Borrelien – Populations – Dynamik

Bakterielle Populations – Dynamik umschreibt bakterielle Resistenzmechanismen – wie sich Bakterien (hier Borrelien) dem wirtseigenen Immunsystem entziehen können.

Pleomorphie oder Pleiomorphie heißt die **Vielgestaltigkeit** von Mikroorganismen oder von Zellen der mehrzelligen Organismen. Pleomorphie ist von der Theorie des Pleomorphismus zu unterscheiden.

Synonyme und Beispiele zu **Pleomorphie: Bakterielle Stress-Varianten**, L-Formen, Round forms, Round bodies, Cyst forms, Blebs, Granules, Cell wall deficient forms, Cell wall defective forms, 'dormant' Borrelia stages, round-body propagules (RBs), Borrelien-Metamorphosen etc..

Bacterial Populations - Dynamics describes bacterial resistance mechanisms - such as bacteria (Borrelia here) can evade the host's own immune system itself.

Pleomorphie or Pleiomorphie is the **diversity** of microorganisms or cells of multicellular organisms. Pleomorphie is to be distinguished from the theory of pleomorphism.

Synonyms and examples of pleomorphie: **Bacterial stress variants**, L-shapes, round forms, round bodies, cyst forms, blebs, Granules, Cell wall deficient forms, Cell wall defective forms, 'dormant' Borrelia stages, round-body propagules (RBs), Borrelia metamorphoses etc..

➔ Selbstorganisation, Symbiose http://www.erlebnishaft.de/selbst_muster_nano.pdf

Ehrenberg CG (1835) **Dritter Beitrag zur Erkenntnis grosser Organisation in der Richtung des kleinsten Raumes.** Abh. Dtsch. Akad. Wiss. Berlin Kl. Cham, Geol. Biol.
http://www.e-rara.ch/zut/content/structure/3929922

Canale-Parola E (1977) **Physiology and evolution of spirochetes.** Bacteriol Rev. 41(1), 181–204. PMCID: PMC413998 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC413998/
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC413998/pdf/bactrev00055-0195.pdf
http://mmbr.asm.org/content/41/1/181.full.pdf

Mattman LH (2001) **Cell Wall Deficient Forms: Stealth Pathogens**. CRC Press.
http://books.google.de/books?id=mincr2Hi81UC&pg=PP1&dq=stealth+pathogens+mattman&ei=SbPIRpbPMYjO6wK5sd3fDw&sig=3JHOeHZ3y43lCELNhajk1fpbJhY&redir_esc=y#v=onepage&q=stealth%20pathogens%20mattman&f=false

---

Lewis K. (2007) **Persister cells, dormancy and infectious disease.** Nat Rev Microbiol 5(1), 48–56.

Lewis K. (2010) **Persister cells.** Annu Rev Microbiol 64(1), 357–372.

Barthold SW, Hodzic E, Imai D, Feng S, Yang X, Luft BJ. (2010) **Ineffectiveness of tigecycline against persistent Borrelia burgdorferi.** Antimicrob Agents Chemother 54, 643–651.

Hopf-Seidel (2013) **Neue Behandlungsstrategien bei Borreliose**. Vortrag 17. 5. 2013 in München.
http://www.dr-hopf-seidel.de/mediapool/87/874128/data/Vortrag_TU_Muenchen_17-5-2013.pdf

Feng J, Wang T, Shi W et al. (2014) **Identification of novel activity against Borrelia burgdorferi persisters using an FDA approved drug library**. Emerg Microbes Infect. 3(7), e49. doi: 10.1038/emi.2014.53. Epub 2014 Jul 2. http://www.ncbi.nlm.nih.gov/pubmed/26038747

Huismans BD (2014) **Abwehr- und Escape- Mechanismen der Borrelien gegen das menschliche Immunsystem und gegenüber Antibiotika und Chemotherapeutika. Warum Borrelien infektiös bleiben trotz intensiver antibiotischer Behandlung** http://www.xerlebnishaft.de/escape.pdf

Huismans BD (2014) **Defense and escape mechanisms of Borrelia against the human immune system and against antibiotics and chemotherapeutics. Why Borrelia remains infectious despite intensive antibiotic treatment.** http://www.xerlebnishaft.de/escape_eng.pdf

MacDonald AB, Berger BW, Schwan TB (1990) Clinical Implictions of Delayed Growth of the Lyme Borreliosis Spirochete, Borrelia Burgdorferi. Acta Tropica 48, 89–94.

Feng J, Wang T, Zhang S, Shi W en Zhang Y. (2014) An optimized SYBR Green I/PI assay for rapid viability assessment and antibiotic susceptibility testing for Borrelia burgdorferi. PLoS One. 9(11), e111809.

Feng J, Wang T, Shi W, Zhang S, Sullivan D, Auwaerter PG en Zhang Y. (2014) Identification of novel activity against Borrelia burgdorferi persisters using an FDA approved drug library. Emerg Microbes Infect. 3(7), e49

Feng J, Zhang S, Shi W en Zhang Y. (2015) Persister mechanisms in Borrelia burgdorferi: implications for improved intervention. Emerg Microbes Infect. 4(8), e51.

Feng J, Auwaerter PG en Zhang Y. (2015) Drug combinations against Borrelia burgdorferi persisters in vitro: eradication achieved by using daptomycin, cefoperazone and doxycycline. PLoS One. 10(3), e0117207.

Sharma B, Brown AV, Matluck NE, Hu LT en Lewis K. (2015) Borrelia burgdorferi, the Causative Agent of Lyme Disease, Forms Drug-Tolerant Persister Cells. Antimicrob Agents Chemother. 59(8), 4616-24.

Hodzic E (2015) **Lyme Borreliosis: Is there a preexisting (natural) variation in antimicrobial susceptibility among Borrelia burgdorferi strains?** Bosn J Basic Med Sci. 15(3), 1-13. doi: 10.17305/bjbms.2015.594. http://www.ncbi.nlm.nih.gov/pubmed/26295288

Feng J, Weitner M, Shi W et al. (2015) **Identification of Additional Anti-Persister Activity against Borrelia burgdorferi from an FDA Drug Library.** Posted on September 17, 2015 by Canlyme http://www.mdpi.com/2079-6382/4/3/397/htm

Caskey JR, Embers ME (2015) **Persister Development by B. burgdorferi Populations In Vitro.** ASM Journals, DOI: http://dx.doi.org/10.1128/aac.00883-15 https://www.growkudos.com/articles/10.1128/aac.00883-15

Sharma B, Brown AV, Matluck NE, Hu LT, Lewis K (2015) **Borrelia burgdorferi, the causative agent of Lyme disease, forms drug-tolerant persister cells.** Antimicrob Agents Chemother. pii: AAC.00864-15. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/26014929

Feng J, Zhang S, Shi W en Zhang Y. (2016) **Ceftriaxone Pulse Dosing Fails to Eradicate Biofilm-Like Microcolony B. burgdorferi Persisters Which Are Sterilized by Daptomycin/ Doxycycline/Cefuroxime without Pulse Dosing.** Front Microbiol. 7, 1744.

Feng J, Shi W, Zhang S, Sullivan D, Auwaerter PG en Zhang Y. A (2016) **Drug Combination Screen Identifies Drugs Active against Amoxicillin-Induced Round Bodies of In Vitro Borrelia burgdorferi Persisters from an FDA Drug Library.** Front Microbiol. 7, 743.

Feng J, Weitner M, Shi W, Zhang S en Zhang Y. (2016) **Eradication of Biofilm-Like Microcolony Structures of Borrelia burgdorferi by Daunomycin and Daptomycin but not Mitomycin C in Combination with Doxycycline and Cefuroxime.** Front Microbiol. 7, 62.

Hübner A (2016) **Update: Therapie der chronischen Borreliose**. Ärztliche Fortbildung AUGSBURG http://www.bca-clinic.de/wp-content/uploads/2016/03/Dr_Axel_H%C3%BCbner_Update_Therapie-der-chronischen-Borreliose_27.02.2016.pdf

Hübner A, Huismans BD (2016) **Thoughts and questions of a clinician related to the infection with borrelia and co-infections.** http://tinyurl.com/zjm7gle (Deutsch entspr.) http://tinyurl.com/okf2zzx http://www.grin.com/en/e-book/313377/thoughts-and-questions-of-a-clinician-related-to-the-infection-with-borrelia

---

Feng J, Zhang S, Shi W en Zhang Y. (2017) **Activity of Sulfa Drugs and Their Combinations against Stationary Phase B. burgdorferi In Vitro.** Antibiotics. 6(1). pii: E10.

Populations – Dynamik

Georgilis K, Peacocke M, Klempner MS (1992) **Fibroblasts protect the Lyme disease spirochete, Borrelia burgdorferi, from ceftriaxone in vitro.** J Infect Dis. 166(2), 440-4. https://www.ncbi.nlm.nih.gov/pubmed/1634816

Liang FT, Jacobs MB, Bowers LC et al. (2002) **An Immune Evasion Mechanism for Spirochetal Persistence in Lyme Borreliosis.** J Exp Med. 195(4), 415–422. doi: 10.1084/jem.20011870 PMCID: PMC2193615 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2193615/

Burkart T (2006) **Motilität und Infektion** Teil VII
http://www.ifik.unibe.ch/unibe/medizin/ifik/content/e7961/e8088/e8446/e8459/07motilitt_und_infektionen_vii_ger.pdf

Marie Kroun (2007) **Microscopy, Culture or PCR-verified cases of persistent [seronegative] Lyme Borreliosis**. http://lymerick.net/persistent-borreliosis.html

Kraiczi P (2011) **Überleben im humanen Wirt: Wie sich Borrelien der Immunabwehr entziehen**. Der Mikrobiologe 21(6), 186-192 http://bibnet.org/vufind/Record/ccmed952197517

Barbour A. (2012) **Remains of infection.** Journal of Clinical Investigation 122(7), 2344-2346
https://dl.dropboxusercontent.com/u/47501788/Remain%20of%20Infection%202012%20Barbour%2CA%20G.pdf

Berntson K (2013) **Review of evidence for immune evasion and persistent infection in Lyme disease**. Int. J. of Gen. Med. Volume 2013, 6 Pages 291 - 306
http://www.dovepress.com/review-of-evidence-for-immune-evasion-and-persistent-infection-in-lyme-peer-reviewed-article-IJGM

Salman-Dilgimen A, Hardy P-O, Radolf JD, Caimano MJ, Chaconas G (2013) **HrpA, an RNA Helicase** Involved in RNA Processing, Is Required for Mouse Infectivity and Tick Transmission of the Lyme Disease Spirochete. PLoS Pathog 9(12): e1003841. doi:10.1371/journal.ppat.1003841
http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1003841

Kraiczy P (2013) **Immunescape-Mechanismen von Borrelia burgdorferi, dem Erreger der Lyme Borreliose. https://www.kgu.de/?id=1764**

Pilloux L, Greub G (2014) ESCMID postgraduate technical workshop on **intracellular bacteria**: from biology to clinic. Microbes Infect. pii: S1286-4579(14)00031-8. doi: 10.1016/j.micinf.2014.03.002.
http://www.ncbi.nlm.nih.gov/pubmed/24727388
„… Bartonella, Chlamydia, Coxiella, Ehrlichia, Listeria, Parachlamydia, Riskettsia, and Waddlia."

➔ (2014) **Excerpts from interview with Willy Burgdorfer, Ph.D., Lyme disease discoverer**
https://www.youtube.com/watch?v=QLIWSkQdCmU&feature=share&fbclid=IwAR0smhE6wJeI3myxzjQ36n-xgA0iXDIgsx6bGtuLREUaUx8IZ2UKAU-JwL8

Berghoff W (2014) **Abwehrmechanismen von Borrelia burgdorferi (Bb) gegenüber dem humanen Immunsystem.**
http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-b_Abwehrmechanismen_von_Bb.pdf

Smith AJ, Oertle J, Prato D (2014) **Borrelia burgdorferi: Cell Biology and clinical Manifestations in Late Chronic Lyme**. Open Journal of Medical Microbiology. 4, 210-223 Full-Text PDF HTML XML

Wallich R (2015) **Immune escape mechanisms of Borrelia and vaccines against Lyme disease.** Nationales Lyme-Borreliose-Symposium. NaBoS 2015 Erfurt, Freitag, 20. März 2015

Hyde JA (2017) **Borrelia burgdorferi Keeps Moving and Carries on: A Review of Borrelial Dissemination and Invasion.** Front. Immunol., https://doi.org/10.3389/fimmu.2017.00114 http://journal.frontiersin.org/article/10.3389/fimmu.2017.00114/full

1. Pleomorphie http://www.erlebnishaft.de/stressvar1.pdf
2. Aufenthalt von Borrelien – Varianten in den Zellen des Wirtsorganismus, Angiopathie http://www.xerlebnishaft.de/angiopathie.pdf
3. Änderung der Borrelien – Oberflächen – Immunogenität, Shedding, Adhäsionsmoleküle
4. Sequestrierung von Wirts – Antikörpern
5. Depression der CD57- Fraktion der natürlichen Killerzellen http://www.erlebnishaft.de/cd57.pdf
6. Depression von Komplement – Fraktionen http://www.xerlebnishaft.de/complement.pdf
7. Biofilm Bildung http://www.erlebnishaft.de/biofilmmed.pdf
8. Horizontaler Gentransfer und Plasmidverlust http://www.erlebnishaft.de/gentransfer.pdf
9. Bakterieller Efflux – Mechanismus

Pleomorphie

MacDonald AB. (1988) **Concorrent neocortical Borreliosis and Alzheimer´s disease: Demonstration of a spirochetal cyst form.** Ann NY Acad Sci 539, 468-470 **In Vivo**

Hulinska D (1989) **Ultrastructure of Borrelia burgdorferi in tissues of patients with Lyme disease.** J Basic Microbiol, 29, 73-83 **In Vivo**

Aberer E, Duray PH (1991) **Morphology of Borrelia burgdorferi**: structural patterns of cultured borreliae in relation to staining methods. J Clin Microbiol. 29(4), 764–772 **In Vivo**

Hulinska D (1994) **Electron microscopy of Langerhans cells and Borrelia burgdorferi in Lyme disease patients.** Zbl Bakt, 280, 348-49 **In Vivo**

Coyle PK; 1995 **Detection of Borrelia burgdorferi-specific antigen in antibody-negative cerebrospinal fluid** Neurology, 45:2010-14 **In Vivo**

Aberer E (1996) **Heterogeneity of Borrelia burgdorferi in the skin.** Am J Dermatopathology, 18(6), 571-9 **In Vivo**

Aberer E (1997) **Why is chronic Lyme borreliosis chronic?** Clinical Infectious Diseases, 25 (Suppl 1), S64-S7 **In Vivo**

Gruntar I, Malovrh T, Murgia R, Cinco M (2001) **Conversion of Borrelia garinii cystic forms to motile spirochetes in vivo** APMIS 109(5) 383-388

Brorson O (2001) **Association between multiple sclerosis and cystic structures in cerebrospinal fluid.** Infection, 29(6), 315 **In Vivo**

Miklossy J, Kasas S, Zurn AD, McCall S, Yu S, McGeer PL. (2008) **Persisting atypical and cystic forms of Borrelia burgdorferi** and local inflammation in Lyme neuroborreliosis. J Neuroinflammation. 25, 5, 40,1-18. http://www.jneuroinflammation.com/content/5/1/40 **In Vivo**

Barbour A (2012) **Remains of infection**. J. Clin. Invest. http://www.jci.org/articles/view/63975 **In Vivo**

MacDonald A. (2013) **Review:** Borrelia burgdorferi **tissue morphologies**, **Imaging methodologies, and Atlases of shapes**. University of New Haven. Borrelia Research Laboratory. [in press] **In Vivo**

MacDonald A. (2013) **Borrelia burgdorferi tissue morphologies and imaging methodologies**. European Journal of Clinical Microbiology & Infectious Diseases 32(8), 1077-1082 http://link.springer.com/article/10.1007/s10096-013-1853-5#page-1 **In Vivo**

Balfour A (1911) **The Infective Granule In Certain Protozoal Infections, As Illustrated By The Spirochaetosis of Sudanese Fowl**, British Medical Journal 752. http://lymerick.net/1911-Balfour.htm

Gross J (1912) **Über Systematik, Struktur und Forpflanzung der Spironemacea.** Zentralbl. f. Bakt. Unz. 65, Heft 1-3.

Spirochetes and their cyst /granule / L-Form. **Leishman's drawings of Borrelia duttoni 'granule's'** (1918) Ann Inst Pasteur 32, 49-59 1918-Leishman-Granule.htm
http://lymerick.net/Spirochetal-cysts.htm

Warthin AS, Olson RE (1930) The **granular transformation of Spirochaeta Pallida** in aortic focal lesions. Am J Syphilis 14, 433-437

Stokes JH, Garner VC (1931) Dermatology and Syphilis. 181 - Issue 3
http://journals.lww.com/amjmedsci/Citation/1931/03000/Granular_Transformation_of_Spirochaeta_Pallida_in.39.aspx

Hampp EG, Scott DB, Wyckoff RWG (1948) Morphologic characteristics of certain cultured strains of oral spirochetes and **Treponema pallidum** as revealed by the electron microscope. J Bacteriol 56, 755-69 http://lymerick.net/1948-Hampp.htm

DeLAMATER ED, WIGGALL RH, HAANES M. (1950) **Studies on the life cycle of spirochetes**; the life cycle of the Nichols pathogenic Treponema pallidum in the rabbit testis as seen by phase contrast microscopy. J Exp Med. 92(3), 239–246. [PMC free article] [PubMed]

DeLamater ED, Wiggall RH, Haanes M (1950) STUDIES ON THE **LIFE CYCLE OF SPIROCHETES** IV. THE LIFE CYCLE OF THE NICHOLS PATHOGENIC TREPONEMA PALLIDUM IN THE RABBIT TESTIS AS VISUALIZED BY MEANS OF STAINED SMEARS. J Exp Med. 92(3), 247–252. PMCID: PMC2136032 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2136032/

DELAMATER ED, NEWCOMER VD, et al. (1950) Studies on the **life cycles of spirochetes**; the use of phase contrast microscopy. Am J Syph Gonorrhea Vener Dis. 34(2), 122–125. [PubMed]

DELAMATER ED, HAANES M, WIGGALL RH, PILLSBURY DM (1951) **STUDIES ON THE LIFE CYCLE OF SPIROCHETES.** THE JOURNAL OF INVESTIGATIVE DERMATOLOGY 16, 231-56 http://lymerick.net/1951-Delamater.htm

Ovchinnikov NM (1951 -1983) http://scholar.google.com/scholar?hl=en ... v+syphilis

Kurtti TJ, Munderloh UG, Johnson RC, et al. (1987) **Colony formation and morphology in Borrelia burgdorferi**. J Clin Microbiol 25(11):2054-8.

MacDonald AB. (1988) **Concorrent neocortical Borreliosis and Alzheimer´s disease: Demonstration of a spirochetal cyst form.** Ann NY Acad Sci 539, 468-470 **In Vivo**

Preac Mursic V, Weber K, Pfister HW, Wilske B et al. (1989) Formation and cultivation of Borrelia burgdorferi spheroplast **L-Form variants**. Infection 17, 355-359

Garon CF, Dorward DW, Corwin MD (1989) **Structural features of Borrelia burgdorferi**—the Lyme disease spirochete: silver staining for nucleic acids. Scanning Microsc Suppl 3, 109-115.

Hulinska D (1989) **Ultrastructure of Borrelia burgdorferi in tissues of patients with Lyme disease.** J Basic Microbiol, 29, 73-83. **In Vivo**

MacDonald AB, Berger BW, Schwan TG. (1990) Clinical implications of delayed growth of the Lyme

borreliosis spirochete, Borrelia burgdorferi. Acta Trop 48(2), 89-94.

Aberer E, Duray PH (1991) **Morphology of Borrelia burgdorferi**: structural patterns of cultured borreliae in relation to staining methods. J Clin Microbiol. 29(4), 764–772. **In Vivo** http://www.ncbi.nlm.nih.gov/pmc/articles/PMC269867/

Schaller M, Neubert U (1994) **Ultrastructure of Borrelia burgdorferi** after exposure to benzylpenicillin. Infection 22 (6), 401–406.

Hulinska D (1994) **Electron microscopy of Langerhans cells and Borrelia burgdorferi in Lyme disease patients.** Zbl Bakt, 280, 348-49 **In Vivo**

Bruck DK, Talbot ML, Cluss RG, Boothby JT (1995) Ultrastructural characterization of the stages of spheroplast preparation of **Borrelia burgdorferi**. J Microbiol Methods 23, 219–228.

Brorson O, Brorson SH (1995) **In Vitro Conversion** of Borrelia burgdorferi to Cystic Forms in Spinal Fluid, and Transformation to Mobile Spirochetes by Incubation in BSK-H Medium. Infection 26(3) 144-150

Coyle PK (1995) **Detection of Borrelia burgdorferi-specific antigen in antibody-negative cerebrospinal fluid** Neurology, 45:2010-14 **In Vivo**

Kersten A, Poitschek C, Rauch S, Aberer E. (1995) **Effects of penicillin, ceftriaxone, and doxycycline on morphology of Borrelia burgdorferi**. Antimicrob Agents Chemother. 39(5), 1127-33 http://aac.asm.org/content/39/5/1127.full.pdf http://www.ncbi.nlm.nih.gov/pubmed/7625800
„According to experiences from studies with other spirochetes it is suggested that encysted borreliae, granules, and the remaining blebs might be responsible for the ongoing antigenic stimulus leading to complaints of chronic Lyme borreliosis.“

Preac-Mursic V, Wanner G, Reinhardt S, Wilske B, Busch U, Marget W (1996) Formation and cultivation of **Borrelia burgdorferi spheroplast L-form variants**. Infection 24, 218–226. http://www.ncbi.nlm.nih.gov/pubmed/8852456

Aberer E (1996) **Heterogeneity of Borrelia burgdorferi in the skin.** Am J Dermatopathology, 18(6), 571-9 **In Vivo**

Aberer E (1997) **Why is chronic Lyme borreliosis chronic?** Clinical Infectious Diseases, 25 (Suppl 1), S64-S7 **In Vivo**

Brorson O, Brorson SH (1997) **Transformation of cystic forms of Borrelia burgdorferi to normal mobile spirochetes**. Infection 25(4) 240-246

Domingue GJ, S, Woody H (1997). Bacterial persistence and expression of disease. Clin. Microbiol. Rev. 10(2), 320-344.

Wainwright M (1997) **Extreme Pleomorphism and the bacterial life cycle: A forgotten controversy**. Perspectives in Biology and Medicine 40, 407-414

Brorson O, Brorson SH (1998) In vitro conversion of Borrelia burgdorferi to **cystic forms in spinal fluid**, and transformation to mobile spirochetes by incubation in BSK-H medium. Infection 26(3) 144-150

Brorson O, Brorson SH (1999) **A rapid method for generating cystic forms of Borrelia burgdorferi, and their reversal to mobile spirochetes**. APMIS 106, 1131–41.

Burgdorfer W (1999) The Complexity of Arthropod-borne Spirochetes (Borrelia spp) FROM 12th International Conference on Lyme Disease and Other Spirochetal and Tick-Borne Disorders Day 1 - April 9 http://www.canlyme.com/burgdorfer.html

Beermann C, Wunderli-Allenspach H, Groscurth P, Filgueira L (2000) Lipoproteins from Borrelia burgdorferi Applied in **Liposomes** and Presented by Dendritic Cells Induce $CD8^+$ T-Lymphocytes in Vitro. Cellular Immunology. 201(2), 124–131 http://www.sciencedirect.com/science/article/pii/S000887490091640X

Alban PS, Johnson PW, Nelson DR. (2000) Serum-starvation-induced changes in protein synthesis and morphology of Borrelia burgdorferi. Microbiology 146, 119–127.

Gruntar I, Malovrh T, Murgia R, Cinco M (2001) **Conversion of Borrelia garinii cystic forms to motile spirochetes in vivo** APMIS 109(5) 383-388

Brorson O (2001) **Association between multiple sclerosis and cystic structures in cerebrospinal fluid.** Infection, 29(6), 315 **In Vivo**

Mattman LH (2001) **Cell Wall Deficient Forms: Stealth Pathogens**. CRC Press. Inc Boca Raton Fla

Murgia R, Piazetta C, Cinco M. (2002) **Cystic forms of Borrelia burgdorferi sensu lato**: induction, development, and the role of RpoS. Wien. Klein. Wochenschr 114(13-14) 574-579

Gruntar I, Malovrh T, Murgia R, Cinco M. (2003) Lyme Disease Studies on the **Cystic Form of Borrelia burgdorferi Mechanisms of Persistence**. http://www.lymeinfo.net/medical/LDCysts.pdf

Murgia R, Cinco M. (2004) **Induction of cystic forms by different stress conditions in Borrelia burgdorferi**. APMIS 112(1), 57-62

Embers ME, Ramamoorthy R, Philipp MT. (2004) Survival strategies of Borrelia burgdorferi, the etiologic agent of Lyme disease. Microbes Infect 6,312–8.

Fritzsche M (2005) Chronic Lyme borreliosis at the root of multiple sclerosis--is a cure with antibiotics attainable? [Journal Article] Med Hypotheses 64(3), 438-48.

MacDonald AB (2006) **A life cycle for Borrelia spirochetes?.** Medical Hypotheses. 67(4), 810-818 http://www.theoneclickgroup.co.uk/documents/Borreliosis/A%20life%20cycle%20for%20Borrelia%20spirochetes.htm

MacDonald AB (2006) **Spirochetal cyst forms** in neurodegenerative disorders,…hiding in plain sight. Med Hypotheses. 67(4), 819-32. http://www.ncbi.nlm.nih.gov/pubmed/16828236

MacDonald AB (2006) Plaques of Alzheimer's disease originate from **cysts of Borrelia burgdorferi**, the Lyme disease spirochete. Med Hypotheses 67(3), 592-600. http://www.joethetick.com/wp-content/uploads/2009/10/Alzheimer_Plaques_Borrelia_Cysts_Med_Hypothesis_May_3.pdf

Lewis K (2007) **Persister cells, dormancy and infectious disease**, Nature Reviews Microbiology 5(1) http://www.nature.com/nrmicro/journal/v5/n1/abs/nrmicro1557.html

Cruz AR, Moore MW, La Vake CJ et al. (2008) Phagocytosis of Borrelia burgdorferi, the Lyme disease spirochete, potentiates innate immune activation and induces apoptosis in human monocytes. Infect Immun 76, 56-70.

Miklossy J, Kasas S, Zurn AD, McCall S, Yu S, McGeer PL. (2008) **Persisting atypical and cystic forms of Borrelia burgdorferi** and local inflammation in Lyme neuroborreliosis. J Neuroinflammation. 25, 5, 40,1-18. http://www.jneuroinflammation.com/content/5/1/40 **In Vivo**

Mattman L.H (2009). **Cell Wall Deficient Forms: Stealth Pathogens**. CRC Press. ISBN-10: 0849335787 ISBN-13: 978-0849335785

Skotarczak B (2009) Adaptation factors of Borrelia for host and vector. Ann Agric Environ Med 16, 1-8.

Brorson Ø, Brorson SH, Scythes J, MacAllister J, Wier A, Margulis L (2009) Destruction of spirochete Borrelia burgdorferi round-body propagules (RBs) by the antibiotic Tigecycline Proceedings of the National Academy of Sciences of the United States of America. 106(44), 18656-18661.

Stricker RB (2009) Challenge to 'Implausibility' of Persistent B. burgdorferi Infection--Contesting the Underlying Basis for Treatment Limitations for Early and Late Lyme Disease and Post-Lyme Syndrome. This challenge is based on Stricker RB. Counterpoint: Long-term antibiotic therapy improves persistent symptoms associated with Lyme disease. Clin Infect Dis. 2007 Jul 15, 45(2), 149-57. Challenge to the following statement from 2006 IDSA Guidelines (p. 1118).
http://www.ilads.org/lyme_disease/written_testimony/6%20Stricker-Challenge%20to%20Implausibility.pdf

Brorson Ø, Brorson SH, Scythes J, et al. (2009) Destruction of spirochete Borrelia burgdorferi round-body propagules (RBs) by the antibiotic tigecycline. Proc Natl Acad Sci U S A 106(44), 18656–18661.

Samiya Al-Robaiy S, Dihazi H, Kacza J et al. (2010) Metamorphosis of Borrelia burgdorferi organisms – RNA, lipid and protein composition in context with the spirochetes' shape. Journal of Basic Microbiology 2010, *50*, 1–13

de Oliveira A, Fonseca AH, da Costa CM et al. (2010) Growth, cysts and kinetics of Borrelia garinii (Spirochaetales: Spirochaetacea) in different culture media. 12 Mem Inst Oswaldo Cruz 105, 717-9.

Binder SC, Telschow A, Meyer-Herman M. (2012) Population dynamics of Borrelia burgdorferi in Lyme disease. Frontiers in Microbiology | Microbial Immunology. 3(104), 2
http://www.frontiersin.org/Microbial_Immunology/10.3389/fmicb.2012.00104/abstract

Bockenstedt LK, Gonzalez DG, Haberman AM (2012) Spirochete antigens persist near cartilage after murine Lyme borreliosis therapy. J Clin Invest. 122(7), 2652–2660. [PMC free article] [PubMed]
http://www.jci.org/articles/view/58813

Barbour A. (2012) **Remains of infection.** Journal of Clinical Investigation 122(7), 2344-2346
doi: 10.1172/JCI63975 PMCID: PMC3386833 PMID: 22728928
https://dl.dropboxusercontent.com/u/47501788/Remain%20of%20Infection%202012%20Barbour%2CA%20G.pdf
http://www.jci.org/articles/view/63975
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3386833/#__ffn_sectitle

Lemgruber L, Brenner C, Kudryashev M (2012) **Formation of 'dormant' Borrelia stages**.
http://www.emc2012.org.uk//documents/Abstracts/Abstracts/EMC2012_0697.pdf

MacDonald A. (2013) Review: Borrelia burgdorferi tissue morphologies, Imaging methodologies, and Atlases of shapes. University of New Haven. Borrelia Research Laboratory. [in press] **In Vivo**

MacDonald A. (2013) **Shape shifting Form Metamorphosis Non-Spiral Borrelia An Image Gallery**
https://www.dropbox.com/s/fq6afgippp9fvls/July%2014%20PDF%20of%20shape%20shifted%20borelia%20lecture%20ABM.pdf
Same document as video http://www.youtube.com/watch?v=pqKaM_J7KDI

MacDonald A (2013) **Round Forms of Borrelia burgdorferi**. Survival of the Microbe and Attack Models. http://alzheimerborreliosis.net/wp-content/uploads/2012/10/April-12-2012-PDF-Cystic-Borrelia-Manifesto.pdf

Lantos PM, Auwaerter PG, Wormser GP (2013) A Systematic Review of **Borrelia burgdorferi Morphologic Variants Does Not Support a Role in Chronic Lyme Disease**. Clin Infect Dis.
http://cid.oxfordjournals.org/content/early/2013/12/12/cid.cit810.abstract
"In the context of the broader medical literature it is not currently possible to ascribe a pathogenic role to morphologic variants of B. burgdorferi in either typical manifestations of Lyme disease or in other chronic disease states that are often labeled chronic Lyme disease. There is no clinical literature to justify specific treatment of B. burgdorferi morphologic variants".

Feng J, Wang T, Shi W et al (2014) **Identification of novel activity against Borrelia burgdorferi persisters using an FDA approved drug library**. Emerging Microbes and Infections. 3, e491-8
[Daptomycin, Cefoperazone, Carbomycin (Veterinärmed. Makrolid), Clofacimin (in Dt. keine Zulassung)]

Miclossy J (2014) http://miklossy.ch/

Feng J, Weitner M, Shi W et al. (2015) **Identification of Additional Anti-Persister Activity against Borrelia burgdorferi from an FDA Drug Library.** Antibiotics 4, 397-410;
doi:10.3390/antibiotics4030397 www.mdpi.com/2079-6382/4/3/397/pdf

"Many antimicrobial agents (antibiotics, antivirals, antifungals, anthelmintics or antiparasitics) used for treating other infections were found to have better activity than the current Lyme antibiotics. These include antibacterials such as rifamycins (3-formal-rifamycin, rifaximin, rifamycin SV), thiostrepton, quinolone drugs (sarafloxacin, clinafloxacin, tosufloxacin), and cell wall inhibitors carbenicillin, tazobactam, aztreonam; antifungal agents such as fluconazole, mepartricin, bifonazole, climbazole, oxiconazole, nystatin; antiviral agents zanamivir, nevirapine, tilorone; antimalarial agents artemisinin, methylene blue, and quidaldine blue; antihelmintic and antiparasitic agents toltrazuril, tartar emetic, potassium antimonyl tartrate trihydrate, oxantel, closantel, hycanthone, pyrimethamine, and tetramisole. Interestingly, drugs used for treating other non-infectious conditions including verteporfin, oltipraz, pyroglutamic acid, pidolic acid, and dextrorphan tartrate, that act on ESS the glutathione/γ-glutamyl pathway involved in protection against free radical damage, and also the antidepressant drug indatraline, were found to have high activity against stationary phase B. burgdorferi. Among the active hits, agents that affect cell membranes, energy production, and reactive oxygen species production are more active against the *B. burgdorferi* persisters than the commonly used antibiotics that inhibit macromolecule biosynthesis".

Meriläinen L, Herranen A, Schwarzbach A, Gilbert L (2015) **Morphological and biochemical features of Borrelia burgdorferi pleomorphic forms.** Microbiology. pii: mic.0.000027. doi: 10.1099/mic.0.000027. http://mic.sgmjournals.org/content/early/2015/01/05/mic.0.000027 http://www.ncbi.nlm.nih.gov/pubmed/25564498
« However, the round bodies displayed lower metabolic activity compared to spirochetes. Furthermore, our results indicated that the different pleomorphic variants were distinguishable by having unique biochemical signatures. Consequently, pleomorphic B. burgdorferi should be taken into consideration as being clinically relevant and influence the development of novel diagnostics and treatment protocols. »

Sharma B, Brown AV, Matluck NE, Hu LT, Lewis K (2015) **Borrelia burgdorferi, the causative agent of Lyme disease, forms drug-tolerant persister cells.** Antimicrob Agents Chemother. pii: AAC.00864-15. http://www.ncbi.nlm.nih.gov/pubmed/26014929#
„After addition of ceftriaxone, the antibiotic was washed away, surviving persisters were allowed to resuscitate, and antibiotic was added again. Four pulse-doses of ceftriaxone killed persisters, eradicating all live bacteria in the culture".

Feng J, Shi W, Zhang Sh, Zhang Y (2015) **Persister mechanisms in *Borrelia burgdorferi*: implications for improved intervention.** Emerg Microbes Infect. 4(8), e51. Published online 2015 Aug 19. doi: 10.1038/emi.2015.51 PMCID: PMC4576169 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4576169/

Meriläinen L, Brander H, Herranen A, Schwarzbach A, Gilbert L (2016) **Pleomorphic forms of Borrelia burgdorferi induce distinct immune responses**. Microbes and Infection, doi: 10.1016/j.micinf.2016.04.002 http://www.sciencedirect.com/science/article/pii/S1286457916300296 http://www.ncbi.nlm.nih.gov/pubmed/27139815
«Here, we demonstrated that round bodies were processed differently in differentiated macrophages, consequently inducing distinct immune responses compared to spirochetes in vitro. Colocalization analysis indicated that the F-actin participates in internalization of both forms. However, round bodies end up less in macrophage lysosomes than spirochetes suggesting that there are differences in processing of these forms in phagocytic cells. Furthermore, round bodies stimulated distinct cytokine and chemokine production in these cells. We confirmed that spirochetes and round bodies present different protein profiles and antigenicity. In a Western blot analysis Lyme disease patients had more intense responses to round bodies when compared to spirochetes. These results suggest that round bodies have a role in Lyme disease pathogenesis. «

Jie Feng, Wanliang Shi, Shuo Zhang et al. (2016) **A Drug Combination Screen Identifies Drugs Active against Amoxicillin-Induced Round Bodies of In Vitro Borrelia burgdorferi Persisters from an FDA Drug Library.** Front. Microbiol, http://dx.doi.org/10.3389/fmicb.2016.00743 http://journal.frontiersin.org/article/10.3389/fmicb.2016.00743/full
"Drug candidates that are preferentially active against the round bodies include artemisinin, ciprofloxacin, nifuroxime, fosfomycin, chlortetracycline, and some sulfa drugs. We found that triple drug combinations artemisinin/cefoperazone/doxycycline, daptomycin/sulfachlorpyridazine/doxycycline and daptomycin/cefoperazone/ doxycycline had among the best activity against both the round body model and the stationary phase persister model. … stationary phase *B. burgdorferi* persisters".

Vancová M, Rudenko N, Vaněček J et al. (2017) **Pleomorphism and Viability of the Lyme Disease Pathogen Borrelia burgdorferi Exposed to Physiological Stress Conditions: A Correlative Cryo-Fluorescence and Cryo-Scanning Electron Microscopy Study.**

Front. Microbiol., https://doi.org/10.3389/fmicb.2017.00596
http://journal.frontiersin.org/article/10.3389/fmicb.2017.00596/full

Jie Feng, Tingting Li, Rebecca Yee, Yuting Yuan, Chunxiang Bai, Menghua Cai, Wanliang Shi, Monica Embers, Cory Brayton, Harumi Saeki, Kathleen Gabrielson, Ying Zhang (2019) **Stationary Phase Persister/Biofilm Microcolony of Borrelia burgdorferi Causes More Severe Disease in a Mouse Model of Lyme Arthritis: Implications for Understanding Persistence, Post-Treatment Lyme Disease Syndrome (PTLDS), and Treatment Failure.** Discovery Medicine 27(148)
http://www.discoverymedicine.com/Jie-Feng/2019/03/persister-biofilm-microcolony-borrelia-burgdorferi-causes-severe-lyme-arthritis-in-mouse-model/
or http://tinyurl.com/y4ahku6q

Rudenko N, Golovchenko M, Kybicova K, Vancova M (2019) **Metamorphoses of Lyme disease spirochetes: phenomenon of Borrelia persisters.**Parasites & Vectors **12,** 237
https://doi.org/10.1186/s13071-019-3495-7
https://parasitesandvectors.biomedcentral.com/articles/10.1186/s13071-019-3495-7
https://www.researchgate.net/publication/333134048_Metamorphoses_of_Lyme_disease_spirochetes_phenomenon_of_Borrelia_persisters

Baker PJ (2020) **A Review of Antibiotic-Tolerant Persisters and Their Relevance to Post-Treatment Lyme Disease Symptoms.** Am J Med. pii: S0002-9343(20)30011-5. doi: 10.1016/j.amjmed.2019.12.007. https://www.ncbi.nlm.nih.gov/pubmed/31926865
« The results described in the present work suggest that the presence of persisters can best be explained by classic biochemical kinetics and that there are alternative explanations for this phenomenon that appears to have no clinical significance ».

Videosequenzen:
MacDonald A (2013) **Non Spiral Borrelia Part I Explanation of Shape shifting and Form Metamorphosis of Spirochetes**. http://www.youtube.com/watch?v=pqKaM_J7KDI
MacDonald A (2013) **Part II Cystic Borrelia and Related Topics Including Round Body Infections of the Brain** http://www.youtube.com/watch?v=1ojq_2-HlNg&feature=youtu.be
MacDonald A (2013) Dr. Alan MacDonald- Pathologist Lyme Disease Expert - **Part III**
http://www.youtube.com/watch?v=FEjNMlNM3l8
http://lymerick.net/videomicroscopy.htm
http://lymerick.net/1948-Hampp.htm
http://lymerick.net/1951-DeLamater.htm

„Warum manche Patienten klassische Bakterien ausbilden und andere Patienten nur intrazellulär persistierende bakterielle Dauerformen (L-Formen, Spheroplasten) (L. Mattman 2001 s.u. S.93)“, d.h. warum Infektionskrankheiten bei einigen Patienten unauffällig verlaufen und bei anderen Patienten chronisch.

Why some patients develop classic bacteria and other patients only intracellularly persistent bacterial survival structures (L-forms, spheroplasts) (L. Mattman 2001 S.U. p.93) ", that is, why infectious diseases in some patients run unobtrusively and chronically in other patients.“

Tabor WC (1962) **Stabilization of protoplasts and spheroplasts by spermine and other polyamides**. J. Bacteriol. 83 1101-1111

Lida Mattman (1964) Cell Wall Deficient Forms. Stealth Pathogens. CRC Press 2001 **Seite 93**
Harold FM. **Stabilization of Streptococcus faecalis protoplasts by spermine**. 88, 1416-1420

Lapinski EM. Flakas ED. (1970) **Reversal of penicillin-induced L-phase growth of Haemophilus influenza by spermine and its effects on antibiotic susceptibility**. Infect. Immun. 1 474-478

Raina A, Jänne J. (1975) **Physiology of the natural polyamines putrescine, spermidine and spermine.** Med Biol. 53(3) 121-47. http://www.ncbi.nlm.nih.gov/pubmed/169440
«Polyamines are able to stimulate protein and ribonucleic acid synthesis in vitro. In several systems characterized by rapid growth polyamines and ribonucleic acid accumulate in parrallel. Evidence that polyamines may have an essential role in protein and/or nucleic acid synthesis is substantiated by recent observations on polyamine-deficient bacterial mutants, although no specific function has been established with certainty as yet. Some clinical applications of polyamine research related to cancer are also discussed briefly ».

US Patent Issued on (1989) http://www.google.com/patents/EP2785766A1?cl=en
Spermine, Spermidine and Putrescine: General Biosynthesis Physiology Literature

Imai A, Matsuyama T, Hanzawa Y (2004) **Spermidine synthase genes are essential for survival of Arabidopsis.** Plant Physiol. 135(3) 1565-73. Epub 2004 Jul 9.
http://www.ncbi.nlm.nih.gov/pubmed/15247389

(2009) **Induction of autophagy by spermidine** promotes longevity. Nature Cell Biology 11, 1305 - 1314 http://www.nature.com/ncb/journal/v11/n11/abs/ncb1975.html

Matt Kaeberlein (2009) **Spermidine surprise for a long life**. Nature Cell Biology 11, 1277 - 1278
http://www.nature.com/ncb/journal/v11/n11/abs/ncb1109-1277.html

http://de.wikipedia.org/wiki/Spermin, http://www.homocystein-netzwerk.de/
https://de.wikipedia.org/wiki/Homocystein, https://de.wikipedia.org/wiki/Methionin

- ➔ **Polyamine, polyamides, spermidine**
  http://www.kabilahsystems.de/biogeneamineundpeptide.pdf
- ➔ **Homocystein, homocysteine** http://www.xerlebnishaft.de/bildmethyl-arginin.pdf

Aufenthalt von Spirochäten in den Zellen ihres Wirtsorganismus, privilegierte Räume, Stay of Borrelia in priviledged sites

Wolbach SB (1919) Studies on Rocky Mountain Spotted Fever. J Med Res 41, 1-197
https://archive.org/details/studiesonrockymo00wolb **["Intranuclear forms", S. 80, 83-86, 106-115]**

Valesova, M., et al., (1989) Detection of Borrelia in the synovial tissue from a patient with Lyme borreliosis by electron microscopy. J Rheumatol, 16(11), 1502-5.

Stanek, G., et al.(1990) Isolation of Borrelia burgdorferi from the myocardium of a patient with longstanding cardiomyopathy. N Engl J Med, 322(4), 249-52

Ma, Y., Sturrock A, Weis J (1991) **Intracellular** localization of Borrelia burgdorferi within human endothelial cells. Infect Immun, 59(2), 671-8

Georgilis K, Peacocke M, Klempner MS.(1992) Fibroblasts protect the Lyme disease spirochete, Borrelia burgdorferi, from ceftriaxone in vitro. J Infect Dis 166(2), 440- 4.

Haupl TH, Krause A, Bittig M. (1992) Persistence of Borrelia burgdorferi in chronic Lyme Disease: altered immune regulation or evasion into immunologically privileged sites? Abstract 149 Fifth International Conference on Lyme Borreliosis, Arlington, VA

Klempner MS, Noring R, Rogers RA.(1993) Invasion of human skin fibroblasts by the Lyme disease spirochete, Borrelia burgdorferi. J Infect Dis. 167(5), 1074- 81.

Haupl, T., et al., (1993) Persistence of Borrelia burgdorferi in ligamentous tissue from a patient with chronic Lyme borreliosis. Arthritis Rheum, 36(11), 1621-6.

Hulinska D, Basta J, Murgia R, Cinco M (1995) **Intracellular** morphological events observed by electron microscopy on neutrophil phagocytosis of Borrelia garinii Journal of Spirochetal and Tick-Borne Diseases. 2(4), 82-86.

Girschick HJ, Huppertz HI, Russmann H, Krenn V, Karch H. (1996) **Intracellular** persistence of Borrelia burgdorferi in human synovial cells. Rheumatol Int 16(3), 125–132

Aberer, E. et al. (1996) Heterogeneity of Borrelia burgdorferi in the skin. Am J Dermatopathol, 18(6), 571-9

Brouqui P, Badiaga S, and Raoult D (1996). "Eucaryotic cells protect Borrelia burgdorferi from the action of penicillin and ceftriaxone but not from the action of doxycycline and erythromycin" (PDF). Antimicrob Agents Chemother 40 (6), 1552–1554.

Nanagara, R., P.H. Duray, and H.R. Schumacher, Jr. (1996) Ultrastructural demonstration of spirochetal antigens in synovial fluid and synovial membrane in chronic Lyme disease: possible factors contributing to persistence of organisms. Hum Pathol, 27(10), 1025-34.

Dorward, D.W., E.R. Fischer, D.M. Brooks, (1997) Invasion and cytopathic killing of human lymphocytes by spirochetes causing Lyme disease. Clin Infect Dis, 25 Suppl 1, S2-8

Priem, S., et al.(1998) Detection of Borrelia burgdorferi by polymerase chain reaction in synovial membrane, but not in synovial fluid from patients with persisting Lyme arthritis after antibiotic therapy. Ann Rheum Dis, 57(2), 118-21

Chary-Valckenaere I, Jaulhac B, Champigneulle J, Piement Y, Mainard D, Pourel J (1998) **Ultrastructural demonstration of intracellular localization of Borrelia burgdorferi in Lyme arthritis**. Br J Rheumatol 37, 468-470.

de Koning, J., et al. (1998) Demonstration of spirochetes in cardiac biopsies of patients with Lyme disease. J Infect Dis, 160(1), 150-3

Chary-Valckenaere I, Jaulhac B, Champigneulle J, et al. (1998) Ultrastructural demonstration of intracellular localization of Borrelia burgdorferi in Lyme arthritis. Br J Rheumatol 37, 468-470.

Kroun M (2003) TNF and interruption of apoptosis (programmed cell death) seem to play an important role in persistence of most (all?) chronic INTRACELLULAR INFECTIONs. http://lymerick.net/NFkB.htm

Duray, P.H., et al. (2005) Invasion of human tissue **ex vivo** by Borrelia burgdorferi. J Infect Dis, 191(10), 1747-54.

Livengood, J.A. and R.D. Gilmore, Jr., (2006) Invasion of human neuronal and glial cells by an infectious strain of Borrelia burgdorferi. Microbes Infect, 8(14-15), 2832-40

Margulis L, Maniotis A, MacAllister J et al. (2009) Position paper. **Spirochete round bodies Syphilis, Lyme disease & AIDS**: Resurgence of „the great imitator“?. Symbiosis 47, 51-58 http://www1.biogema.de/WEK/312-Margulis-final.pdf

Müller, KE (2009) Erkrankung der elastischen und kollagenen Fasern von Haut, Sehnen und Bändern bei Lyme-Borreliose. Umwelt Medizin Gesellschaft 22, 112-118. http://www.schattenblick.de/infopool/medizin/fachmed/mz1um194.html

Chmielewski T, Tylewska-Wierzhanowska S (2011) Inhibition of fibroblast apoptosis by Borrelia afzelii, Coxiella burnetii and Bartonella henselae. Poll Microbiol 60(3). 269-72

- ➔ **Bakterielle Stressvarianten, L-Formen** http://www.erlebnishaft.de/stressvar1.pdf
- ➔ **Symbiogenese** http://www.erlebnishaft.de/symbiogenese.pdf

Änderung der Borrelien – Immunogenität, Schedding, Adhäsionsmoleküle

Urban C, Rahal JJ, Luft B (1991) **Effect of a beta-lactamase inhibitor, tazobactam, on growth and penicillin-binding proteins of Borrelia burgdorferi.** FEMS Microbiol Lett. 66(1), 113-6 http://www.ncbi.nlm.nih.gov/pubmed/1657694
http://www.researchgate.net/publication/21497431_Effect_of_a_beta-lactamase_inhibitor_tazobactam_on_growth_and_penicillin-binding_proteins_of_Borrelia_burgdorferi

Gasser R, Reisinger E, Eber B (1995) Cases of Lyme borreliosis resistant to conventional treatment: improved symptoms with cephalosporin plus **specific beta-lactamase inhibition.** Microb Drug Resist. 1(4), 341-4. http://www.ncbi.nlm.nih.gov/pubmed/9158807

Schwann TG, Piesman J, Golde WT, Dolan MC, Ros PA (1995) Induction of an outer surface protein on Bburgdorferi during tick feeding. Proc Natl Acad Sci USA 92, 2909-2913

Zhang J-R, Hardham JM, Barbour AG, Norris SJ (1997) Antigenic variation in Lyme Disease Borreliae by Promiscuous Recombination of VMP-Like Sequence Cassettes. Cell, 89, 275-285

Zhang J-R, Norris SJ (1998) Genetic Variation of the Borrelia burgdorferi Gene. vlsE Involves Cassette-Specific, Segmental Gene Conversion. Infection and Immunity. 66, 3698-3704

Liang FT, Yan J, Mbow ML et al. (2004). "Borrelia burgdorferi changes its surface antigenic expression in response to host immune responses". Infect Immun 72 (10), 5759–5767.

Aberer E, Bergmann AR, Derler AM, et al. (2007) Course of Borrelia burgdorferi DNA shedding in urine after treatment. Acta Derm Venereol 87 (1), 39-42. Abstract

Hurdle JG, O'Neill AJ, Chopra I, Lee RE (2011) **Targeting bacterial membrane function: an underexploited mechanism for treating persistent infections.** Nature Reviews Microbiology 9, 62–75 doi:10.1038/nrmicro2474 http://www.nature.com/nrmicro/journal/v9/n1/glossary/nrmicro2474.html

Riede I (2014) Membrane Fluidity : About the Origin of Autoimmunity. Open Journal of Immunology. 4, 9-13 http://dx.doi.org/10.4236/oji.2014.41002
http://www.scirp.org/journal/PaperInformation.aspx?paperID=43791#.VACBOGNVhws

Ritchie JA, Coburn J (2015) **A short-term Borrelia burgdorferi infection model identifies tissue tropisms and bloodstream survival conferred by adhesion proteins.** Infect Immun. pii: IAI.00349-15. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/26015482

Pianta A, Drouin EE, Crowley JT et al. (2015) **Annexin A2 Is a Target of Autoimmune T and B Cell Responses Associated with Synovial Fibroblast Proliferation in Patients with Antibiotic-Refractory Lyme Arthritis.** Clin Immunol. pii: S1521-6616(15)30009-7. doi: 10.1016/j.clim.2015.07.005. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/26187145

Sequestrierung von Wirts-Antikörpern

Schutzer SE, Coyle PK, Belman AL et al. (1990) Sequestration of antibody to Borrelia burgdorferi in immune complexes in sero-negative Lyme disease. Lancet 335(8685), 312-315

Brunner M, Sigal LH (2000) Immune complexes from serum of patients with lyme disease contain Borrelia burgdorferi antigen and antigen-specific antibodies: potential use for improved testing. J Infect Dis 182(2), 534-9. Abstract

Depression der CD57 Fraktion der natürlichen Killerzellen

Literatur: http://www.erlebnishaft.de/cd57.pdf

Depression von Komplement - Faktoren

Literatur: http://www.xerlebnishaft.de/complement.pdf

Biofilme in der Medizin

Literatur: http://www.erlebnishaft.de/biofilmmed.pdf

Horizontaler Gentransfer

Literatur: http://www.erlebnishaft.de/gentransfer.pdf

Gen Dynamik

Literatur: http://www.xerlebnishaft.de/gen_dynamik.pdf

Efflux – Mechanismus, Zellmembran - Transportproteine

Webber MA, Piddock LJV (2003) **The importance of efflux pumps in bacterial antibiotic resistance**. J. Antimicrob. Chemother. 51(1), 9-11.

Gibbons S1, Oluwatuyi M, Kaatz GW (2003) A novel inhibitor of multidrug efflux pumps in Staphylococcus aureus. J Antimicrob Chemother. 51(1), 13-7.
http://www.ncbi.nlm.nih.gov/pubmed/12493782
« GG918, a synthetic inhibitor of P-glycoprotein-mediated mammalian tumour multidrug resistance, was found to be equipotent to reserpine in enhancing the in vitro activity of norfloxacin and ciprofloxacin against strains of Staphylococcus aureus expressing distinct efflux-related multidrug resistance pumps. … Using GG918 as a lead compound, a structure-activity evaluation may reveal a more potent and broader spectrum inhibitor of S. aureus antibiotic efflux pumps. »

Mahamoud A, Chevalier J, Alibert-Franco S (2007) **Antibiotic efflux pumps in Gram-negative bacteria: the inhibitor response strategy**. J. Antimicrob. Chemother. 59(6), 1223-1229.

Schlager MA, Hoogenraad CC (2009) **Basic mechanisms for recognition and transport of synaptic cargos**. (Review). In: Molecular brain. Band 2, 25, ISSN 1756-6606. doi:10.1186/1756-6606-2-25. PMID 19653898. PMC 2732917

Ejim L et al., (2011) Combinations of antibiotics and nonantibiotic drugs enhance antimicrobial efficacy. Nature Chemical Biology, doi:10.1038/nchembio.559
http://fhs.mcmaster.ca/media/cf_therapy/cf_therapy_paper.pdf

Garvey MI, Rahman MM, Gibbons S et al. (2011) **Medicinal plant extracts with efflux inhibitory activity against Gram-negative bacteria**. International Journal of Antimicrobial Agents. 37, 145-151
http://www.ncbi.nlm.nih.gov/pubmed/21194895

Amaral L, Fanning, Pagès JM (2011) **Efflux pumps of Gram-negative bacteria**: Genetic responses to stress and the modulation of their activity by pH, inhibitors and phenothiazines. Advances in Enzymology 77, 61-108. PMID

Amaral L, Molnar J (2012) **Inhibitors of efflux pumps of Gram-negative bacteria inhibit Quorum Sensing**. Open J Pharmacology 2-2, 16th July.

Amaral L, Spengler G, Martins A et al. (2012) **Inhibitors of efflux pumps of bacteria that also inhibit efflux pumps of cancer cells**. Anticancer Research Special Issue 32, 2947-2957. PMID

Varga Z, Amaral L, Subki AM et al. (2012) **Inhibition of quorum sensing by proton pump inhibitor trifluoromethyl ketones** In Vivo 26, 277-285. PMID

Yu EW, Zhang Q, Brown MH (2013) **Microbial Efflux Pumps**: Current Research. Caister Academic Press. http://www.horizonpress.com/efflux-pumps

JE Kristiansen, J Molnar, Amaral, S Dastidar (2013) **Role of Phenothiazines and Structurally Similar Compounds of Plant Origin in the Fight against Infections by Drug Resistant Bacteria, Efflux Pumps of Multi-Drug Resistant Pathogenic Bacteria**: Their Genetic Regulation, Molecular Biology and Possible Control with Newly Designed Agents. Biochemistry & Pharmacology Open Access Journal 2, 58. 1.

Amaral L, Spengler G, Martins A, Molnar J (2013) **Efflux pumps** that bestow multi-drug resistance of pathogenic Gram-negative bacteria. Biochem Pharmacol Open Access 2, 3. August. DOI

Amaral L (2013) Preface - **Regulation and Control of Efflux Pumps that Mediate Multi-drug Resistance of Pathogenic Bacteria** The Open Microbiology Journal 7, 21. DOI

Amaral L, Martins A, Spengler G, Molnar J (2014) **Efflux pumps of Gram-negative bacteria**: what they do, how they do it, with what and how to deal with them. Frontiers In Pharmacology Open Access Jan. DOI

- **Pyrazinamid** http://www.xerlebnishaft.de/pyrazinamid.pdf

- **MACDONALD AB** http://www.molecularalzheimer.org/
- **MACDONALD AB The Biology of Lyme Disease: An Expert's Perspective (1 - 3)** https://www.youtube.com/watch?v=r8tESJVvM88 https://www.youtube.com/watch?v=2RATCS-3v9Q https://www.youtube.com/watch?v=FEjNMlNM3l8
- **SHOR S. LYME DISEASE EVIDENCE BASED STATE OF ART** http://vimeo.com/41466006
- **STRICKER R** http://foreignaffairs.house.gov/112/HHRG-112-FA16-WState-StrickerR-20120717.pdf
- **INVISIBLY ILL. Stealth infections and their role in chronic pain and illness** http://beyondthebandaid.com.au/?page_id=1002

- **Huismans BD (2017) Chronic Inflammatory Disorders, Multisystem diseases caused by pathogens.** http://www.kabilahsystems.de/ko-erreg_eupd1.pdf

- **Huismans BD (2018) Diagnostik / Therapie und biologische Grundlagen zu Cavete-Diagnosen bei Multisystem-Krankheiten durch Krankheits-Erreger. Literatursammlung und Kommentar** https://www.grin.com/document/432181 In German and English at the same time. **Diagnostic / therapy and biological foundations, a contribution to cavete - diagnoses in MSIDS (Multiple Systemic Infectious Disease Syndromes). An annotated literature collection.** www.grin.com/document/432181

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