

## 9 Literatur

1. Hoffmann, J.A., et al., *Phylogenetic perspectives in innate immunity*. Science, 1999. **284**(5418): p. 1313-8.
2. Medzhitov, R. and C.A. Janeway, Jr., *Innate immunity: the virtues of a nonclonal system of recognition*. Cell, 1997. **91**(3): p. 295-8.
3. Janeway, C.A. and P. Travers, *Immunobiology*. 5 ed. The Immune System in Health and Disease. 2001, Heidelberg Berlin Oxford: Garland Publishing.
4. Kaisho, T. and S. Akira, *Toll-like receptors as adjuvant receptors*. Biochim Biophys Acta, 2002. **1589**(1): p. 1-13.
5. Akira, S. and H. Hemmi, *Recognition of pathogen-associated molecular patterns by TLR family*. Immunol Lett, 2003. **85**(2): p. 85-95.
6. Pasare, C. and R. Medzhitov, *Toll-like receptors: linking innate and adaptive immunity*. Microbes Infect, 2004. **6**(15): p. 1382-7.
7. Anderson, K.V., L. Bokla, and C. Nusslein-Volhard, *Establishment of dorsal-ventral polarity in the Drosophila embryo: the induction of polarity by the Toll gene product*. Cell, 1985. **42**(3): p. 791-8.
8. Anderson, K.V., G. Jurgens, and C. Nusslein-Volhard, *Establishment of dorsal-ventral polarity in the Drosophila embryo: genetic studies on the role of the Toll gene product*. Cell, 1985. **42**(3): p. 779-89.
9. Gay, N.J. and F.J. Keith, *Drosophila Toll and IL-1 receptor*. Nature, 1991. **351**(6325): p. 355-6.
10. Belvin, M.P. and K.V. Anderson, *A conserved signaling pathway: the Drosophila toll-dorsal pathway*. Annu Rev Cell Dev Biol, 1996. **12**: p. 393-416.
11. Lemaitre, B., et al., *The dorsoventral regulatory gene cassette spatzle/Toll/cactus controls the potent antifungal response in Drosophila adults*. Cell, 1996. **86**(6): p. 973-83.
12. O'Neill, L.A., *The interleukin-1 receptor/Toll-like receptor superfamily: signal transduction during inflammation and host defense*. Sci STKE, 2000. **2000**(44): p. RE1.
13. Aravind, L., V.M. Dixit, and E.V. Koonin, *Apoptotic molecular machinery: vastly increased complexity in vertebrates revealed by genome comparisons*. Science, 2001. **291**(5507): p. 1279-84.
14. Hultmark, D., *Macrophage differentiation marker MyD88 is a member of the Toll/IL-1 receptor family*. Biochem Biophys Res Commun, 1994. **199**(1): p. 144-6.
15. Medzhitov, R., P. Preston-Hurlburt, and C.A. Janeway, Jr., *A human homologue of the Drosophila Toll protein signals activation of adaptive immunity*. Nature, 1997. **388**(6640): p. 394-7.

16. Takeda, K., T. Kaisho, and S. Akira, *Toll-like receptors*. Annu Rev Immunol, 2003. **21**: p. 335-76.
17. Takeda, K. and S. Akira, *Microbial recognition by Toll-like receptors*. J Dermatol Sci, 2004. **34**(2): p. 73-82.
18. Heil, F., et al., *Species-specific recognition of single-stranded RNA via toll-like receptor 7 and 8*. Science, 2004. **303**(5663): p. 1526-9.
19. Yarovinsky, F., et al., *TLR11 activation of dendritic cells by a protozoan profilin-like protein*. Science, 2005. **308**(5728): p. 1626-9.
20. Kobe, B. and A.V. Kajava, *The leucine-rich repeat as a protein recognition motif*. Curr Opin Struct Biol, 2001. **11**(6): p. 725-32.
21. Takeuchi, O. and S. Akira, *Toll-like receptors; their physiological role and signal transduction system*. Int Immunopharmacol, 2001. **1**(4): p. 625-35.
22. Zarembek, K.A. and P.J. Godowski, *Tissue expression of human Toll-like receptors and differential regulation of Toll-like receptor mRNAs in leukocytes in response to microbes, their products, and cytokines*. J Immunol, 2002. **168**(2): p. 554-61.
23. Hornung, V., et al., *Quantitative expression of toll-like receptor 1-10 mRNA in cellular subsets of human peripheral blood mononuclear cells and sensitivity to CpG oligodeoxynucleotides*. J Immunol, 2002. **168**(9): p. 4531-7.
24. McKenna, K., A.S. Beignon, and N. Bhardwaj, *Plasmacytoid dendritic cells: linking innate and adaptive immunity*. J Virol, 2005. **79**(1): p. 17-27.
25. Visintin, A., et al., *Regulation of Toll-like receptors in human monocytes and dendritic cells*. J Immunol, 2001. **166**(1): p. 249-55.
26. Mempel, M., et al., *Toll-like receptor expression in human keratinocytes: nuclear factor kappaB controlled gene activation by Staphylococcus aureus is toll-like receptor 2 but not toll-like receptor 4 or platelet activating factor receptor dependent*. J Invest Dermatol, 2003. **121**(6): p. 1389-96.
27. Seibl, R., et al., *Expression and regulation of Toll-like receptor 2 in rheumatoid arthritis synovium*. Am J Pathol, 2003. **162**(4): p. 1221-7.
28. Abreu, M.T., et al., *TLR4 and MD-2 expression is regulated by immune-mediated signals in human intestinal epithelial cells*. J Biol Chem, 2002. **277**(23): p. 20431-7.
29. Tulic, M.K., et al., *Role of toll-like receptor 4 in protection by bacterial lipopolysaccharide in the nasal mucosa of atopic children but not adults*. Lancet, 2004. **363**(9422): p. 1689-97.
30. Zeuke, S., et al., *TLR4-mediated inflammatory activation of human coronary artery endothelial cells by LPS*. Cardiovasc Res, 2002. **56**(1): p. 126-34.

31. Janeway, C.A., Jr. and R. Medzhitov, *Innate immune recognition*. Annu Rev Immunol, 2002. **20**: p. 197-216.
32. Guha, M. and N. Mackman, *LPS induction of gene expression in human monocytes*. Cell Signal, 2001. **13**(2): p. 85-94.
33. Schumann, R.R., *Endotoxin-bindende Proteine: neue Ansätze in der Sepsisbehandlung*, in *Die gelben Hefte*. 1997.
34. Chamaillard, M., et al., *Nods, Nalps and Naip: intracellular regulators of bacterial-induced inflammation*. Cell Microbiol, 2003. **5**(9): p. 581-92.
35. Medzhitov, R., *Toll-like receptors and innate immunity*. Nat Rev Immunol, 2001. **1**(2): p. 135-45.
36. Hahn, H., Falke, D., Kaufmann, S.H.E., Ullmann, U., *Medizinische Mikrobiologie und Infektiologie*. Vol. 4. Auflage. 2001, Berlin, Heidelberg, New York: Springer-Verlag.
37. Philpott, D.J. and S.E. Girardin, *The role of Toll-like receptors and Nod proteins in bacterial infection*. Mol Immunol, 2004. **41**(11): p. 1099-108.
38. Thiemermann, C., *Interactions between lipoteichoic acid and peptidoglycan from Staphylococcus aureus: a structural and functional analysis*. Microbes Infect, 2002. **4**(9): p. 927-35.
39. Schroder, N.W., et al., *Lipoteichoic acid (LTA) of Streptococcus pneumoniae and Staphylococcus aureus activates immune cells via Toll-like receptor (TLR)-2, lipopolysaccharide-binding protein (LBP), and CD14, whereas TLR-4 and MD-2 are not involved*. J Biol Chem, 2003. **278**(18): p. 15587-94.
40. Manukyan, M., et al., *Binding of lipopeptide to CD14 induces physical proximity of CD14, TLR2 and TLR1*. Eur J Immunol, 2005. **35**(3): p. 911-21.
41. Schroder, N.W., et al., *Lipopolysaccharide binding protein binds to triacylated and diacylated lipopeptides and mediates innate immune responses*. J Immunol, 2004. **173**(4): p. 2683-91.
42. Krieg, A.M., *Immune effects and mechanisms of action of CpG motifs*. Vaccine, 2000. **19**(6): p. 618-22.
43. Ito, T., et al., *Interferon-alpha and interleukin-12 are induced differentially by Toll-like receptor 7 ligands in human blood dendritic cell subsets*. J Exp Med, 2002. **195**(11): p. 1507-12.
44. Underhill, D.M., *Toll-like receptors: networking for success*. Eur J Immunol, 2003. **33**(7): p. 1767-75.
45. Netea, M.G., et al., *Toll-like receptors and the host defense against microbial pathogens: bringing specificity to the innate-immune system*. J Leukoc Biol, 2004. **75**(5): p. 749-55.
46. Akira, S., K. Takeda, and T. Kaisho, *Toll-like receptors: critical proteins linking innate and acquired immunity*. Nat Immunol, 2001. **2**(8): p. 675-80.
47. Kaisho, T. and S. Akira, *Pleiotropic function of Toll-like receptors*. Microbes Infect, 2004. **6**(15): p. 1388-94.

48. Wild, J.S. and S. Sur, *CpG oligonucleotide modulation of allergic inflammation*. Allergy, 2001. **56**(5): p. 365-76.
49. Matsuguchi, T., et al., *Gene expressions of Toll-like receptor 2, but not Toll-like receptor 4, is induced by LPS and inflammatory cytokines in mouse macrophages*. J Immunol, 2000. **165**(10): p. 5767-72.
50. Mita, Y., et al., *Toll-like receptor 4 surface expression on human monocytes and B cells is modulated by IL-2 and IL-4*. Immunol Lett, 2002. **81**(1): p. 71-5.
51. Staeger, H., A. Schaffner, and M. Schneemann, *Human toll-like receptors 2 and 4 are targets for deactivation of mononuclear phagocytes by interleukin-4*. Immunol Lett, 2000. **71**(1): p. 1-3.
52. Flo, T.H., et al., *Differential expression of Toll-like receptor 2 in human cells*. J Leukoc Biol, 2001. **69**(3): p. 474-81.
53. Mita, Y., et al., *Toll-like receptor 2 and 4 surface expressions on human monocytes are modulated by interferon-gamma and macrophage colony-stimulating factor*. Immunol Lett, 2001. **78**(2): p. 97-101.
54. Bosisio, D., et al., *Stimulation of toll-like receptor 4 expression in human mononuclear phagocytes by interferon-gamma: a molecular basis for priming and synergism with bacterial lipopolysaccharide*. Blood, 2002. **99**(9): p. 3427-31.
55. Leung, D.Y. and T. Bieber, *Atopic dermatitis*. Lancet, 2003. **361**(9352): p. 151-60.
56. Verboom, P., et al., *The cost of atopic dermatitis in the Netherlands: an international comparison*. Br J Dermatol, 2002. **147**(4): p. 716-24.
57. Novak, N., T. Bieber, and D.Y. Leung, *Immune mechanisms leading to atopic dermatitis*. J Allergy Clin Immunol, 2003. **112**(6 Suppl): p. S128-39.
58. Bunikowski, R., et al., *Prevalence and role of serum IgE antibodies to the Staphylococcus aureus-derived superantigens SEA and SEB in children with atopic dermatitis*. J Allergy Clin Immunol, 1999. **103**(1 Pt 1): p. 119-24.
59. Pastore, S., et al., *Interferon-gamma promotes exaggerated cytokine production in keratinocytes cultured from patients with atopic dermatitis*. J Allergy Clin Immunol, 1998. **101**(4 Pt 1): p. 538-44.
60. Strachan, D.P., *Hay fever, hygiene, and household size*. Bmj, 1989. **299**(6710): p. 1259-60.
61. Braun-Fahrlander, C., et al., *Environmental exposure to endotoxin and its relation to asthma in school-age children*. N Engl J Med, 2002. **347**(12): p. 869-77.
62. Eisenbarth, S.C., et al., *Lipopolysaccharide-enhanced, toll-like receptor 4-dependent T helper cell type 2 responses to inhaled antigen*. J Exp Med, 2002. **196**(12): p. 1645-51.
63. Gehring, U., et al., *Exposure to endotoxin decreases the risk of atopic eczema in infancy: a cohort study*. J Allergy Clin Immunol, 2001. **108**(5): p. 847-54.

64. Gereda, J.E., et al., *Relation between house-dust endotoxin exposure, type 1 T-cell development, and allergen sensitisation in infants at high risk of asthma*. Lancet, 2000. **355**(9216): p. 1680-3.
65. Zeuner, R.A., et al., *Influence of stimulatory and suppressive DNA motifs on host susceptibility to inflammatory arthritis*. Arthritis Rheum, 2003. **48**(6): p. 1701-7.
66. Schmidt, M., et al., *Cytokine and Ig-production by CG-containing sequences with phosphodiester backbone and dumbbell-shape*. Allergy, 2006. **61**(1): p. 56-63.
67. Kalliomaki, M., et al., *Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial*. Lancet, 2001. **357**(9262): p. 1076-9.
68. Grewe, M., et al., *A role for Th1 and Th2 cells in the immunopathogenesis of atopic dermatitis*. Immunol Today, 1998. **19**(8): p. 359-61.
69. Lauener, R.P., et al., *Expression of CD14 and Toll-like receptor 2 in farmers' and non-farmers' children*. Lancet, 2002. **360**(9331): p. 465-6.
70. Yang, I.A., et al., *Toll-like receptor 4 polymorphism and severity of atopy in asthmatics*. Genes Immun, 2004. **5**(1): p. 41-5.
71. Ahmad-Nejad, P., et al., *The toll-like receptor 2 R753Q polymorphism defines a subgroup of patients with atopic dermatitis having severe phenotype*. J Allergy Clin Immunol, 2004. **113**(3): p. 565-7.
72. Schultz Larsen, F. and J.M. Hanifin, *Secular change in the occurrence of atopic dermatitis*. Acta Derm Venereol Suppl (Stockh), 1992. **176**: p. 7-12.
73. *Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis*. Dermatology, 1993. **186**(1): p. 23-31.
74. Kunz, B., et al., *Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis*. Dermatology, 1997. **195**(1): p. 10-9.
75. Livak, K.J., et al., *Oligonucleotides with fluorescent dyes at opposite ends provide a quenched probe system useful for detecting PCR product and nucleic acid hybridization*. PCR Methods Appl, 1995. **4**(6): p. 357-62.
76. Cardullo, R.A., et al., *Detection of nucleic acid hybridization by nonradiative fluorescence resonance energy transfer*. Proc Natl Acad Sci U S A, 1988. **85**(23): p. 8790-4.
77. Holland, P.M., et al., *Detection of specific polymerase chain reaction product by utilizing the 5'--3' exonuclease activity of Thermus aquaticus DNA polymerase*. Proc Natl Acad Sci U S A, 1991. **88**(16): p. 7276-80.
78. Vandesompele, J., et al., *Accurate normalization of real-time quantitative RT-PCR data by geometric averaging of multiple internal control genes*. Genome Biol, 2002. **3**(7): p. RESEARCH0034.

- 
79. Radonic, A., et al., *Guideline to reference gene selection for quantitative real-time PCR*. Biochem Biophys Res Commun, 2004. **313**(4): p. 856-62.
  80. Pfaffl, *Real-time RT-PCR: Neue Ansätze zur exakten mRNA Quantifizierung*. BIOSpektrum, 2004. Sonderausgabe PCR, 10 (2004)(10): p. S. 92-95.
  81. van der Heijden, I.M., et al., *Presence of bacterial DNA and bacterial peptidoglycans in joints of patients with rheumatoid arthritis and other arthritides*. Arthritis Rheum, 2000. **43**(3): p. 593-8.
  82. Bustin, S.A., *Absolute quantification of mRNA using real-time reverse transcription polymerase chain reaction assays*. J Mol Endocrinol, 2000. **25**(2): p. 169-93.
  83. Ding, C. and C.R. Cantor, *Quantitative analysis of nucleic acids--the last few years of progress*. J Biochem Mol Biol, 2004. **37**(1): p. 1-10.
  84. Dvorak, Z., J.M. Pascussi, and M. Modriansky, *Approaches to messenger RNA detection - comparison of methods*. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub, 2003. **147**(2): p. 131-5.
  85. Wittwer, C.T., *Der LightCycler: Schnelle Real-time-PCR*, in *transkript Laborwelt*. 2000. p. 47-48.
  86. Stahlberg, A., Kubista, M. *Quantitative gene expression analysis by Real-time PCR- How to optimize the reverse transcription and real-time PCR reaction*. in *1st International qPCR Symposium and Application Workshop- Transcriptomics, Clinical Diagnostic and Gene Quantification*. 2004. Freising-Weihenstephan, Germany.
  87. Nagata, N., et al., *Analysis of highly expressed genes in monocytes from atopic dermatitis patients*. Int Arch Allergy Immunol, 2003. **132**(2): p. 156-67.
  88. Petit-Bertron, A.F., et al., *Adherence influences monocyte responsiveness to interleukin-10*. J Leukoc Biol, 2003. **73**(1): p. 145-54.
  89. Reynolds, N.J. and W.I. Al-Daraji, *Calcineurin inhibitors and sirolimus: mechanisms of action and applications in dermatology*. Clin Exp Dermatol, 2002. **27**(7): p. 555-61.
  90. Wahn, U., et al., *Efficacy and safety of pimecrolimus cream in the long-term management of atopic dermatitis in children*. Pediatrics, 2002. **110**(1 Pt 1): p. e2.
  91. Simon, D., et al., *Reduced dermal infiltration of cytokine-expressing inflammatory cells in atopic dermatitis after short-term topical tacrolimus treatment*. J Allergy Clin Immunol, 2004. **114**(4): p. 887-95.
  92. Kis, K., et al., *Budesonide, but not tacrolimus, affects the immune functions of normal human keratinocytes*. Int Immunopharmacol, 2006. **6**(3): p. 358-68.
  93. Leyden, J.J., R.R. Marples, and A.M. Kligman, *Staphylococcus aureus in the lesions of atopic dermatitis*. Br J Dermatol, 1974. **90**(5): p. 525-30.

- 
94. Ellingsen, E., et al., *Induction of cytokine production in human T cells and monocytes by highly purified lipoteichoic acid: involvement of Toll-like receptors and CD14*. Med Sci Monit, 2002. **8**(5): p. BR149-56.
  95. Miethke, T., et al., *Superantigens: the paradox of T-cell activation versus inactivation*. Int Arch Allergy Immunol, 1995. **106**(1): p. 3-7.
  96. Armstrong, L., et al., *Differential expression of Toll-like receptor (TLR)-2 and TLR-4 on monocytes in human sepsis*. Clin Exp Immunol, 2004. **136**(2): p. 312-9.
  97. Hoflich, C. and H.D. Volk, *[Immunomodulation in sepsis]*. Chirurg, 2002. **73**(11): p. 1100-4.
  98. Zollner, T.M., et al., *Colonization with superantigen-producing Staphylococcus aureus is associated with increased severity of atopic dermatitis*. Clin Exp Allergy, 2000. **30**(7): p. 994-1000.
  99. Strachan, D.P., *Family size, infection and atopy: the first decade of the "hygiene hypothesis"*. Thorax, 2000. **55** Suppl 1: p. S2-10.
  100. Ibs, K.-H. and L. Rink, *Das Immunsystem im Alter*. Zeitschrift für Gerontologische Geriatrie, 2001. **34**: p. 480-485.
  101. Sindermann, J., et al., *Investigations of the lymphokine system in elderly individuals*. Mech Ageing Dev, 1993. **70**(1-2): p. 149-59.
  102. Renshaw, M., et al., *Cutting edge: impaired Toll-like receptor expression and function in aging*. J Immunol, 2002. **169**(9): p. 4697-701.
  103. Boehmer, E.D., et al., *Age-dependent decrease in Toll-like receptor 4-mediated proinflammatory cytokine production and mitogen-activated protein kinase expression*. J Leukoc Biol, 2004. **75**(2): p. 342-9.
  104. Kalliomaki, M., et al., *Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial*. Lancet, 2003. **361**(9372): p. 1869-71.
  105. Helin, T., S. Haahtela, and T. Haahtela, *No effect of oral treatment with an intestinal bacterial strain, Lactobacillus rhamnosus (ATCC 53103), on birch-pollen allergy: a placebo-controlled double-blind study*. Allergy, 2002. **57**(3): p. 243-6.
  106. Michel, O., et al., *Severity of asthma is related to endotoxin in house dust*. Am J Respir Crit Care Med, 1996. **154**(6 Pt 1): p. 1641-6.
  107. Morath, S., A. Geyer, and T. Hartung, *Structure-function relationship of cytokine induction by lipoteichoic acid from Staphylococcus aureus*. J Exp Med, 2001. **193**(3): p. 393-7.
  108. Takeuchi, O., et al., *Cutting edge: role of Toll-like receptor 1 in mediating immune response to microbial lipoproteins*. J Immunol, 2002. **169**(1): p. 10-4.
  109. Jacobi, A., et al., *Infliximab in the treatment of moderate to severe atopic dermatitis*. J Am Acad Dermatol, 2005. **52**(3 Pt 1): p. 522-6.

- 
110. Riordan, S.M., et al., *Peripheral blood mononuclear cell expression of toll-like receptors and relation to cytokine levels in cirrhosis*. Hepatology, 2003. **37**(5): p. 1154-64.
  111. Arbour, N.C., et al., *TLR4 mutations are associated with endotoxin hyporesponsiveness in humans*. Nat Genet, 2000. **25**(2): p. 187-91.
  112. Bernasconi, N.L., N. Onai, and A. Lanzavecchia, *A role for Toll-like receptors in acquired immunity: up-regulation of TLR9 by BCR triggering in naive B cells and constitutive expression in memory B cells*. Blood, 2003. **101**(11): p. 4500-4.
  113. Ruprecht, C.R. and A. Lanzavecchia, *Toll-like receptor stimulation as a third signal required for activation of human naive B cells*. Eur J Immunol, 2006. **36**(4): p. 810-6.
  114. Sakai, T., et al., *Defect of toll-like receptor 9-mediated activation in NC/Nga mouse macrophages*. Immunol Lett, 2006.
  115. Nahori, M.A., et al., *Differential TLR recognition of leptospiral lipid A and lipopolysaccharide in murine and human cells*. J Immunol, 2005. **175**(9): p. 6022-31.
  116. Sacre, S.M., et al., *Endotoxin signaling in human macrophages: signaling via an alternate mechanism*. J Endotoxin Res, 2004. **10**(6): p. 445-52.
  117. Pallisgaard, N., et al., *Rapid and sensitive minimal residual disease detection in acute leukemia by quantitative real-time RT-PCR exemplified by t(12;21) TEL-AML1 fusion transcript*. Genes Chromosomes Cancer, 1999. **26**(4): p. 355-65.