Das angeborene Immunsystem, innate immunity, Komplement, Faktor H, C3, C4, Mannose bindendes Lektin, Chaperone, N-Acetylglucosaminidase, Inflammasom, 25-Hydroxycholesterol

Das angeborene (unspezifische) Immunsystem besteht aus den **anatomische Barrieren** (Haut, Eingeweide- und Lungen- Oberflächen) und aus **speziellen chemischen Wirk-Stoffen**.

The innate (non-specific) immune system consists of the **anatomical barriers** (skin, gut and lung surfaces) and from **special chemical active substances**.

Gaestel M, et al. (2009) Targeting innate immunity protein kinase signalling in inflammation. Nat Rev Drug Discov. 8(6), 480-99.

Ramaglia V, et al. (2009) Innate immunity in the nervous system. Prog Brain Res. 175, 95-123.

Metz M, et al. (2009) Innate immunity and allergy in the skin. Curr Opin Immunol. 21(6), 687-93.

Artis D, et al. (2010) Innate immunity. Curr Opin Immunol. 22(1), 1-3.

Harding M, Kubes P. (2011) Innate immunity in the vasculature: interactions with pathogenic bacteria. Current Opinion in Microbiology 15, 1–7

Casanova JL, Abel L (2013) The genetic theory of infectious diseases: a brief history and selected illustrations. Annu Rev Genomics Hum Genet 14, 215-243. http://www.ncbi.nlm.nih.gov/pubmed/23724903

Komplement, Complement

Carlsson J, Edlund MB, Hänström L (1984) Bactericidal and cytotoxic effects of **hypothiocyanite-hydrogen peroxide mixtures**. In: Infect Immun. 44(3), 581–6.

Mikola H, Waris M, Tenovuo J. (1995) Inhibition of herpes simplex virus type 1, respiratory syncytial virus and echovirus type 11 by peroxidase-generated **hypothiocyanite**. Antiviral Res. 26(2), 161-71

Law SK, Dodds AW (1997) **The internal thioester and the covalent binding properties of the complement proteins C3 and C4.** Protein Sci. 6(2), 263–274. doi: 10.1002/pro.5560060201 PMCID: PMC2143658 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2143658/

Kraicy P, Skerka, C, Kirschenfink, M et al. (2001) Mechanism of complement resistance of pathogenic **Borrelia burgdorferi** isolates. Int Immunopharmacol 1, 393–401

Kraicy P, Skerka, C, Kirschenfink, M et al. (2002) Immune evasion of **Borrelia burgdorferi** – Insufficient killing of the pathogens by complement and antibody. Int J Med Microbiol 291 141–146

Kraicy P, Skerka, C, Zipfel, PF et al (2002) Complement regulator-acquiring surface proteins of **Borrelia burgdorferi** – A new protein family involved in complement resistance. Wien Klin Wochenschr 114 568–573

Sorensen B, Streib JE, Strand M, et al. (2003) Complement Activation in a Model of **Chronic Fatigue Syndrome.** Journal of Allergy and Clinical Immunology, 112, 397-403. http://dx.doi.org/10.1067/mai.2003.1615

Kraicy P (2004) Natürliche Komplementresistenz und humorale Immunabwehr bei **Borrelia burgdorferi**, dem Erreger der Lyme-Borreliose. Aachen

Rus H, et al. (2006) The complement system in central nervous system diseases. Autoimmunity. 39(5), 395-402.

Endo Y, et al. (2006) **Lectin** complement system and pattern recognition. Immunobiology. 211(4), 283-93.

Basta M. (2008) Ambivalent effect of immunoglobulins on the complement system: activation versus inhibition. Mol Immunol. 45(16), 4073-9.

Di Muzio G, Perricone C, Ballanti E, et al. (2011) Complement system and **rheumatoid arthritis**: relationships with autoantibodies, serological, clinical features, and anti-TNF treatment. Int J Immunopathol Pharmacol 24(2), 357-66. Abstract

Sladkova V, Mareš J, Lubenova B, et al. (2011) Degenerative and inflammatory markers in the cerebrospinal fluid of multiple sclerosis patients with relapsing-remitting course of disease and after clinical isolated syndrome. Neurol Res 33(4), 415-20. Abstract

Perricone C, De Carolis C, Giacomelli R, et al. (2011) Inhibition of the complement system by **glutathione**: molecular mechanisms and potential therapeutic implications. Int J Immunopathol Pharmacol 24(1), 63-8. Abstract

Speidl WS, Kastl SP, Huber K, et al. (2011) Complement in **atherosclerosis**: friend or foe? J Thromb Haemost 9(3), 428-40. Abstract

Bradley DT, Badger SA, Bown MJ, et al. (2011) Coding polymorphisms in the genes of the alternative complement pathway and **abdominal aortic aneurysm**. Int J Immunogenet 38(3), 243-8. Abstract

Sta M, Sylva-Steenland RM, Casula M, et al. (2011) Innate and adaptive immunity in **amyotrophic lateral sclerosis**: evidence of complement activation. Neurobiol Dis 42(3), 211-20. Abstract

Skattum L, van Deuren M, van der Poll T, Truedsson L (2011) Complement deficiency states and associated infections. Mol Immunol 48, 1643-1655.

Teodorovich OV, Shatokhin MN, Mykolaenko TV, et al. (2011) Correction of complement system failure in patients with **chronic prostatitis**. Urologiia (4), 29-32. Abstract

Mayer G, (2011) IMMUNOLOGY - CHAPTER ONE. INNATE (NON-SPECIFIC) IMMUNITY. University of South Carolina. Shool of Medicine. http://pathmicro.med.sc.edu/ghaffar/innate.htm
"The elements of the innate (non-specific) immune system include anatomical barriers, secretory molecules and cellular components. Among the mechanical anatomical barriers are the skin and internal epithelial layers, the movement of the intestines and the oscillation of broncho-pulmonary cilia. Associated with these protective surfaces are chemical and biological agents".

Perl M, Denk S, Kalbitz M, et al. (2012) **Granzyme B**: a new crossroad of complement and apoptosis. Adv Exp Med Biol 135-46. Abstract

de Taeye SW, Kreuk L, van Dam AP et al. (2013) Complement evasion by **Borrelia burgdorferi**: it takes three to tango. Trends in Parasitology. http://www.cell.com/trends/parasitology/abstract/S1471-4922%2812%2900199-7

Bhattacharjee A, Oeemig JS, Kolodziejczyk R et al. (2013) Structural basis for complement evasion by **Lyme disease pathogen Borrelia burgdorferi**. J Biol Chem. 288(26), 18685-95. doi: 10.1074/jbc.M113.459040. http://www.ncbi.nlm.nih.gov/pubmed/23658013

Teegler A, Herzberger P, Margos G, Fingerle V, Kraiczy P (2014) The relapsing fever spirochete **Borrelia miyamotoi resists complement-mediated killing by human serum**. Ticks and Tick-borne Diseases 5(6), 898-901 http://www.sciencedirect.com/science/article/pii/S1877959X14001484

Hawley KL, et al. (2012) **CD14 cooperates with complement receptor 3 to mediate MyD88-independent phagocytosis of Borrelia burgdorferi**. Proc Natl Acad Sci USA 109(4):1228–1232 http://www.ncbi.nlm.nih.gov/pubmed/22232682

Hawley KL, Martín-Ruiz I, Iglesias-Pedraz JM et al. (2013) **CD14 Targets Complement Receptor 3 to Lipid Rafts during Phagocytosis of Borrelia burgdorferi.** Int J Biol Sci. 9(8), 803–810. Published online 2013 Aug 20. doi: 10.7150/ijbs.7136 PMCID: PMC3753444 PMID: 23983613 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3753444/

Teegler A, Herzberger P, Margos G et al. (2014) **The relapsing fever spirochete *Borrelia miyamotoi* resists complement-mediated killing by human serum.** Ticks Tick Borne Dis. 5(6), 898-901. doi: 10.1016/j.ttbdis.2014.07.011. Epub 2014 Jul 22. http://www.ncbi.nlm.nih.gov/pubmed/25104575 http://www.researchgate.net/publication/264643996_The_relapsing_fever_spirochete_Borrelia_miyamotoi_resists_complement-mediated_killing_by_human_serum

« The data presented here provide strong evidence that B. miyamotoi overcome human complement by affecting the central complement component C3, thereby inhibiting formation of the C3 convertase and downstream activation of the complement cascade. »

Sandholm K, Henningsson AJ, Sa¨ve S et al. (2014**) Early Cytokine Release in Response to Live Borrelia burgdorferi Sensu Lato Spirochetes Is Largely Complement Independent**. PLOS one. 9(9), e108013 http://www.plosone.org/article/fetchObject.action?uri=info%3Adoi%2F10.1371%2Fjournal.pone.0108013&representation=PDF

Lukas M, Adrian K, (2014) **Komplementdefekte** http://www.viomecum.ch/index.cfm?AD0ADE7609EA45FEBE3CB8025A33948E

Kraiczy P (2016) **Hide and Seek: How Lyme Disease Spirochetes Overcome Complement Attack.** Front Immunol. 7, 385. doi: 10.3389/fimmu.2016.00385 PMCID: PMC5036304 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5036304/

Factor H

Kraiczy P, Hellwage J, Skerka C et al. (2003) **Immune evasion of Borrelia burgdorferi**: mapping of a complement-inhibitor factor H-binding site of BbCRASP-3, a novel member of the Erp protein family. Eur J Immunol. 33(3), 697-707. http://www.ncbi.nlm.nih.gov/pubmed/12616490

„In conclusion, BbCRASP-3 has been identified as a novel factor H-binding protein on B. burgdorferi which by conferring complement resistance to the pathogen may contribute to its persistence in the mammalian host.“

Cordes FS, Roversi P, Kraiczy P et al. (2005) A novel fold for the factor H-binding protein BbCRASP-1 of **Borrelia burgdorferi**. Nat Struct Mol Biol. 12(3), 276-7. http://www.ncbi.nlm.nih.gov/pubmed/15711564

Alitalo A, Meri T, et al. (2005) Expression of complement factor H binding immunoevasion proteins in Borrelia garinii isolated from patients with neuroborreliosis. Eur. J. Imrnunol. 35 (10), 3043-3053.

Ferreira VP, Pangburn MK, Cortés C. (2010) Complement control protein factor H: the good, the bad, and the inadequate. Mol Immunol 47(13), 2187-97. Abstract

Dieterich R, Hammerschmidt C, Richter D, et al. (2010) Inadequate binding of immune regulator factor H is associated with sensitivity of Borrelia lusitaniae to human complement. Infect Immun 78(11), 4467-76. Abstract

Schejbel L, Schmidt IM, Kirchhoff M, et al. (2011) Complement factor H deficiency and endocapillary glomerulonephritis due to paternal isodisomy and a novel factor H mutation. Genes Immun 2011 Mar; 12(2), 90-9. Abstract

Schmidt CQ, Slingsby FC, Richards A, et al. (2011) Production of biologically active complement factor H in therapeutically useful quantities. Protein Expr Purif 2011 Apr; 76(2), 254-63. Abstract

Heurich M, Martínez-Barricarte R, Francis NJ, et al. (2011) Common polymorphisms in C3, factor B, and factor H collaborate to determine systemic complement activity and disease risk. Proc Natl Acad Sci U S A 108(21), 8761-6. Abstract

Brangulis K, Petrovski I, Kazaks A et al. (2015) Crystal structures of Erp protein family members ErpP and ErpC from Borrelia burgdorferi reveal the reason for different affinities for complement regulator factor H. Biochemica et Biophysica Acta http://www.ncbi.nlm.nih.gov/pubmed/25582082

C3, C4

Diagnostik: http://www.laborlexikon.de/Lexikon/Infoframe/k/Komplement-Untersuchungen.htm

Therapie: Nur Systemdestruktions-Methoden, keine letztlich heilende Therapie bekannt.
Therapy: Only system Destruktions methods, ultimately no known curative therapy.

Alitalo A, Meri T, Rämö L, Jokiranta TS, Heikkilä T, Seppälä IJ, Oksi J, Viljanen M, Meri S (2001) Complement evasion by **Borrelia burgdorferi**: serum-resistant strains promote C3b inactivation. Infect Immun. 69(6), 3685-91.

Mocco J, Wilson DA, Komotar RJ et al. (2006) Alterations in Plasma Complement Levels after Human **Ischemic Stroke**. Neurosurgery, 59, 28-33. http://dx.doi.org/10.1227/01.NEU.0000219221.14280.65

Mack, W.J., Ducruet, A.F., Hickman, Z.L., et al. (2007) Early Plasma Complement C3a Levels Correlate with Func-tional Outcome after **Aneurysmal Subarachnoid Hemorrhage**. Neurosurgery, 61, 255-260. http://dx.doi.org/10.1227/01.NEU.0000255518.96837.8E

Shoemaker RC, et al. (2008) Complement split products C3a and C4a are early markers of **acute lyme disease** in tick bite patients in the United States. Int Arch Allergy Immunol. 146(3), 255-61. http://www.ncbi.nlm.nih.gov/m/pubmed/18270493/ http://dx.doi.org/10.1159/000116362
CONCLUSIONS: These findings suggest that C3a and C4a may be useful markers of Lyme disease in patients seen shortly after tick bite, even in those without EM.

Stricker RB, Savely VR, Motanya NC, Giclas PC. (2009) Complement split products C3a and C4a in **chronic Lyme disease**. Scand J Immunol. 69, 64–69. PubMed
http://dx.doi.org/10.1111/j.1365-3083.2008.02191.x
Stricker RB (2012) "One of the benefits of doing C3a and C4a testing in a Lyme patient with positive ANA is that if the C3a is normal prior to antibiotic treatment, the patient is unlikely to have an autoimmune disease no matter how high the ANA titer is. Like the ANA, C4a is an inflammatory marker that can be high in any condition that involves inflammation."

Abdel Fattah M, El Baz M, Sherif A, et al. (2010) Complement components (C3, C4) as inflammatory markers in asthma. Indian J Pediatr 77(7), 771-3. Abstract

Jamali S, Salzmann A, Perroud N, et al. (20120) Functional variant in complement C3 gene promoter and genetic susceptibility to temporal lobe epilepsy and febrile seizures. PLoS One 5(9) Abstract

Peruzzi B, Serra M, Pescucci C, et al. (2010) Easy genotyping of complement C3 'slow' and 'fast' allotypes by tetra-primer amplification refractory mutation system PCR. Mol Cell Probes 24(6), 401-2. Abstract

Martínez-Barricarte R, Heurich M, Valdes-Cañedo F, et al. (2010) Human C3 mutation reveals a mechanism of dense deposit disease pathogenesis and provides insights into complement activation and regulation. J Clin Invest 120(10), 3702-12. Abstract

Wang JJ, Huang Y, Wu C, et al. (2011) Levels of serum acylation-stimulating protein and C3 in children with primary nephrotic syndrome. Zhongguo Dang Dai Er Ke Za Zhi 13(10), 817-9. Abstract

Kenyon KD, Cole C, Crawford F, et al. (2011) IgG autoantibodies against deposited C3 inhibit macrophage-mediated apoptotic cell engulfment in systemic autoimmunity. J Immunol 187(5), 2101-11. Abstract

Guo Q, Subramanian H, Gupta K, et al. (2011) Regulation of C3a receptor signaling in human mast cells by G protein coupled receptor kinases. PLoS One 6(7), e22559. Abstract

Bridoux F, Desport E, Frémeaux-Bacchi V, et al. (2011) Glomerulonephritis with isolated C3 deposits and monoclonal gammopathy: a fortuitous association? Clin J Am Soc Nephrol 6(9), 2165-74. Abstract

Wang Y, Hancock AM, Bradner J, et al. (2011) Complement 3 and factor h in human cerebrospinal fluid in Parkinson's disease, Alzheimer's disease, and multiple-system atrophy. Am J Pathol 178(4), 1509-16. Abstract

Stokowska A, Olsson S, Holmegaard L, et al. (2011) Plasma C3 and C3a levels in cryptogenic and large-vessel disease stroke: associations with outcome. Cerebrovasc Dis 32(2), 114-22. Abstract

Ignatius A, Schoengraf P, Kreja L, et al. (2011) Complement C3a and C5a modulate osteoclast formation and inflammatory response of osteoblasts in synergism with IL-1β. J Cell Biochem 112(9), 2594-605. Abstract

De Pergola G, Ciccone MM, Guida P, et al. (2011) Relationship between C3 levels and common carotid intima-media thickness in overweight and obese patients. Obes Facts 2011; 4(2):159-63. Abstract

Okura Y, Yamada M, Takezaki S, et al. (2011) Novel compound heterozygous mutations in the C3 gene: hereditary C3 deficiency. Pediatr Int 2011 Apr; 53(2), e16-9. Full Citation

TAN JY, LI FX, WU D, et al. (2011) Association of the C3 gene polymorphisms with susceptibility to adult asthma. Zhonghua Yi Xue Yi Chuan Xue Za Zhi 28(2):204-7. Abstract

Onat A, Can G, Rezvani R, et al. (2011) Complement C3 and cleavage products in cardiometabolic risk. Clin Chim Acta 2011 Jun 11; 412(13-14), 1171-9. Abstract

Ganesalingam J, An J, Shaw CE, et al. (2011) Combination of neurofilament heavy chain and complement C3 as CSF biomarkers for ALS. J Neurochem 117(3), 528-37. Abstract

Yang S, Li Q, Song Y, et al. (2011) Serum complement C3 has a stronger association with insulin resistance than high-sensitivity C-reactive protein in women with polycystic ovary syndrome. Fertil Steril 95(5), 1749-53. Abstract

Sartz L, Olin AI, Kristoffersson AC, et al. (2012) A novel C3 mutation causing increased formation of the C3 convertase in familial atypical hemolytic uremic syndrome. J Immunol; 188(4), 2030-7. Abstract

Ramaglia V, Hughes TR, Donev RM, et al. (2012) C3-dependent mechanism of microglial priming relevant to multiple sclerosis. Proc Natl Acad Sci U S A 109(3), 965-70. Abstract

Mazumdar B, Kim H, Meyer K, et al. (2012) Hepatitis C virus proteins inhibit C3 complement production. J Virol 86(4), 2221-8. Abstract

Bosmann M, Ward PA (2012) Role of C3, C5 and anaphylatoxin receptors in acute lung injury and in sepsis. Adv Exp Med Biol 147-59. Abstract

Unbound MEDLINE results for: Complement AND human| Refine this search
77713 journal articles in the PubMed database
Unbound MEDLINE results for: innate immunity AND human| Refine this search
42520 journal articles in the PubMed database

Mannose bindende Lektine, mannose-binding lectins

Das **Mannose-bindende Lektin (MBL)** gehört zu den wichtigsten Komponenten der angeborenen Immunabwehr.
The **mannose-binding lectin (MBL)** is one of the most important components of the innate immune response.

(2014) **Diagnostik:** z.B. Institut für medizinische Diagnostik, Berlin-Potsdam
http://www.imd-berlin.de/leistungsschwerpunkte/immundefekte/untersuchungsverfahren/mannose-bindendes-lektin-mbl.html

(214) **Therapie, therapy:** Griffithsin (**viral entry inhibitor**)

Catanzaro PJ et. al. (1971) Spectrum and Possible Mechanism of Carrageenan Cytotoxicity. Am J Pathol, 64(2), 387–404. PMC 2047576
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2047576/

Dieg EF. et al. (1974) Inhibition of herpesvirus replication by marine algae extracts. Anitimicrb. Ag. Chemother 6, 524-525 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC444684/

Eresmann DW, Deig EF, Hatch MT et al. (1977) **ANTIVIRAL SUBSTANCES FROM CALIFORNIA MARINE ALGAE**. Journal of Phycology 13(1), 37–40**.** http://onlinelibrary.wiley.com/doi/10.1111/j.1529-8817.1977.tb02883.x/abstract

Rumjanek VM et al. (1977) A re-evaluation of the role of macrophages in carrageenan-induced immunosuppression. Immunology, 33(3), 423–432. PMC 1445637 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1445637/

Richards JT, Kern RE, Glasgow LA et al. (1978) Antiviral activity of extracts from marine algae. Antimicrob. Agents Chemother. 14(1), 24-30 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC352400/

Thomson AW, Fowler EF (1981) Carrageenan: A review of its effects on the immune system: Agents and Actions. 11(3), 265-273 http://www.ncbi.nlm.nih.gov/pubmed/7020378

Gonzales ME et al. (1987) Polysaccharides as antiviral agents: antiviral activity of carrageenan. Antimicrobial Agents and Chemotherapy, 31,1388-1393 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC174948/

Neushul M (1990) Antiviral carbohydrates from marine red algae. Hydrobiologia 204/205, 99-104. (heparin-like sulfated polysaccharides) http://link.springer.com/article/10.1007%2FBF00040220#page-1

Cole KM, Sheath RG (1990/2011) Biology of the Red Algae, Cambridge University Press, Cambridge. http://www.amazon.com/Biology-Red-Algae-Kathleen-Cole/dp/0521202469

Koch A et al. (2001) Acute respiratory tract infections and **mannose- binding lectin insufficiency** during early childhood. JAMA 285, 1316- 1321

Alan R. et al. (2001) Mannose-binding lectin in prediction of susceptibility to infection, Lancet, 358, 597-680. http://www.ncbi.nlm.nih.gov/pubmed/11530141

Kilpatrick DC. (2002) **Mannan- binding lectin and its role in innate immunity.** Transfusion Med. 12, 335- 351. http://www.ncbi.nlm.nih.gov/pubmed/12473150

Eisen DP et al. (2003) Impact of Mannose-Binding Lectin on Susceptibility to Infectious Diseases. Clin Infect Dis 37, 1496-1505

Ezekowitz RA. (2003) Role of the mannose-binding lectin in innate immunity. J Infect Dis 187(Suppl 2), S335-9

Tsutsumi et al. (2005) **Mannose binding lectin: Genetics and autoimmmun disease**. Autoimmunity Reviews 4, 364-372. http://www.ncbi.nlm.nih.gov/pubmed/16081027

Emau P, Tian B, O'keefe BR et al (2007) **Griffithsin, a potent HIV entry inhibitor, is an excellent candidate for anti-HIV microbicide.** J Med Primatol. 36(4-5), 244-53. http://www.ncbi.nlm.nih.gov/pubmed/17669213

O´Keefe BR, Vojdani F, Buffa V et al. (2009) Scaleable manufacture of HIV-1 entry inhibitor **griffithsin** and validation of its safety and efficacy **as a topical microbicide** component. PNAS Early Edition. http://www.pnas.org/content/early/2009/03/27/0901506106.full.pdf+html Proc. Natl. Acad. Sci. U. S. A. 106, 6099-6104. http://www.ncbi.nlm.nih.gov/pubmed/19332801

“Plant-produced GRFT (GRFT-P) was shown as active against HIV at picomolar concentrations, directly virucidal via binding to HIV envelope glycoproteins, and capable of blocking cell-to-cell HIV transmission.”

Moulaei T, R. Shenoy SR, Giomarelli B et al. (2010) **Monomerization of Viral Entry Inhibitor Griffithsin Elucidates the Relationship between Multivalent Binding to Carbohydrates and anti-HIV Activity.** Structure 18(9), 1104–1115
http://www.cell.com/structure/abstract/S0969-2126%2810%2900268-6
http://ac.els-cdn.com/S0969212610002686/1-s2.0-S0969212610002686-main.pdf?_tid=253d3a08-76fe-11e4-bf25-00000aacb35e&acdnat=1417179644_c3e0e40a207215894536297938786bab

(2012) **Anti-viral griffiths** in compounds, compositions and methods of use. US 8088729 B2
http://www.google.com/patents/US8088729 (**mannose-binding lectins** such as griffithsin)
« A method of inhibiting a viral infection of a host comprising administering to the host an anti-viral polypeptide comprising SEQ ID NO: 3, where in the viral infection is a Hepatitis C viral infection, a Severe Acute Respiratory Syndrome (SARS) viral infection, an H5N1 viral infection, or an Ebola viral infection, and where upon the viral infection is inhibited. »

Barton Chr, Kouokam JC, Lasnik AB et al. (2014) **Activity of and Effect of Subcutaneous Treatment with the Broad-Spectrum Antiviral Lectin Griffithsin in Two Laboratory Rodent Models.** Antimicrob Agents Chemother. 58(1), 120–127. doi: 10.1128/AAC.01407-13
PMCID: PMC3910741 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3910741/
http://www.ncbi.nlm.nih.gov/pubmed/24145548
„The results presented in this work show that minimal toxicity was induced by a range of single and repeated daily subcutaneous doses of GRFT in two rodent species, although we noted treatment-associated increases in spleen and liver mass suggestive of an antidrug immune response. …
Overall, our data presented here show that GRFT accumulates to relevant therapeutic concentrations which are tolerated with minimal toxicity. »

Sajanti EM, Gröndahl-Yli-Hannuksela K, Kauko T et al. (2014) **Lyme Borreliosis and Deficient Mannose-Binding Lectin Pathway of Complement.** J Immunol. pii: 1402128.
http://www.jimmunol.org/content/early/2014/11/21/jimmunol.1402128.abstract

Chaperone, HSP60/GroEL, HSP70, HSP90, HSP100/Clp, kleinere Hitzeschockproteine

Helmes C. (1995) Molekulaare und immunologische Charakterisierung der immundominanten Antigene HSP60, HSP70 und LpLA7 von **Borrelia burgdorferi**, dem Erreger der Lyme-Borreliose. Heidelberg, Univ. Diss., 1997
http://katalog.ub.uni-heidelberg.de/cgi-bin/titel.cgi?katkey=9714870
http://books.google.de/books/about/Molekulare_und_immunologische_Charakteri.html?id=tbepHAAACAAJ&redir_esc=y

Bukau B, Horwich AL (1998) The Hsp70 and Hsp60 Chaperone Machines. Cell Vol 92, 351-366 (Abstract) http://www.cell.com/fulltext/S0092-8674%2800%2980928-9
http://homepages.bw.edu/~mbumbuli/cell/chaplec/
https://www.researchgate.net/publication/13753859_The_Hsp70_and_Hsp60_chaperone_machines

Bukau B et al. (2000) Getting newly synthesized proteins into shape. Cell) 101, 119-122 (Abstract)

Ferbitz et al. (2004) Structure of the trigger factor chaperone in complex with the ribosome defines the molecular environment of the emerging nascent protein chain. Nature 431, 590-596. (Abstract)

Tyedmers, J. et al. Cellular strategies for controlling protein aggregation. Nat. Rev. Cell Biol. (2010) 11, 777-788 (Abstract)

Oh E et al. (2011) Selective ribosome profiling reveals the cotranslational chaperone action of trigger factor in vivo. Cell 147, 1295-1308 (Abstract).

Lu M et al. (2014) Opposing unfolded-protein-response signals converge on death receptor 5 to control apoptosis Science, 345, 98-101
http://www.sciencemag.org/content/345/6192/98.short

- **Chaperones (Anstandsdamen)**
  http://www.ncbi.nlm.nih.gov/pubmed/?term=chaperones
- **Heat shock protein 70** (**HSP70**) http://www.ncbi.nlm.nih.gov/pubmed/?term=hsp70

N-acetylgalactosaminidase (Nagalase) Aktivität und Gc-MAF

Nagalase (Alpha-N-acetylgalactosaminidase) ist ein in **Bakterien**, in **Tumoren, Tieren, Menschen** physiologisch vorkommendes Enzym, eine Glycosid-Hydrolase. Das Enzym inaktiviert durch Zuckerabspaltung den Immun-Booster GcMAF (MAF = Makrophagen aktivierender Faktor).

Nagalase wirkt immunsuppressiv durch Inaktivierung der Makrophagen.
Quelle u.a.: http://dr-bieger.de/nagalase-und-gcmaf-dezember-2012/

Nagalase (alpha-N-acetylgalactosaminidase) is a physiologically occurring enzyme in **bacteria**, **tumors** and in **animals**, it is a glycoside hydrolase. The enzyme inactivates the immune Booster GcMAF (MAF = macrophage activating factor) by cleavage of the sugar.

Nagalase has an immunosuppressive effect by inactivation of macrophages.
Source, inter alia: http://dr-bieger.de/nagalase-und-gcmaf-dezember-2012/

Laboratorien, laboratories:
ELN http://www.hdri-usa.com/tests/nagalase/ http://www.europeanlaboratory.nl/documents/Nagalase%20in%20bloed%20eng.pdf
RED Laboratories
http://www.google.de/url?sa=t&rct=j&q=&esrc=s&source=web&cd=9&ved=0CHcQFjAI&url=http%3A%2F%2Fwww.arydol.es%2Farchivos%2Ftemas%2Fdolor-cronico-sindrome-fatiga-cronica%2Fdownload.php%3Ff%3Dsindrome-intestino-permeable.pdf&ei=f661UoyyK4bItAaQlIC4CA&usg=AFQjCNH7iw77cCamJa68mLwTSUbAlcox7Q&bvm=bv.58187178,d.Yms
Prof. Dr. med. M. Kramer Facharzt für Laboratoriumsmedizin Mönchhofstraße 52 69120 Heidelberg, Germany
http://nagalase-test.de/wp-content/uploads/2013/11/Untersuchungsauftrag-Nagalase.pdf

Wang AM, Schindler D, Desnick R (1990) Schindler disease: the molecular lesion in the alpha-N-acetylgalactosaminidase gene that causes an infantile neuroaxonal dystrophy. J. Clin. Invest. 86 (5), 1752–6. doi:10.1172/JCI114901. PMC 296929. PMID 2243144.

Saharuddin BM, Nagasawa H, Uto Y, Hori H (2002) Tumor cell alpha-N-acetylgalactosaminidase activity and its involvement in GcMAF-related macrophage activation Elsevier, 132(1), 1–8, Comparative Biochemistry and Physiology - Part A: Molecular & Integrative Physiology

Yamamoto N, Suyama H, Yamamoto N, Ushijima N. (2008) Immunotherapy of metastatic breast cancer patients with vitamin D-binding protein-derived macrophage activating factor (GcMAF) Int J Cancer. 122, 461–7. doi: 10.1002/ijc.23107. [PubMed] [Cross Ref]

Pacini S, Punzi T, Morucci G, Gulisano M, Ruggiero M. (2012) Effects of **vitamin D-binding protein**-derived macrophage-activating factor on human breast cancer cells. Anticancer Res. 32, 45–52. [PubMed]

Thyer L, Ward E, Smith R et al. (2013) GC protein-derived macrophage-activating factor decreases α-N-acetylgalactosaminidase levels in advanced cancer patients. Oncoimmunology. 2(8), e25769. doi: 10.4161/onci.25769 PMCID: PMC3812199
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3812199/
„…However, the response to GcMAF was often relatively robust and certain trends stand out.“

Sample records for **serum nagalase activity** from WorldWideScience.org
http://worldwidescience.org/topicpages/s/serum+nagalase+activity.html

Inflammation http://en.wikipedia.org/wiki/Inflammation
http://de.wikipedia.org/wiki/Entz%C3%BCndung

Gc-MAF

Wang AM, Schindler D, Desnick R (1990) Schindler disease: the molecular lesion in the alpha-N-acetylgalactosaminidase gene that causes an infantile neuroaxonal dystrophy. J. Clin. Invest. 86 (5), 1752–6. doi:10.1172/JCI114901. PMC 296929. PMID 2243144.

Saharuddin BM, Nagasawa H, Uto Y, Hori H (2002) Tumor cell alpha-N-acetylgalactosaminidase activity and its involvement in GcMAF-related macrophage activation Elsevier, 132(1), 1–8, Comparative Biochemistry and Physiology - Part A: Molecular & Integrative Physiology

Yamamoto N, Suyama H, Yamamoto N, Ushijima N. (2008) Immunotherapy of metastatic breast cancer patients with vitamin D-binding protein-derived macrophage activating factor (GcMAF) Int J Cancer. 122, 461–7. doi: 10.1002/ijc.23107. [PubMed] [Cross Ref]

Yamamoto N, Hirofumi Suyama H, Yamamoto N (2008) Immunotherapy for Prostate Cancer with Gc Protein-Derived Macrophage-Activating Factor, **GcMAF1** - Translational Oncology 1 (2), 65–72 PDF
http://www.biologischekrebstherapie.net/wp-content/uploads/2013/11/tlo0102_0065-Yamamoto-GcMAF-prostrate-cancer.pdf

Pacini S, Punzi T, Morucci G, Gulisano M, Ruggiero M. (2012) Effects of **vitamin D-binding protein**-derived macrophage-activating factor on human breast cancer cells. Anticancer Res. 32, 45–52. [PubMed]

Thyer L, Ward E, Smith R et al. (2013) GC protein-derived macrophage-activating factor decreases α-N-acetylgalactosaminidase levels in advanced cancer patients. Oncoimmunology. Landes Bioscience 2(8), e25769. doi: 10.4161/onci.25769 PMCID: PMC3812199 PDF
http://www.biologischekrebstherapie.net/wp-content/uploads/2013/11/2013ONCOIMM0155R.pdf
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3812199/
„…However, the response to GcMAF was often relatively robust and certain trends stand out.“

KUCHIIKE D, UTO Y, MUKAI H et al. (2013) **Degalactosylated/Desialylated Human Serum Containing GcMAF Induces Macrophage Phagocytic Activity and In Vivo Antitumor Activity.** ANTICANCER RESEARCH 33, 2881-2886
http://www.biologischekrebstherapie.net/wp-content/uploads/2013/11/2013-degalactosylated-desialylated-human-serum-containing-gcmaf-induces-macrophage-phagocytic-antitumor-activity.pdf
« We demonstrated that GcMAF-containing human serum can be used as a potential macrophage activator for cancer immunotherapy.“

INUI T, KUCHIIKE D, KUBO K et al. (2013) **Clinical Experience of Integrative Cancer Immunotherapy with GcMAF.** ANTICANCER RESEARCH 33, 2917-2920 PDF

http://www.biologischekrebstherapie.net/wp-content/uploads/2013/11/2013-clinical-experience-integrative-cancer-immunotherapy-gcmaf.pdf
„The results of our integrativeimmunotherapy seem hopeful. We also plan to conduct a comparative clinical study. Immunotherapy has become an attractive new strategy in the treatment of cancer. »

Sample records for serum nagalase activity from WorldWideScience.org
http://worldwidescience.org/topicpages/s/serum+nagalase+activity.html
http://www.gcmaf-immuntherapie.com/
http://www.biologischekrebstherapie.net/gcmaf/
https://en.wikipedia.org/wiki/Gc-MAF
http://www.firstimmune.de/
http://immunocentre.eu/what-is-gcmaf/
http://www.firstimmune.de/patient-resources/treatment-strategies/

Gc-MAF explained - The start (www.bgli.nl to order Gc-MAF)
https://www.youtube.com/watch?v=y7BLpR214t0#t=49
Noakes D (2015) How GcMAF eradicates cancers
https://www.youtube.com/watch?v=z998HfHbi7w
~ http://www.himmunitas.org/pages/english/index_en.php?page=home_en ~

Inflammasom

Das Inflammasom ist ein cytosolischer Proteinkomplex in Makrophagen und neutrophilen Granulozyten, der durch Bestandteile von Bakterien oder Kristalle aus Harnsäure, Siliziumdioxyd, Titanoxyd, Cholesterin, Asbest, Nanopartikel von spezieller Größe) stimuliert wird. Quelle: http://de.wikipedia.org/wiki/Inflammasom
Inflammasomes (2014) http://www.adipogen.com/inflammasomes/

Martinon F, Burns K, Tschopp J (2002) **The inflammasome: a molecular platform triggering activation of inflammatory caspases and processing of proIL-beta.** Mol Cell. 10(2), 417-26.

Martinon F, Tschopp J (2004) **Inflammatory caspases: linking an intracellular innate immune system to autoinflammatory diseases.** Cell. 117(5), 561-74.

Agostini L, Martinon F, Bruns K et al. (2004) NALP3 forms an IL1 beta –proccessing inflammasome with increased activity in Muckle-Wells autoinflammators disorder. Immunity 20, 319-325 http://www.ncbi.nlm.nih.gov/pubmed/15030775

Goldbach-Mansky R. et al.(2006) Neonatal-Onset Multisystem Inflammatory Disease Responsive to Interleukin-1β Inhibition. In: New England Journal of Medicine. 355, 581-592 (Abstract).

Drenth JP, van der Meer JW (2006) The Inflammasome -- A Linebacker of Innate Defense. In: New England Journal of Medicine. 355(7), 730-732 Abstract
http://www.ncbi.nlm.nih.gov/pubmed/16914711

Watanabe H, Gaide O, Petrilli V et al. (2007) Activation of the IL-1 beta processing inflammasome is involved in contact hypersensitivity. J Invest Dermatol. 127, 1956-1963
http://www.ncbi.nlm.nih.gov/pubmed/17429439

Mariathasan S, Monack DM (2007) Inflammasome adaptors and sensors: intracellular regulators of infection and inflammation. In: Nature Reviews Immunology. 7, 31-40 (Artikel).

Halle A et al. (2008) The NALP3 inflammasome is involved in the innate immune response to amyloid-bold beta, Nature Immunology 9, 857 - 865
http://www.nature.com/ni/journal/v9/n8/abs/ni.1636.html

Keller M, Rüegg A, Werner S, Beer HD et al. (2008) Active **Caspase-1** is a regulator of unconventional protein secretion. Cell, 132(5), 818-31 doi:10.1016/j.cell. 12.040
http://www.ncbi.nlm.nih.gov/pubmed/18329368

Stutz A, Golenbock DT, Latz E. (2009) **Inflammasomes: too big to miss.** J Clin Invest 119, 3502-11 http://www.ncbi.nlm.nih.gov/pubmed/19955661

Martinon F, Mayor A, Tschopp J (2009) **The inflammasomes: Guardians of the body**. Annu Rev Immunol. 277, 21119-21122 http://www.ncbi.nlm.nih.gov/pubmed/19302040

So A, Pazár B (2010) **The Expanded Role of the Inflammasome in Human Disease.** The Rheumatologist.
http://www.the-rheumatologist.org/details/article/863227/The_Expanded_Role_of_the_Inflammasome_in_Human_Disease.html

Yazdi AS, Guarda G, Riteau N, Drexler SK, Tardivel A, Couillin I, Tschopp J (2010) Nanoparticles activate the NLR pyrin domain containing 3 (Nlrp3) inflammasome and cause pulmonary inflammation through release of IL-1? and IL-1?. In: Proceedings of the National Academy of Sciences of the United States of America. 107, 45, 19449–19454, ISSN 1091-6490. doi:10.1073/pnas.1008155107. PMID 20974980. PMC 2984140 (freier Volltext).

Schorn C, Frey B, Lauber K, Janko Ch, Strysio M, Keppeler H, Gaipl US, Voll RE, Springer E, Munoz LE, Schett G, Herrmann M (2010) Sodium Overload and Water Influx Activate the NALP3 Inflammasome. In: The Journal of Biological Chemistry, 286, 35-41. PMID 21051542 doi:10.1074/jbc.M110.139048

Meixenberger K. Mechanismen der Inflammasom-Aktivierung durch Listeria monocytogenes. Dissertation Charité Berlin. http://www.diss.fu-berlin.de/diss/servlets/MCRFileNodeServlet/FUDISS_derivate_000000007467/Upload.pdf;jsessionid=4E3542F69A2C71C7DE66A8C769DA9B75?hosts=

Kambe N, Satoh T, Nakamura Y et al. (2010) **Autoinflammatory diseases and the inflammasome: mechanisms of IL-1beta activation leading to neutrophil-rich skin disorders**. http://www.jsir.gr.jp/journal/Vol31No1/pdf/09_S4_72.pdf

Shaw PJ, McDermott MF, Kannegant T-D (2011) **Inflammasomes and autoimmunity. Trends in Molecular Medicine 17(2), 57-64**
DOI: http://dx.doi.org/10.1016/j.molmed.2010.11.001

Düwell P. (2011) **Die Rolle des NLRP3-Inflammasoms in der Pathogenese entzündlicher Erkrankungen am Beispiel von Atherosklerose und der experimentellen Colitis**. Dissertation Universität München. http://edoc.ub.uni-muenchen.de/13060/1/Duewell_Peter.pdf

Davis BK, Wen H, Ting JP-Y (2011) T**he Inflammasome NLRs in Immunity, Inflammation, and Associated Diseases.** Annu Rev Immunol. 2011; 29: 707–735. doi: 10.1146/annurev-immunol-031210-101405 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4067317/

Bscheider M. (2012) **Inflammasom Aktivierung durch RNA-Viren und Pilze.** Dissertation Universität München. http://edoc.ub.uni-muenchen.de/14996/1/Bscheider_Michael.pdf

Franchi L, Muñoz-Planillo R, Núñez G (2012) Sensing and reacting to microbes through the inflammasomes Nature Immunology 13, 325–332 (2012)

Luigi Franchi, Raul Muñoz-Planillo, Gabriel Núñez (2012) **Sensing and reacting to microbes through the inflammasomes.** Nature Immunology 13, 325–332 (2012) Alexander So, Borbála Pazár.

McIlwain DR, Berger T, Mak TW (2013) Caspase Functions in Cell Death and Disease. doi: 10.1101/cshperspect.a008656 Cold Spring Harbor Laboratory Press http://cshperspectives.cshlp.org/content/5/4/a008656.full

Ranson N, Eri R (2013) **The Role of Inflammasomes in Intestinal Inflammation.** American Journal of Medical and Biological Research, 1 (3), 64-76. DOI: 10.12691/ajmbr-1-3-3 http://pubs.sciepub.com/ajmbr/1/3/3/

Davis BK, Wen H, Ting JP-Y (2014) **The Inflammasome NLRs in Immunity, Inflammation, and Associated Diseases.** Annu Rev Immunol. 2011; 29: 707–735. doi: 10.1146/annurev-immunol-031210-101405 PMCID: PMC4067317 NIHMSID: NIHMS596973 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4067317/

Sollberger G, Strittmatter GE, Garstkiewicz M et al. (2014) **Caspase -1: The inflammasome and beyond.** Innate Immunity. 20(2), 115-125 http://ini.sagepub.com/content/20/2/115.full

Samstad EO, Niyonzima N, Nymo S, Aune MH, Ryan L (2014) **Cholesterol crystals induce complement-dependent inflammasome activation and cytokine release.** J Immunol. 192(6), 2837-45. doi: 10.4049/jimmunol.1302484. Epub 2014 Feb 19. http://www.ncbi.nlm.nih.gov/pubmed/24554772
„We conclude that CC [cholesterol crystals] employ the complement system to induce cytokines and activate the inflammasome/caspase-1 by regulating several cellular responses in human monocytes. In light of this, complement inhibition might be an interesting therapeutic approach for treatment of atherosclerosis.“

Kono H, Kimura Y, Latz E (2014) **Inflammasome activation in response to dead cells and their metabolites**. Current Opinion in Immunology 2014, 30, 91–98

Inflammasome, Wikipedia, the free encyclopedia http://en.wikipedia.org/wiki/Inflammasome

25-Hydroxycholesterol

Huismans BD. (1973) **Serum lipid values and lipid electrophoreses in a hospital for vascular diseases**. Med Welt. 24(20), 820-1. http://www.ncbi.nlm.nih.gov/pubmed/4753901

Nishio, E. et al. (1996) Oxysterols induced apoptosis in cultured smooth muscle cells through CPP32 protease activation and bcl-2 protein downregulation. Biochem. Biophys. Res. Commun. 226, 928-934

Chen JJ, Lukyanenko Y, Hutson JC (2002). 25-hydroxycholesterol is produced by testicular macrophages during the early postnatal period and influences differentiation of Leydig cells in vitro. Biol. Reprod. 66 (5), 1336–41. doi:10.1095/biolreprod66.5.1336. PMID 11967195.

Lukyanenko Y, Chen JJ, Hutson JC (2002). Testosterone regulates 25-hydroxycholesterol production in testicular macrophages. Biol. Reprod. 67 (5), 1435–8. doi:10.1095/biolreprod.102.007575. PMID 12390873

Lim HK, et al. (2003) Oxysterols induce apoptosis and accumulation of cell cycle at G(2)/M phase in the human monocytic THP-1 cell line. Life Sci. 72, 1389-1399

Brown MS, Goldstein JL (2009) Cholesterol feedback: from Schoenheimer's bottle to Scap's MELADL. J. Lipid Res. 50, 15–S27.

Diczfalusy U, Olofsson KE, Carlsson AM et al. (2009) Marked up-regulation of cholesterol 25-hydroxylase expression by lipopolysaccharide. J. Lipid Res. 50, 2258–2264.

Bauman DR, Bitmansour AD, McDonald JG et al. (2009) **25-Hydroxycholesterol secreted by macrophages in response to Toll-like receptor activation suppresses immunoglobulin A production**. Proc. Natl. Acad. Sci. USA 106, 16764–16769.

Park K, Scott AL (2010) **Cholesterol 25-hydroxylase production by dendritic cells and macrophages is regulated by type I interferons**. J. Leukoc. Biol. 88, XXX–XXX. Search Google Scholar

McDonald JG, Russell DW (2010) **Editorial: 25-Hydroxycholesterol: a new life in immunology**. Journal of Leukocyte Biology 88 (6) 1071-1072 http://www.ncbi.nlm.nih.gov/pubmed/21123296

Liu, Su-Yang et al. (2013) Interferon-Inducible Cholesterol-25-Hydroxylase Broadly Inhibits Viral Entry by Production of **25-Hydroxycholesterol**. Immunity **38** (1), 92–105. doi:10.1016/j.immuni.2012.11.005. PMID 23273844

Lathe R, Sapronova A, Kotelevtsev Y (2014) **Atherosclerosis and Alzheimer – disease with a common cause? Inflammation, oxysterols, vasculature.** BMC Geriatr. 14(1), 36 http://www.biomedcentral.com/1471-2318/14/36/abstract

- **Immunitaet** http://www.erlebnishaft.de/danger_model.pdf
- **Mitochondrien** http://www.xerlebnishaft.de/mitochondrien.pdf
- **Zytoskelett** http://www.xerlebnishaft.de/zytoskelett.pdf
- **Zellmembran, Fettsäuren, Amine und Proteine** http://www.kabilahsystems.de/ungesaettfetts.pdf http://www.kabilahsystems.de/biogeneamineundpeptide.pdf
- **Selbstorganisation** http://www.erlebnishaft.de/selbst_muster_nano.pdf
- **Symbiogenese** http://www.erlebnishaft.de/symbiogenese.pdf

- **Entzündungshemmung** http://www.kabilahsystems.de/antizyt-chem.pdf

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