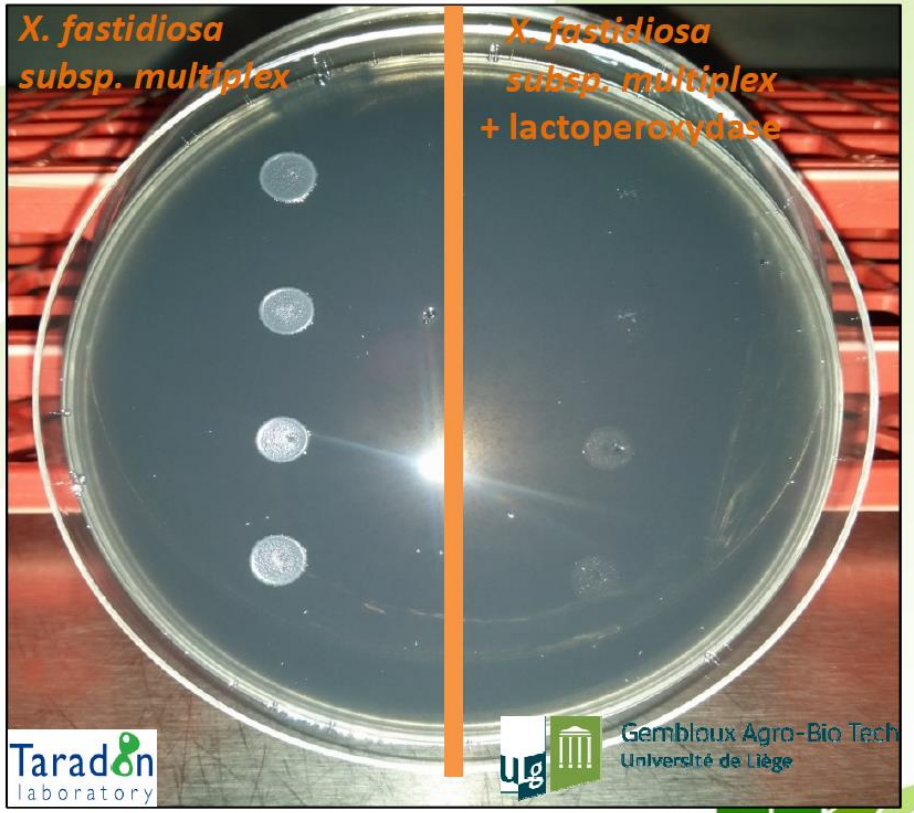

GALLIPOLI 8
Mancaversa 6
MATINO 8
LECCE 45
LIDO PIZZO
Marina di Gallipoli
lido Punta della Suina
marina di Gallipoli

In vitro antibacterial effectiveness of LP-A

***Xylella fastidiosa subsp. fastidiosa* (LMG 17159)**



***Xylella fastidiosa subsp. multiplex* (LMG 09063)**



Taradon laboratory

Gembloux Agro-Bio Tech
Université de Liège

Laboratory of Phytopathology