
REFERENCES

1. Ahn, S. H., Kramvis, A., Kawai, S., Spangenberg, H. C., Li, J., Kimbi, G., Kew, M., Wands, J. and Tong, S. (2003). Sequence variation upstream of precore translation initiation codon reduces hepatitis B virus e antigen production. *Gastroenterology* **125**, 1370-8.
2. Ahn, Y. O. (1996). Strategy for vaccination against hepatitis B in areas with high endemicity: focus on Korea. *Gut* **38 Suppl 2**, S63-6.
3. Akuta, N. and Kumada, H. (2005). Influence of hepatitis B virus genotypes on the response to antiviral therapies. *J Antimicrob Chemother* **55**, 139-42.
4. Alberti, A., Clumeck, N., Collins, S., Gerlich, W., Lundgren, J., Palu, G., Reiss, P., Thiebaut, R., Weiland, O., Yazdanpanah, Y., Zeuzem, S. and ECC Jury. (2005). Short statement of the first European Consensus Conference on the treatment of chronic hepatitis B and C in HIV co-infected patients. *J Hepatol* **42**, 615-24.
5. Allain, J. P. (2004). Occult hepatitis B virus infection. *Transfus Clin Biol* **11**, 18-25.
6. Almeida, J. D. (1971). Electron microscope findings in the field of serum hepatitis. *Proc R Soc Med* **64**, 276.
7. Antonucci, T. K. and Rutter, W. J. (1989). Hepatitis B virus (HBV) promoters are regulated by the HBV enhancer in a tissue-specific manner. *J Virol* **63**, 579-83.

-
8. Araujo, N. M., Mello, F. C., Yoshida, C. F., Niel, C. and Gomes, S. A. (2004). High proportion of subgroup A' (genotype A) among Brazilian isolates of Hepatitis B virus. *Arch Virol* **149**, 1383-95.
 9. Arauz-Ruiz, P., Norder, H., Robertson, B. H. and Magnus, L. O. (2002). Genotype H: a new Amerindian genotype of hepatitis B virus revealed in Central America. *J Gen Virol* **83**, 2059-73.
 10. Arii, M., Takada, S. and Koike, K. (1992). Identification of three essential regions of hepatitis B virus X protein for trans-activation function. *Oncogene* **7**, 397-403.
 11. B. E., Lingappa, V. R. and Ganem, D. (1990). The N-terminal (pre-S2) domain of a hepatitis B virus surface glycoprotein is translocated across membranes by downstream signal sequences. *J Virol* **64**, 1414-9.
 12. Baptista, M., Kramvis, A. and Kew, M. C. (1999). High prevalence of 1762(T) 1764(A) mutations in the basic core promoter of hepatitis B virus isolated from black Africans with hepatocellular carcinoma compared with asymptomatic carriers. *Hepatology* **29**, 946-53.
 13. Bartenschlager, R. & Schaller, H. (1988). The amino-terminal domain of the hepadnaviral P-gene encodes the terminal protein (genome-linked protein) believed to prime reverse transcription. *Embo J* **7**, 4185-92.
 14. Bayer, M. E., Blumberg, B. S. and Werner, B. (1968). Particles associated with Australia antigen in the sera of patients with leukaemia, Down's Syndrome and hepatitis. *Nature* **218**, 1057-9.

-
15. Beasley, R. P. (1988). Hepatitis B virus. The major etiology of hepatocellular carcinoma. *Cancer* **61**, 1942-56.
 16. Beasley, R. P., Hwang, L. Y., Lin, C. C. and Chien, C. S. (1981). Hepatocellular carcinoma and hepatitis B virus. A prospective study of 22 707 men in Taiwan. *Lancet* **2**, 1129-33.
 17. Beckel-Mitchener, A. and Summers, J. (1997). A novel transcriptional element in circular DNA monomers of the duck hepatitis B virus. *J Virol* **71**, 7917-22.
 18. Blackberg, J. and Kidd-Ljunggren, K. (2003). Mutations within the hepatitis B virus genome among chronic hepatitis B patients with hepatocellular carcinoma. *J Med Virol* **71**, 18-23.
 19. Bonino, F., Rosina, F., Rizzetto, M., Rizzi, R., Chiaberge, E., Tardanico, R., Callea, F. and Verme, G. (1986). Chronic hepatitis in HBsAg carriers with serum HBV-DNA and anti-HBe. *Gastroenterology* **90**, 1268-73.
 20. Bosch, F. X. and Ribes, J. (2000). Epidemiology of liver cancer in Europe. *Can J Gastroenterol* **14**, 621-30.
 21. Bosch, F. X., Ribes, J. and Borrás, J. (1999). Epidemiology of primary liver cancer. *Semin Liver Dis* **19**, 271-85.
 22. Bosch, V., Bartenschlager, R., Radziwill, G. & Schaller, H. (1988). The duck hepatitis B virus P-gene codes for protein strongly associated with the 5'-end of the viral DNA minus strand. *Virology* **166**, 475-85.
 23. Bowyer, S. M. and Sim, J. G. (2000). Relationships within and between genotypes of hepatitis B virus at points across the genome: footprints of recombination in certain isolates. *J Gen Virol* **81**, 379-92.

-
24. Bowyer, S. M., van Staden, L., Kew, M. C. and Sim, J. G. (1997). A unique segment of the hepatitis B virus group A genotype identified in isolates from South Africa. *J Gen Virol* **78** (Pt 7), 1719-29.
 25. Bruss, V. & Gerlich, W. H. (1988). Formation of transmembraneous hepatitis B e-antigen by cotranslational in vitro processing of the viral precore protein. *Virology* **163**, 268-75.
 26. Buckwold, V. E., Xu, Z., Chen, M., Yen, T. S. and Ou, J. H. (1996). Effects of a naturally occurring mutation in the hepatitis B virus basal core promoter on precore gene expression and viral replication. *J Virol* **70**, 5845-51.
 27. Buendia, M. A. (1992). Hepatitis B viruses and hepatocellular carcinoma. *Adv Cancer Res* **59**, 167-226.
 28. Cabrerizo, M., Bartolom inverted question marke, J., Caramelo, C., Barril, G. and Carreno, V. (2000). Molecular analysis of hepatitis B virus DNA in serum and peripheral blood mononuclear cells from hepatitis B surface antigen-negative cases. *Hepatology* **32**, 116-23.
 29. Cabrerizo, M., Bartolome, J. and Carreno, V. (2002). In vitro infection of human peripheral blood mononuclear cells by a defective hepatitis B virus with a deletion in the PreS1 region of the viral genome. *J Viral Hepat* **9**, 265-71.
 30. Calkhoven, C. F., Muller, C. and Leutz, A. (2000). Translational control of C/EBPalpha and C/EBPbeta isoform expression. *Genes Dev* **14**, 1920-32.
 31. Cao, J. and Geballe, A. P. (1996a). Coding sequence-dependent ribosomal arrest at termination of translation. *Mol Cell Biol* **16**, 603-8.

-
32. Cao, J. and Geballe, A. P. (1996b). Inhibition of nascent-peptide release at translation termination. *Mol Cell Biol* **16**, 7109-14.
33. Carman, W. F., Jacyna, M. R., Hadziyannis, S., Karayiannis, P., McGarvey, M. J., Makris, A. and Thomas, H. C. (1989). Mutation preventing formation of hepatitis B e antigen in patients with chronic hepatitis B infection. *Lancet* **2**, 588-91.
34. Carman, W. F., Korula, J., Wallace, L., MacPhee, R., Mimms, L. and Decker, R. (1995). Fulminant reactivation of hepatitis B due to envelope protein mutant that escaped detection by monoclonal HBsAg ELISA. *Lancet* **345**, 1406-7.
35. Carman, W. F., Zanetti, A. R., Karayiannis, P., Waters, J., Manzillo, G., Tanzi, E., Zuckerman, A. J. and Thomas, H. C. (1990). Vaccine-induced escape mutant of hepatitis B virus. *Lancet* **336**, 325-9.
36. Cattaneo, R., Will, H., Hernandez, N. and Schaller, H. (1983). Signals regulating hepatitis B surface antigen transcription. *Nature* **305**, 336-8.
37. Chami, M., Gozuacik, D., Saigo, K., Capiod, T., Falson, P., Lecoecur, H., Urashima, T., Beckmann, J., Gougeon, M. L., Claret, M., le Maire, M., Brechot, C. and Paterlini-Brechot, P. (2000). Hepatitis B virus-related insertional mutagenesis implicates SERCA1 gene in the control of apoptosis. *Oncogene* **19**, 2877-86.
38. Chan, H. L., Tsui, S. K., Tse, C. H., Ng, E. Y., Au, T. C., Yuen, L., Bartholomeusz, A., Leung, K. S., Lee, K. H., Locarnini, S. and Sung, J. J. (2005) Epidemiological and virological characteristics of 2 subgroups of hepatitis B virus genotype C. *Infect Dis* **191**, 2022-32.

-
39. Chang, C., Zhou, S., Ganem, D. & Standring, D. N. (1994). Phenotypic mixing between different hepadnavirus nucleocapsid proteins reveals C protein dimerization to be cis preferential. *J Virol* **68**, 5225-31.
40. Chang, H. K., Wang, B. Y., Yuh, C. H., Wei, C. L. and Ting, L. P. (1989). A liver-specific nuclear factor interacts with the promoter region of the large surface protein gene of human hepatitis B virus. *Mol Cell Biol* **9**, 5189-97.
41. Chang, L. J., Ganem, D. & Varmus, H. E. (1990). Mechanism of translation of the hepadnaviral polymerase (P) gene. *Proc Natl Acad Sci U S A* **87**, 5158-62.
42. Chang, L. J., Pryciak, P., Ganem, D. & Varmus, H. E. (1989). Biosynthesis of the reverse transcriptase of hepatitis B viruses involves de novo translational initiation not ribosomal frameshifting. *Nature* **337**, 364-8.
43. Chayama, K., Suzuki, Y., Kobayashi, M., Tsubota, A., Hashimoto, M., Miyano, Y., Koike, H., Koida, I., Arase, Y., Saitoh, S., Murashima, N., Ikeda, K. and Kumada, H. (1998). Emergence and takeover of YMDD motif mutant hepatitis B virus during long-term lamivudine therapy and re-takeover by wild type after cessation of therapy. *Hepatology* **27**, 1711-6.
44. Chen, H. S., Kaneko, S., Girones, R., Anderson, R. W., Hornbuckle, W. E., Tennant, B. C., Cote, P. J., Gerin, J. L., Purcell, R. H. and Miller, R. H. (1993). The woodchuck hepatitis virus X gene is important for establishment of virus infection in woodchucks. *J Virol* **67**, 1218-26.
45. Chen, M. T., Billaud, J. N., Sallberg, M., Guidotti, L. G., Chisari, F. V., Jones, J., Hughes, J. and Milich, D. R. (2004). A function of the hepatitis B virus

-
- precure protein is to regulate the immune response to the core antigen. *Proc Natl Acad Sci U S A* **101**, 14913-8.
46. Chen, Y. C., Delbrook, K., Dealwis, C., Mimms, L., Mushahwar, I. K. and Mandecki, W. (1996). Discontinuous epitopes of hepatitis B surface antigen derived from a filamentous phage peptide library. *Proc Natl Acad Sci U S A* **93**, 1997-2001.
47. Chiaramonte, M., Stroffolini, T., Ngatchu, T., Rapicetta, M., Lantum, D., Kaptue, L., Chionne, P., Conti, S., Sarrecchia, B. and Naccarato, R. (1991). Hepatitis B virus infection in Cameroon: a seroepidemiological survey in city school children. *J Med Virol* **33**, 95-9.
48. Cho, G., Park, S. G. and Jung, G. (2000). Localization of HSP90 binding sites in the human hepatitis B virus polymerase. *Biochem Biophys Res Commun* **269**, 191-6.
49. Colgrove, R., Simon, G. and Ganem, D. (1989). Transcriptional activation of homologous and heterologous genes by the hepatitis B virus X gene product in cells permissive for viral replication. *J Virol* **63**, 4019-26.
50. Dane, D. S., Cameron, C. H. and Briggs, M. (1970). Virus-like particles in serum of patients with Australia-antigen-associated hepatitis. *Lancet* **1**, 695-8.
51. Das, K., Xiong, X., Yang, H., Westland, C. E., Gibbs, C. S., Sarafianos, S. G. and Arnold, E. (2001). Molecular modeling and biochemical characterization reveal the mechanism of hepatitis B virus polymerase resistance to lamivudine (3TC) and emtricitabine (FTC). *J Virol* **75**, 4771-9.

-
52. De Falco, S., Ruvoletto, M. G., Verdoliva, A., Ruvo, M., Raucci, A., Marino, M., Senatore, S., Cassani, G., Alberti, A., Pontisso, P. & Fassina, G. (2001). Cloning and expression of a novel hepatitis B virus-binding protein from HepG2 cells. *J Biol Chem* **276**, 36613-23.
53. Devarbhavi, H. C., Cohen, A. J., Patel, R., Wiesner, R. H., Dickson, R. C. and Ishitani, M. B. (2002). Preliminary results: outcome of liver transplantation for hepatitis B virus varies by hepatitis B virus genotype. *Liver Transpl* **8**, 550-5.
54. Ducrest, A. L., Amacker, M., Lingner, J. and Nabholz, M. (2002). Detection of promoter activity by flow cytometric analysis of GFP reporter expression. *Nucleic Acids Res* **30**, e65.
55. Eble, B. E., MacRae, D. R., Lingappa, V. R. and Ganem, D. (1987). Multiple topogenic sequences determine the transmembrane orientation of the hepatitis B surface antigen. *Mol Cell Biol* **7**, 3591-601.
56. Feitelson, M. A. (1994). Biology of hepatitis B virus variants. *Lab Invest* **71**, 324-49.
57. Felsenstein, J. (1995). PHYLIP (Phylogeny Inference Package). Department of Genetics, University of Washington, Seattle, Washington.
<http://evolution.genetics.washington.edu/phylip.html>.
58. Fernholz, D., Galle, P. R., Stemler, M., Brunetto, M., Bonino, F. and Will, H. (1993). Infectious hepatitis B virus variant defective in pre-S2 protein expression in a chronic carrier. *Virology* **194**, 137-48. and & Lolekha, S. (1995). Hepatitis B virus strains in Thailand: genomic variants in chronic carriers. *J Med Virol* **47**, 454-61.

-
59. Fukuda, R., Ishimura, N., Kushiya, Y., Moriyama, N., Ishihara, S., Chowdhury, A., Tokuda, A., Sakai, S., Akagi, S., Watanabe, M. and Fukumoto, S. (1996). Hepatitis B virus with X gene mutation is associated with the majority of serologically "silent" non-b, non-c chronic hepatitis. *Microbiol Immunol* **40**, 481-8.
60. Galibert, F., Mandart, E., Fitoussi, F., Tiollais, P. and Charnay, P. (1979). Nucleotide sequence of the hepatitis B virus genome (subtype ayw) cloned in *E. coli*. *Nature* **281**, 646-50.
61. Garcia, A. D., Ostapchuk, P. and Hearing, P. (1993). Functional interaction of nuclear factors EF-C, HNF-4, and RXR alpha with hepatitis B virus enhancer I. *J Virol* **67**, 3940-50.
62. Garcia, A. D., Ostapchuk, P. and Hearing, P. (1993). Functional interaction of nuclear factors EF-C, HNF-4, and RXR alpha with hepatitis B virus enhancer I. *J Virol* **67**, 3940-50.
63. Gerlich, W. H. and Robinson, W. S. (1980). Hepatitis B virus contains protein attached to the 5' terminus of its complete DNA strand. *Cell* **21**, 801-9.
64. Gerlich, W. H., Heermann, K. H. & Lu, X. (1992). Functions of hepatitis B surface proteins. *Arch Virol Suppl* **4**, 129-32.
65. Gerner, P. R., Friedt, M., Oettinger, R., Lausch, E. and Wirth, S. (1998). The hepatitis B virus seroconversion to anti-HBe is frequently associated with HBV genotype changes and selection of preS2-defective particles in chronically infected children. *Virology* **245**, 163-72.

-
66. Gong, S. S., Jensen, A. D. and Rogler, C. E. (1996). Loss and acquisition of duck hepatitis B virus integrations in lineages of LMH-D2 chicken hepatoma cells. *J Virol* **70**, 2000-7.
67. Gong, S. S., Jensen, A. D., Chang, C. J. & Rogler, C. E. (1999). Double-stranded linear duck hepatitis B virus (DHBV) stably integrates at a higher frequency than wild-type DHBV in LMH chicken hepatoma cells. *J Virol* **73**, 1492-502.
68. Gong, S. S., Jensen, A. D., Wang, H. and Rogler, C. E. (1995). Duck hepatitis B virus integrations in LMH chicken hepatoma cells: identification and characterization of new episomally derived integrations. *J Virol* **69**, 8102-8.
69. Gozuacik, D., Murakami, Y., Saigo, K., Chami, M., Mugnier, C., Lagorce, D., Okanoue, T., Urashima, T., Brechot, C. and Paterlini-Brechot, P. (2001). Identification of human cancer-related genes by naturally occurring Hepatitis B Virus DNA tagging. *Oncogene* **20**, 6233-40.
70. Grandjacques, C., Pradat, P., Stuyver, L., Chevallier, M., Chevallier, P., Pichoud, C., Maisonnas, M., Trepo, C. and Zoulim, F. (2000). Rapid detection of genotypes and mutations in the pre-core promoter and the pre-core region of hepatitis B virus genome: correlation with viral persistence and disease severity. *J Hepatol* **33**, 430-9.
71. Grethe, S., Heckel, J. O., Rietschel, W. and Hufert, F. T. Molecular epidemiology of hepatitis B virus variants in nonhuman primates. *J Virol* **74**, 5377-81.

-
72. Gunther, S., Baginski, S., Kissel, H., Reinke, P., Kruger, D. H., Will, H. and Meisel, H. (1996a). Accumulation and persistence of hepatitis B virus core gene deletion mutants in renal transplant patients are associated with end-stage liver disease. *Hepatology* **24**, 751-8.
73. Gunther, S., Li, B. C., Miska, S., Kruger, D. H., Meisel, H. and Will, H. (1995). A novel method for efficient amplification of whole hepatitis B virus genomes permits rapid functional analysis and reveals deletion mutants in immunosuppressed patients. *J Virol* **69**, 5437-44.
74. Gunther, S., Piwon, N. and Will, H. (1998). Wild-type levels of pregenomic RNA and replication but reduced pre-C RNA and e-antigen synthesis of hepatitis B virus with C(1653) --> T, A(1762) --> T and G(1764) --> A mutations in the core promoter. *J Gen Virol* **79 (Pt 2)**, 375-80.
75. Gunther, S., Piwon, N., Iwanska, A., Schilling, R., Meisel, H. and Will, H. (1996a). Type, prevalence, and significance of core promoter/enhancer II mutations in hepatitis B viruses from immunosuppressed patients with severe liver disease. *J Virol* **70**, 8318-31.
76. Guo, W. T., Bell, K. D. and Ou, J. H. (1991). Characterization of the hepatitis B virus EnhI enhancer and X promoter complex. *J Virol* **65**, 6686-92.
77. Hansen, L. J., Tennant, B. C., Seeger, C. and Ganem, D. (1993). Differential activation of myc gene family members in hepatic carcinogenesis by closely related hepatitis B viruses. *Mol Cell Biol* **13**, 659-67.

-
78. Hardie, D. R. and Williamson, C. (1997). Analysis of the preS1 gene of hepatitis B virus (HBV) to define epidemiologically linked and un-linked infections in South Africa. *Arch Virol* **142**, 1829-41.
79. Heermann, K. H., Goldmann, U., Schwartz, W., Seyffarth, T., Baumgarten, H. and Gerlich, W. H. (1984). Large surface proteins of hepatitis B virus containing the pre-s sequence. *J Virol* **52**, 396-402.
80. Heermann, K. H., Kruse, F., Seifer, M. and Gerlich, W. H. (1987). Immunogenicity of the gene S and Pre-S domains in hepatitis B virions and HBsAg filaments. *Intervirology* **28**, 14-25.
81. Henkler, F., Hoare, J., Waseem, N., Goldin, R. D., McGarvey, M. J., Koshy, R. and King, I. A. (2001). Intracellular localization of the hepatitis B virus HBx protein. *J Gen Virol* **82**, 871-82.
82. Hildt, E., Urban, S., Eckerskorn, C. and Hofschneider, P. H. (1996). Isolation of highly purified, functional carboxy-terminally truncated hepatitis B virus middle surface protein activators from eucaryotic expression systems. *Hepatology* **24**, 502-7.
83. Hoare, J., Henkler, F., Dowling, J. J., Errington, W., Goldin, R. D., Fish, D. & McGarvey, M. J. (2001). Subcellular localisation of the X protein in HBV infected hepatocytes. *J Med Virol* **64**, 419-26.
84. Hollinger, F. B., Goyal, R. K., Hersh, T., Powell, H. C., Schulman, R. J. and Malnick, J. L. (1972). Immune response to hepatitis virus type B in Down's syndrome and other mentally retarded patients. *Am J Epidemiol* **95**, 356-62.

-
85. Hou, J., Karayiannis, P., Waters, J., Luo, K., Liang, C. and Thomas, H. C. (1995). A unique insertion in the S gene of surface antigen--negative hepatitis B virus Chinese carriers. *Hepatology* **21**, 273-8.
86. Hou, J., Lin, Y., Waters, J., Wang, Z., Min, J., Liao, H., Jiang, J., Chen, J., Luo, K. and Karayiannis, P. (2002). Detection and significance of a G1862T variant of hepatitis B virus in Chinese patients with fulminant hepatitis. *J Gen Virol* **83**, 2291-8.
87. Hruska, J. F., Clayton, D. A., Rubenstein, J. L. and Robinson, W. S. (1977). Structure of hepatitis B Dane particle DNA before and after the Dane particle DNA polymerase reaction. *J Virol* **21**, 666-72.
88. Hsu, T., Moroy, T., Etiemble, J., Louise, A., Trepo, C., Tiollais, P. and Buendia, M. A. (1988). Activation of c-myc by woodchuck hepatitis virus insertion in hepatocellular carcinoma. *Cell* **55**, 627-35.
89. <http://web.hku.hk/-xxia/software/software.htm>
90. <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed>.
91. <http://www.orange-street-church.org/text/huguenot.htm>.
92. <http://www.stanford.edu/group/virus/1999/tchang/replication.htm>.
93. <http://www.who.int>.
94. Hu, J. and Seeger, C. (1996). Hsp90 is required for the activity of a hepatitis B virus reverse transcriptase. *Proc Natl Acad Sci U S A* **93**, 1060-4.
95. Hu, K. Q. and Siddiqui, A. (1991). Regulation of the hepatitis B virus gene expression by the enhancer element I. *Virology* **181**, 721-6.

-
96. Huang, M. & Summers, J. (1994). pet, a small sequence distal to the pregenome cap site, is required for expression of the duck hepatitis B virus pregenome. *J Virol* **68**, 1564-72.
97. Hunt, C. M., McGill, J. M., Allen, M. I. and Condreay, L. D. (2000). Clinical relevance of hepatitis B viral mutations. *Hepatology* **31**, 1037-44.
98. Huy, T. T., Ushijima, H., Quang, V. X., Win, K. M., Luengrojanakul, P., Kikuchi, K., Sata, T. and Abe, K. (2004). Genotype C of hepatitis B virus can be classified into at least two subgroups. *J Gen Virol* **85**, 283-92.
99. *J Biol Chem*, **278**, 891-5.
100. Jahr, S., Hentze, H., Englisch, S., Hardt, D., Fackelmayer, F. O., Hesch, R. D. and Knippers, R. (2001). DNA fragments in the blood plasma of cancer patients: quantitations and evidence for their origin from apoptotic and necrotic cells. *Cancer Res* **61**, 1659-65.
101. Jung, M. C. & Pape, G. R. (2002). Immunology of hepatitis B infection. *Lancet Infect Dis* **2**, 43-50.
102. Junker-Niepmann, M., Bartenschlager, R. and Schaller H. (1990). A short cis-acting sequence is required for hepatitis B virus pregenome encapsidation and sufficient for packaging of foreign RNA. *EMBO J* **9**, 3389-96.
103. Kane, M. (1995). Global programme for control of hepatitis B infection. *Vaccine* **13 Suppl 1**, S47-9.
104. Kao, J. H. (2002). Hepatitis B viral genotypes: clinical relevance and molecular characteristics. *J Gastroenterol Hepatol* **17**, 643-50.

-
105. Kao, J. H. (2002). Hepatitis B viral genotypes: clinical relevance and molecular characteristics. *J Gastroenterol Hepatol* **17**, 643-50.
106. Kao, J. H. and Chen, D. S. (2002). Global control of hepatitis B virus infection. *Lancet Infect Dis* **2**, 395-403.
107. Kao, J. H., Chen, P. J., Lai, M. Y. and Chen, D. S. (2000a). Hepatitis B genotypes correlate with clinical outcomes in patients with chronic hepatitis B. *Gastroenterology* **118**, 554-9.
108. Kao, J. H., Chen, P. J., Lai, M. Y. and Chen, D. S. (2002). Genotypes and clinical phenotypes of hepatitis B virus in patients with chronic hepatitis B virus infection. *J Clin Microbiol* **40**, 1207-9.
109. Kao, J. H., Wu, N. H., Chen, P. J., Lai, M. Y. and Chen, D. S. (2000). Hepatitis B genotypes and the response to interferon therapy. *J Hepatol* **33**, 998-1002.
110. Kato, H., Gish, R. G., Bzowej, N., Newsom, M., Sugauchi, F., Tanaka, Y., Kato, T., Orito, E., Usuda, S., Ueda, R., Miyakawa, Y. and Mizokami, M. (2004). Eight genotypes (A-H) of hepatitis B virus infecting patients from San Francisco and their demographic, clinical, and virological characteristics. *J Med Virol* **73**, 516-521.
111. Kato, H., Orito, E., Gish, R. G., Bzowej, N., Newsom, M., Sugauchi, F., Suzuki, S., Ueda, R., Miyakawa, Y. and Mizokami, M. (2002a). Hepatitis B e antigen in sera from individuals infected with hepatitis B virus of genotype G. *Hepatology* **35**, 922-9.

-
112. Kato, H., Orito, E., Gish, R. G., Sugauchi, F., Suzuki, S., Ueda, R., Miyakawa, Y. and Mizokami, M. (2002b). Characteristics of hepatitis B virus isolates of genotype G and their phylogenetic differences from the other six genotypes (A through F). *J Virol* **76**, 6131-7.
113. Kay, A., Mandart, E., Trepo, C. and Galibert, F. (1985). The HBV HBX gene expressed in *E. coli* is recognised by sera from hepatitis patients. *Embo J* **4**, 1287-92.
114. Kew, M. C. (1996b). Progress towards the comprehensive control of hepatitis B in Africa: a view from South Africa. *Gut* **38 Suppl 2**, S31-6.
115. Kew, M. C. (2002). Epidemiology of hepatocellular carcinoma. *Toxicology* **181-182**, 35-8.
116. Kew, M. C. and Popper, H. (1984). Relationship between hepatocellular carcinoma and cirrhosis. *Semin Liver Dis* **4**, 136-46.
117. Kew, M. C., Kramvis, A., Yu, M. C., Arakawa, K. and Hodgkinson, J. (2005). Increased hepatocarcinogenic potential of hepatitis B virus genotype A in Bantu-speaking sub-saharan Africans. *J Med Virol* **75**, 513-21.
118. Kew, M. C., Miller, R. H., Chen, H. S., Tennant, B. C. and Purcell, R. H. (1993). Mutant woodchuck hepatitis virus genomes from virions resemble rearranged hepadnaviral integrants in hepatocellular carcinoma. *Proc Natl Acad Sci USA* **90**, 10211-5.
119. Kew, M.C. (1992). Chronic Hepatitis B virus infection in Africa and Hepatocellular Carcinoma in Africa. *S Afr J Sci* **88**, 524-28.

-
120. Kiire, C. F. (1996). The epidemiology and prophylaxis of hepatitis B in sub-Saharan Africa: a view from tropical and subtropical Africa. *Gut* **38 Suppl 2**, S5-12.
121. Kim, C. M., Koike, K., Saito, I., Miyamura, T. and Jay, G. (1991). HBx gene of hepatitis B virus induces liver cancer in transgenic mice. *Nature* **351**, 317-20.
122. Knoll, A., Rohrhofer, A., Kochanowski, B., Wurm, E. M. and Jilg, W. (1999). Prevalence of precore mutants in anti-HBe-positive hepatitis B virus carriers in Germany. *J Med Virol* **59**, 14-8.
123. Koike, K., Shirakata, Y., Yaginuma, K., Arai, M., Takada, S., Nakamura, I., Hayashi, Y., Kawada, M. and Kobayashi, M. (1989). Oncogenic potential of hepatitis B virus. *Mol Biol Med* **6**, 151-60.
124. Kozak, M. (1977). Nucleotide sequences of 5'-terminal ribosome-protected initiation regions from two reovirus messages. *Nature* **269**, 391-4.
125. Kozak, M. (1978). How do eucaryotic ribosomes select initiation regions in messenger RNA? *Cell* **15**, 1109-23.
126. Kozak, M. (1986). Influences of mRNA secondary structure on initiation by eukaryotic ribosomes. *Proc Natl Acad Sci U S A* **83**, 2850-4.
127. Kozak, M. (1986a). Point mutations define a sequence flanking the AUG initiator codon that modulates translation by eukaryotic ribosomes. *Cell* **44**, 283-92.
128. Kozak, M. (1987a). At least six nucleotides preceding the AUG initiator codon enhance translation in mammalian cells. *J Mol Biol* **196**, 947-50.

-
129. Kozak, M. (1987b). An analysis of 5'-noncoding sequences from 699 vertebrate messenger RNAs. *Nucleic Acids Res* **15**, 8125-48.
130. Kozak, M. (1997). Recognition of AUG and alternative initiator codons is augmented by G in position +4 but is not generally affected by the nucleotides in positions +5 and +6. *Embo J* **16**, 2482-92.
131. Kozak, M. (1999). Initiation of translation in prokaryotes and eukaryotes. *Gene* **234**, 187-208.
132. Kramvis, A. & Kew, M. C. (1998). Structure and function of the encapsidation signal of hepadnaviridae. *J Viral Hepat* **5**, 357-67.
133. Kramvis, A. and Kew, M. C. (1999). The core promoter of hepatitis B virus. *J Viral Hepat* **6**, 415-27.
134. Kramvis, A., Bukofzer, S., Kew, M. C. and Song, E. (1997). Nucleic acid sequence analysis of the precore region of hepatitis B virus from sera of southern African black adult carriers of the virus. *Hepatology* **25**, 235-40.
135. Kramvis, A., Kew, M. C. & Bukofzer, S. (1998). Hepatitis B virus precore mutants in serum and liver of Southern African Blacks with hepatocellular carcinoma. *J Hepatol* **28**, 132-41.
136. Kramvis, A., Kew, M. C. and Francois, G. (2005). Hepatitis B virus genotypes. *Vaccine*. **23**, 2409-23.
137. Kramvis, A., Restorp, K., Norder, H., Botha, J. F., Magnius, L. O. and Kew, M. C. (2005) Full genome analysis of Hepatitis B virus genotype E strains from south-western Africa and Madagascar reveals low genetic variability. *J Gen Virol* (in press).

-
138. Kramvis, A., Weitzmann, L., Owiredo, W. K. and Kew, M. C. (2002). Analysis of the complete genome of subgroup A' hepatitis B virus isolates from South Africa. *J Gen Virol* **83**, 835-9.
139. Kratz, P. A., Bottcher, B. and Nassal, M. (1999). Native display of complete foreign protein domains on the surface of hepatitis B virus capsids. *Proc Natl Acad Sci U S A* **96**, 1915-20.
140. Kuroki, K., Cheung, R., Marion, P. L. & Ganem, D. (1994). A cell surface protein that binds avian hepatitis B virus particles. *J Virol* **68**, 2091-6.
141. Kuroki, K., Eng, F., Ishikawa, T., Turck, C., Harada, F. & Ganem, D. (1995). gp180, a host cell glycoprotein that binds duck hepatitis B virus particles, is encoded by a member of the carboxypeptidase gene family. *J Biol Chem* **270**, 15022-8.
142. Kwok, S. and Higuchi, R. (1989). Avoiding false positives with PCR. *Nature* **339**, 237-8.
143. Landers, T. A., Greenberg, H. B. and Robinson, W. S. (1977). Structure of hepatitis B Dane particle DNA and nature of the endogenous DNA polymerase reaction. *J Virol* **23**, 368-76.
144. Lanford, R. E., Chavez, D., Brasky, K. M., Burns, R. B 3rd. and Rico-Hesse, R. (1998). Isolation of a hepadnavirus from the woolly monkey, a New World primate. . *Proc Natl Acad Sci U S A* **95**, 5757-61.
145. Lanford, R. E., Chavez, D., Rico-Hesse, R. and Mootnick, A. (2000). Hepadnavirus infection in captive gibbons. *J Virol* **74**, 2955-9.

-
146. Laskus, T., Rakela, J., Tong, M. J., Nowicki, M. J., Mosley, J. W. and Persing, D. H. (1994). Naturally occurring hepatitis B virus mutants with deletions in the core promoter region. *J Hepatol* **20**, 837-41.
147. Li, J. S., Tong, S. P., Wen, Y. M., Vitvitski, L., Zhang, Q. and Trepo, C. (1993). Hepatitis B virus genotype A rarely circulates as an HBe-minus mutant: possible contribution of a single nucleotide in the precore region. *J Virol* **67**, 5402-10.
148. Li, M., Xie, Y., Wu, X., Kong, Y. and Wang, Y. (1995). HNF3 binds and activates the second enhancer, ENII, of hepatitis B virus. *Virology* **214**, 371-8.
149. Lindh, M., Horal, P., Dhillon, A. P., Furuta, Y. and Norkrans, G. (1996). Hepatitis B virus carriers without precore mutations in hepatitis B e antigen-negative stage show more severe liver damage. *Hepatology* **24**, 494-501.
150. Lo, W. Y. and Ting, L. P. (1994). Repression of enhancer II activity by a negative regulatory element in the hepatitis B virus genome. *J Virol* **68**, 1758-64.
151. Lok, A. S., Akarca, U. S. and Greene, S. (1995). Predictive value of precore hepatitis B virus mutations in spontaneous and interferon-induced hepatitis B e antigen clearance. *Hepatology* **21**, 19-24.
152. Lok, A. S., Akarca, U. and Greene, S. (1994). Mutations in the pre-core region of hepatitis B virus serve to enhance the stability of the secondary structure of the pre-genome encapsidation signal. *Proc Natl Acad Sci U S A* **91**, 4077-81.
153. Lioriot, M. A., Marcellin, P., Talbodec, N., Guignon, V., Gigou, M., Boyer, N., Bezeaud, A., Erlinger, S. and Benhamou, J. P. (1995). Low frequency of

- precure hepatitis B virus mutants in anti-hepatitis B e-positive reactivation after loss of hepatitis B e antigen in patients with chronic hepatitis B. *Hepatology* **21**, 627-31.
154. Machida, A., Kishimoto, S., Ohnuma, H., Baba, K., Ito, Y., Miyamoto, H., Funatsu, G., Oda, K., Usuda, S., Togami, S. & et al. (1984). A polypeptide containing 55 amino acid residues coded by the pre-S region of hepatitis B virus deoxyribonucleic acid bears the receptor for polymerized human as well as chimpanzee albumins. *Gastroenterology* **86**, 910-8.
155. Maddrey, W. C. (2001). Hepatitis B--an important public health issue. *Clin Lab* **47**, 51-5.
156. Magnius, L. O. and Norder, H. (1995). Subtypes, genotypes and molecular epidemiology of the hepatitis B virus as reflected by sequence variability of the S-gene. *Intervirology* **38**, 24-34.
157. Mahoney, F. J. (1999). Update on diagnosis, management, and prevention of hepatitis B virus infection. *Clin Microbiol Rev* **12**, 351-66.
158. Marinos, G., Torre, F., Gunther, S., Thomas, M. G., Will, H., Williams, R. and Naoumov, N. V. (1996). Hepatitis B virus variants with core gene deletions in the evolution of chronic hepatitis B infection. *Gastroenterology* **111**, 183-92.
159. Marion, P. L., Oshiro, L. S., Regnery, D. C., Scullard, G. H. and Robinson, W. S. (1980). A virus in Beechey ground squirrels that is related to hepatitis B virus of humans. *Proc Natl Acad Sci U S A* **77**, 2941-5.
160. Martindale, D. W., Wilson, M. D., Wang, D., Burke, R. D., Chen, X., Duronio, V. and Koop, B. F. (2000). Comparative genomic sequence analysis of the

-
- Williams syndrome region (LIMK1-RFC2) of human chromosome 7q11.23. *Mamm Genome* **11**, 890-8.
161. Matsubara, K. and Tokino, T. (1990). Integration of hepatitis B virus DNA and its implications for hepatocarcinogenesis. *Mol Biol Med* **7**, 243-60.
162. Mayerat, C., Mantegani, A. and Frei, P. C. (1999). Does hepatitis B virus (HBV) genotype influence the clinical outcome of HBV infection? *J Viral Hepat* **6**, 299-304.
163. McMahon, B. J., Alward, W. L., Hall, D. B., Heyward, W. L., Bender, T. R., Francis, D. P. and Maynard, J. E. (1985). Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis* **151**, 599-603.
164. Melegari, M., Scaglioni, P. P. and Wands, J. R. (1998). Hepatitis B virus mutants associated with 3TC and famciclovir administration are replication defective. *Hepatology* **27**, 628-33.
165. Messageot, F., Salhi, S., Eon, P. and Rossignol, J. M. Proteolytic processing of the hepatitis B virus e antigen precursor. Cleavage at two furin consensus sequences.
166. Milich, D. R., Chen, M. K., Hughes, J. L. & Jones, J. E. (1998). The secreted hepatitis B precore antigen can modulate the immune response to the nucleocapsid: a mechanism for persistence. *J Immunol* **160**, 2013-21.
167. Milich, D. R., Jones, J. E., Hughes, J. L., Price, J., Raney, A. K. & McLachlan, A. (1990). Is a function of the secreted hepatitis B e antigen to induce immunologic tolerance in utero? *Proc Natl Acad Sci U S A* **87**, 6599-603.

-
168. Miller, R. H., Kaneko, S., Chung, C. T., Girones, R. and Purcell, R. H. (1989). Compact organization of the hepatitis B virus genome. *Hepatology* **9**, 322-7.
169. Minuk, G. Y., Orr, P. S., Brown, R., Macdonald, S., Chaudhary, R. K. and Temple, P. (2000). Pre-core mutant infections in the Canadian Inuit. *J Hepatol* **33**, 781-4.
170. Miyakawa, Y. and Mizokami, M. (2003). Classifying hepatitis B virus genotypes. *Intervirology* **46**, 329-38.
171. Mizokami, M., Orito, E., Ohba, K., Ikeo, K., Lau, J. Y. and Gojobori, T. Constrained evolution with respect to gene overlap of hepatitis B virus. (1997). *J Mol Evol* **44**, S83-90.
172. Moolla, N., Kew, M. and Arbuthnot, P. (2002). Regulatory elements of hepatitis B virus transcription. *J Viral Hepat* **9**, 323-31.
173. Moradpour, D. and Wands, J. R. (1994). The molecular pathogenesis of hepatocellular carcinoma. *J Viral Hepat* **1**, 17-31.
174. Moriyama, K. (1997). Reduced antigen production by hepatitis B virus harbouring nucleotide deletions in the overlapping X gene and precore-core promoter. *J Gen Virol* **78 (Pt 6)**, 1479-86.
175. Mphahlele, M. J., Tshatsinde, E. A., Burnett, R. J. and Aspinall, S. (2002). Protective efficacy and antibody follow-up of hepatitis B vaccine within the South African expanded programme on immunisation. *S Afr Med J* **92**, 612-3.
176. Mulders, M. N., Venard, V., Njayou, M., Edoth, A. P., Bola Oyefolu, A. O., Kehinde, M. O., Muyembe Tamfum, J. J., Nebie, Y. K., Maiga, I., Ammerlaan, W., Fack, F., Omilabu, S. A., Le Faou, A. and Muller, C. P. (2004). Low genetic

- diversity despite hyperendemicity of hepatitis B virus genotype E throughout West Africa. *J Infect Dis* **190**, 400-8.
177. Murakami, Y., Minami, M., Daimon, Y. and Okanoue, T. (2004). Hepatitis B virus DNA in liver, serum, and peripheral blood mononuclear cells after the clearance of serum hepatitis B virus surface antigen. *J Med Virol* **72**, 203-14.
178. Nakao, K., Nakata, K., Yamashita, M., Tamada, Y., Hamasaki, K., Ishikawa, H., Kato, Y., Eguchi, K. and Ishii, N. (1999). p48 (ISGF-3gamma) is involved in interferon-alpha-induced suppression of hepatitis B virus enhancer-1 activity. *J Biol Chem* **274**, 28075-8.
179. Nassal, M. & Schaller, H. (1993). Hepatitis B virus replication. *Trends Microbiol* **1**, 221-8.
180. Neurath, A. R., Kent, S. B., Strick, N. & Parker, K. (1986). Identification and chemical synthesis of a host cell receptor binding site on hepatitis B virus. *Cell* **46**, 429-36.
181. Ngui, S. L., Hallet, R. and Teo, C. G. (1999). Natural and iatrogenic variation in hepatitis B virus. *Rev Med Virol* **9**, 183-209.
182. Nicholas, K., B. and Nicholas, H. .B. (1997). GeneDoc: Analysis and Visualization of Genetic Variation. www.psc.edu/biomed/genedoc.
183. Norder, H., Arauz-Ruiz, P., Blitz, L., Pujol, F. H., Echevarria, J. M. and Magnius, L. O. (2003). The T(1858) variant predisposing to the precore stop mutation correlates with one of two major genotype F hepatitis B virus clades. *J Gen Virol* **84**, 2083-7.

-
184. Norder, H., Courouce, A. M. and Magnius, L. O. (1994). Complete genomes, phylogenetic relatedness, and structural proteins of six strains of the hepatitis B virus, four of which represent two new genotypes. *Virology* **198**, 489-503.
185. Norder, H., Courouce, A. M., Coursaget, P., Echevarria, J. M., Lee, S. D., Mushahwar, I. K., Robertson, B. H., Locarnini, S. and Magnius, L. O. (2004). Genetic diversity of hepatitis B virus strains derived worldwide: genotypes, subgenotypes, and HBsAg subtypes. *Intervirology* **47**, 289-309.
186. Norder, H., Ebert, J. W., Fields, H. A., Mushahwar, I. K. and Magnius, L. O. (1996). Complete sequencing of a gibbon hepatitis B virus genome reveals a unique genotype distantly related to the chimpanzee hepatitis B virus. *Virology* **218**, 214-23.
187. Norder, H., Hammas, B., Lee, S. D., Bile, K., Courouce, A. M., Mushahwar, I. K. and Magnius, L. O. (1993). Genetic relatedness of hepatitis B viral strains of diverse geographical origin and natural variations in the primary structure of the surface antigen. *J Gen Virol* **74 (Pt 7)**, 1341-8.
188. Norder, H., Hammas, B., Lofdahl, S., Courouce, A. M. and Magnius, L. O. (1992). Comparison of the amino acid sequences of nine different serotypes of hepatitis B surface antigen and genomic classification of the corresponding hepatitis B virus strains. *J Gen Virol* **73 (Pt 5)**, 1201-8.
189. Odemuyiwa, S. O., Mulders, M. N., Oyedele, O. I., Ola, S. O., Odaibo, G. N., Olaleye, D. O. and Muller, C. P. (2001). Phylogenetic analysis of new hepatitis B virus isolates from Nigeria supports endemicity of genotype E in West Africa. *J Med Virol* **65**, 463-9.

-
190. Oess, S. and Hildt, E. (2000). Novel cell permeable motif derived from the PreS2-domain of hepatitis-B virus surface antigens. *Gene Ther* **7**, 750-8.
191. Ogston, C. W., Jonak, G. J., Rogler, C. E., Astrin, S. M. and Summers, J. (1982). Cloning and structural analysis of integrated woodchuck hepatitis virus sequences from hepatocellular carcinomas of woodchucks. *Cell* **29**, 385-94.
192. Okamoto, H., Tsuda, F., Akahane, Y., Sugai, Y., Yoshida, M., Moriyama, K., Tanaka, T., Miyakawa, Y. and Mayumi, M. (1994). Hepatitis B virus with mutations in the core promoter for an e antigen-negative phenotype in carriers with antibody to e antigen. *J Virol* **68**, 8102-10.
193. Omata, M., Ehata, T., Yokosuka, O., Hosoda, K. and Ohto, M. (1991). Mutations in the precore region of hepatitis B virus DNA in patients with fulminant and severe hepatitis. *N Engl J Med* **324**, 1699-704.
194. Ong, S. S., Jensen, A. D., Chang, C. J. and Rogler, C. E. (1999). Double-stranded linear duck hepatitis B virus (DHBV) stably integrates at a higher frequency than wild-type DHBV in LMH chicken hepatoma cells. *J Virol* **73**, 1492-502.
195. Ono-Nita, S. K., Kato, N., Shiratori, Y., Lan, K. H., Yoshida, H., Carrilho, F. J. and Omata, M. (1999a). Susceptibility of lamivudine-resistant hepatitis B virus to other reverse transcriptase inhibitors. *J Clin Invest* **103**, 1635-40.
196. Ono-Nita, S. K., Kato, N., Shiratori, Y., Masaki, T., Lan, K. H., Carrilho, F. J. and Omata, M. (1999b). YMDD motif in hepatitis B virus DNA polymerase influences on replication and lamivudine resistance: A study by in vitro full-length viral DNA transfection. *Hepatology* **29**, 939-45.

-
197. Oon, C. J., Chen, W. N., Lim, N., Koh, S., Lim, G. K., Leong, A. L. and Tan, G. S. (1999). Hepatitis B virus variants with lamivudine-related mutations in the DNA polymerase and the 'a' epitope of the surface antigen are sensitive to ganciclovir. *Antiviral Res* **41**, 113-8.
198. Orito, E., Mizokami, M., Sakugawa, H., Michitaka, K., Ishikawa, K., Ichida, T., Okanoue, T., Yotsuyanagi, H. and Iino, S. (2001). A case-control study for clinical and molecular biological differences between hepatitis B viruses of genotypes B and C. Japan HBV Genotype Research Group. *Hepatology* **33**, 218-23.
199. Osborne, L. R., Martindale, D., Scherer, S. W., Shi, X. M., Huizenga, J., Heng, H. H., Costa, T., Pober, B., Lew, L., Brinkman, J., Rommens, J., Koop, B. and Tsui, L. C. (1996). Identification of genes from a 500-kb region at 7q11.23 that is commonly deleted in Williams syndrome patients. *Genomics* **36**, 328-36.
200. Ou, J. H., Laub, O. & Rutter, W. J. (1986). Hepatitis B virus gene function: the precore region targets the core antigen to cellular membranes and causes the secretion of the e antigen. *Proc Natl Acad Sci U S A* **83**, 1578-82.
201. Owiredun, W. K., Kramvis, A. and Kew, M. C. (2001a). Hepatitis B virus DNA in serum of healthy black African adults positive for hepatitis B surface antibody alone: possible association with recombination between genotypes A and D. *J Med Virol* **64**, 441-54.
202. Owiredun, W. K., Kramvis, A. and Kew, M. C. (2001b). Molecular analysis of hepatitis B virus genomes isolated from black African patients with fulminant hepatitis B. *J Med Virol* **65**, 485-92.

-
203. Page, R. D. M. (1996). TREEVIEW: An application to display phylogenetic trees on personal computers. *Comput Appl Biosci* **12**, 357-58.
<http://taxonomy.zoology.gla.ac.uk/rod/treeview.html>.
204. Papatheodoridis, G. V., Dimou, E., Laras, A., Papadimitropoulos, V. and Hadziyannis, S. J. (2002). Course of virologic breakthroughs under long-term lamivudine in HBeAg-negative precore mutant HBV liver disease. *Hepatology* **36**, 219-26.
205. Patel, N. U., Jameel, S., Isom, H. and Siddiqui, A. (1989). Interactions between nuclear factors and the hepatitis B virus enhancer. *J Virol* **63**, 5293-301.
206. Paterson, A. C., Kew, M. C., Herman, A. A., Becker, P. J., Hodgkinson, J. and Isaacson, C. (1985). Liver morphology in southern African blacks with hepatocellular carcinoma: a study within the urban environment. *Hepatology* **5**, 72-8.
207. Petersen, J., Dandri, M., Burkle, A., Zhang, L. and Rogler, C. E. (1997). Increase in the frequency of hepadnavirus DNA integrations by oxidative DNA damage and inhibition of DNA repair. *J Virol* **71**, 5455-63.
208. Pontesilli, O., van Nunen, A. B., van Riel, D., Carotenuto, P., Niesters, H. G., Uytdehaag, F. G., De Man, R. A. and Osterhaus, A. D. (2004). Hepatitis B virus-specific T cell response in chronic hepatitis B patients treated with lamivudine and interferon-alpha. *Liver Int* **24**, 308-15.

-
209. Pontisso, P., Ruvoletto, M. G., Gerlich, W. H., Heermann, K. H., Bardini, R. and Alberti, A. (1989). Identification of an attachment site for human liver plasma membranes on hepatitis B virus particles. *Virology* **173**, 522-30.
210. Popper, H., Shih, J. W., Gerin, J. L., Wong, D. C., Hoyer, B. H., London, W. T., Sly, D. L. and Purcell, R. H. (1981). Woodchuck hepatitis and hepatocellular carcinoma: correlation of histologic with virologic observations. *Hepatology* **1**, 91-8.
211. Poussin, K., Dienes, H., Sirma, H., Urban, S., Beaugrand, M., Franco, D., Schirmacher, P., Brechot, C. and Paterlini Brechot, P. (1999). Expression of mutated hepatitis B virus X genes in human hepatocellular carcinomas. *Int J Cancer* **80**, 497-505.
212. Pult, I., Netter, H. J., Bruns, M., Prassolov, A., Sirma, H., Hohenberg, H., Chang, S. F., Frolich, K., Krone, O., Kaleta, E. F. and Will, H. (2001). Identification and analysis of a new hepadnavirus in white storks. *Virology* **289**, 114-28.
213. Pumpens, P. and Grens, E. (2001). HBV core particles as a carrier for B cell/T cell epitopes. *Intervirology* **44**, 98-114.
214. Radziwill, G., Tucker, W. and Schaller, H. (1990). Mutational analysis of the hepatitis B virus P gene product: domain structure and RNase H activity. *J Virol* **64**, 613-20.
215. Raimondo, G., Burk, R. D., Lieberman, H. M., Muschel, J., Hadziyannis, S. J., Will, H., Kew, M. C., Dusheiko, G. M. and Shafritz, D. A. (1988). Interrupted

-
- replication of hepatitis B virus in liver tissue of HBsAg carriers with hepatocellular carcinoma. *Virology* **166**, 103-12.
216. Repp, R., Keller, C., Borkhardt, A., Csecke, A., Schaefer, S., Gerlich, W. H. and Lampert, F. (1992). Detection of a hepatitis B virus variant with a truncated X gene and enhancer II. *Arch Virol* **125**, 299-304.
217. Richter-Cook, N. J., Dever, T. E., Hensold, J. O. and Merrick, W. C. (1998). Purification and characterization of a new eukaryotic protein translation factor. Eukaryotic initiation factor 4H. *J Biol Chem* **273**, 7579-87.
218. Robinson, W. S. (1994). Molecular events in the pathogenesis of hepadnavirus-associated hepatocellular carcinoma. *Annu Rev Med* **45**, 297-323.
219. Robinson, W. S. and Greenman, R. L. (1974). DNA polymerase in the core of the human hepatitis B virus candidate. *J Virol* **13**, 1231-6.
220. Robinson, W. S., Clayton, D. A. and Greenman, R. L. (1974). DNA of a human hepatitis B virus candidate. *J Virol* **14**, 384-91.
221. Robinson, W. S., Miller, R. H. & Marion, P. L. (1987). Hepadnaviruses and retroviruses share genome homology and features of replication. *Hepatology* **7**, 64S-73S.
222. Rodriguez-Frias, F., Buti, M., Jardi, R., Cotrina, M., Viladomiu, L., Esteban, R. and Guardia, J. (1995). Hepatitis B virus infection: precore mutants and its relation to viral genotypes and core mutations. *Hepatology* **22**, 1641-7.
223. Rogler, C. E. and Summers, J. (1982). Novel forms of woodchuck hepatitis virus DNA isolated from chronically infected woodchuck liver nuclei. *J Virol* **44**, 852-63.

-
224. Rogler, C. E. and Summers, J. (1984). Cloning and structural analysis of integrated woodchuck hepatitis virus sequences from a chronically infected liver. *J Virol* **50**, 832-7.
225. Ruiz-Opazo, N., Chakraborty, P. R. & Shafritz, D. A. (1982a). Characterization of viral genomes in the liver and serum of chimpanzee long-term hepatitis B virus carriers: a possible role for supercoiled HBV-DNA in persistent HBV infection. *J Cell Biochem* **19**, 281-92.
226. Ruiz-Opazo, N., Chakraborty, P. R. & Shafritz, D. A. (1982b). Evidence for supercoiled hepatitis B virus DNA in chimpanzee liver and serum Dane particles: possible implications in persistent HBV infection. *Cell* **29**, 129-36.
227. Russnak, R. H. (1991). Regulation of polyadenylation in hepatitis B viruses: stimulation by the upstream activating signal PS1 is orientation-dependent, distance-independent, and additive. *Nucleic Acids Res* **19**, 6449-56.
228. Sallam, T. A. and William Tong, C. Y. (2004). African links and hepatitis B virus genotypes in the Republic of Yemen. *J Med Virol* **73**, 23-8.
229. Schaller, H. and Fischer, M. (1991). Transcriptional control of hepadnavirus gene expression. *Curr Top Microbiol Immunol* **168**, 21-39.
230. Schlicht, H. J., Radziwill, G. & Schaller, H. (1989). Synthesis and encapsidation of duck hepatitis B virus reverse transcriptase do not require formation of core-polymerase fusion proteins. *Cell* **56**, 85-92.
231. Seeger, C. and Mason, W. S. (2000). Hepatitis B virus biology. *Microbiol Mol Biol Rev* **64**, 51-68.

-
232. Seeger, C., Ganem, D. and Varmus, H. E. (1986). Biochemical and genetic evidence for the hepatitis B virus replication strategy. *Science* **232**, 477-84.
233. Seeger, C., Summers, J. and Mason, W. S. (1991). Viral DNA synthesis. *Curr Top Microbiol Immunol* **168**, 41-60.
234. Seto, E., Mitchell, P. J. & Yen, T. S. (1990). Transactivation by the hepatitis B virus X protein depends on AP-2 and other transcription factors. *Nature* **344**, 72-4.
235. Severini, A., Liu, X. Y., Wilson, J. S. and Tyrrell, D. L. (1995). Mechanism of inhibition of duck hepatitis B virus polymerase by (-)-beta-L-2',3'-dideoxy-3'-thiacytidine. *Antimicrob Agents Chemother* **39**, 1430-5.
236. Shaul, Y., Garcia, P. D., Schonberg, S. and Rutter, W. J. (1986). Integration of hepatitis B virus DNA in chromosome-specific satellite sequences. *J Virol* **59**, 731-4.
237. Shih, C., Burke, K., Chou, M. J., Zeldis, J. B., Yang, C. S., Lee, C. S., Isselbacher, K. J., Wands, J. R. and Goodman, H. M. (1987). Tight clustering of human hepatitis B virus integration sites in hepatomas near a triple-stranded region. *J Virol* **61**, 3491-8.
238. Simonetti, R. G., Camma, C., Fiorello, F., Politi, F., D'Amico, G. & Pagliaro, L. (1991). Hepatocellular carcinoma. A worldwide problem and the major risk factors. *Dig Dis Sci* **36**, 962-72.
239. Sirma, H., Giannini, C., Poussin, K., Paterlini, P., Kremsdorf, D. and Brechot, C. (1999). Hepatitis B virus X mutants, present in hepatocellular carcinoma

- tissue abrogate both the antiproliferative and transactivation effects of HBx. *Oncogene* **18**, 4848-59.
240. Slagle, B. L., Lee, T. H. and Butel, J. S. (1992). Hepatitis B virus and hepatocellular carcinoma. *Prog Med Virol* **39**, 167-203.
241. Sprengel, R., Kaleta, E. F. & Will, H. (1988). Isolation and characterization of a hepatitis B virus endemic in herons. *J Virol* **62**, 3832-9.
242. Standring, D. N., Ou, J. H., Masiarz, F. R. & Rutter, W. J. (1988). A signal peptide encoded within the precore region of hepatitis B virus directs the secretion of a heterogeneous population of e antigens in *Xenopus* oocytes. *Proc Natl Acad Sci U S A* **85**, 8405-9.
243. Standring, D. N., Rutter W. J., Varmus, H. E. and Ganem, D. (1984). Transcription of the hepatitis B surface antigen gene in cultured murine cells initiates within the presurface region. *J Virol* **50**, 563-71.
244. Staprans, S., Loeb, D. D. and Ganem, D. (1991). Mutations affecting hepadnavirus plus-strand DNA synthesis dissociate primer cleavage from translocation and reveal the origin of linear viral DNA. *J Virol* **65**, 1255-62.
245. Stuyver, L., De Gendt, S., Van Geyt, C., Zoulim, F., Fried, M., Schinazi, R. F. & Rossau, R. (2000). A new genotype of hepatitis B virus: complete genome and phylogenetic relatedness. *J Gen Virol* **81**, 67-74.
246. Sugouchi, F., Chutaputti, A., Orito, E., Kato, H., Suzuki, S., Ueda, R. and Mizokami, M. (2002). Hepatitis B virus genotypes and clinical manifestation among hepatitis B carriers in Thailand. *J Gastroenterol Hepatol* **17**, 671-6.

-
247. Sugauchi, F., Kumada, H., Acharya, S. A., Shrestha, S. M., Gamutan, M. T., Khan, M., Gish, R. G., Tanaka, Y., Kato, T., Orito, E., Ueda, R., Miyakawa, Y. and Mizokami, M. (2004). Epidemiological and sequence differences between two subtypes (Ae and Aa) of hepatitis B virus genotype A. *J Gen Virol* **85**, 811-20.
248. Sugauchi, F., Kumada, H., Sakugawa, H., Komatsu, M., Niitsuma, H., Watanabe, H., Akahane, Y., Tokita, H., Kato, T., Tanaka, Y., Orito, E., Ueda, R., Miyakawa, Y. and Mizokami, M. (2004). Two subtypes of genotype B (Ba and Bj) of hepatitis B virus in Japan. *Clin Infect Dis* **38**, 1222-8.
249. Sugauchi, F., Orito, E., Ichida, T., Kato, H., Sakugawa, H., Kakumu, S., Ishida, T., Chutaputti, A., Lai, C. L., Ueda, R., Miyakawa, Y. and Mizokami, M. (2002). Hepatitis B virus of genotype B with or without recombination with genotype C over the precore region plus the core gene. *J Virol* **76**, 5985-92.
250. Sugauchi, F., Orito, E., Kato, H., Suzuki, S., Kawakita, S., Sakamoto, Y., Fukushima, K., Akiba, T., Yoshihara, N., Ueda, R. and Mizokami, M. (2003). Genotype, serotype, and phylogenetic characterization of the complete genome sequence of hepatitis B virus isolates from Malawian chronic carriers of the virus. *J Med Virol* **69**, 33-40.
251. Summers, J. & Mason, W. S. (1982). Replication of the genome of a hepatitis B--like virus by reverse transcription of an RNA intermediate. *Cell* **29**, 403-15.
252. Summers, J., O'Connell, A. & Millman, I. (1975). Genome of hepatitis B virus: restriction enzyme cleavage and structure of DNA extracted from Dane particles. *Proc Natl Acad Sci U S A* **72**, 4597-601.

-
253. Summers, J., Smolec, J. M. and Snyder, R. (1978). A virus similar to human hepatitis B virus associated with hepatitis and hepatoma in woodchucks. *Proc Natl Acad Sci U S A* **75**, 4533-7.
254. Suzuki, H., Sata, M., Sasaki, M., Murashima, S., Akiyoshi, F., Noguchi, S. & Tanikawa, K. (1998). Mutations of glucocorticoid responsive element of HBV DNA. *Kurume Med J* **45**, 171-4.
255. Suzuki, Y., Ishihara, D., Sasaki, M., Nakagawa, H., Hata, H., Tsunoda, T., Watanabe, M., Komatsu, T., Ota, T., Isogai, T., Suyama, A. and Sugano, S. (2000). Statistical analysis of the 5' untranslated region of human mRNA using "Oligo-Capped" cDNA libraries. *Genomics* **64**, 286-97.
256. Szmuness, W., Prince, A. M., Goodman, M., Ehrlich, C., Pick, R. and Ansari, M. (1974). Hepatitis B immune serum globulin in prevention of nonparenterally transmitted hepatitis B. *N Engl J Med* **290**, 701-6.
257. Takada, S. and Koike, K. (1990). X protein of hepatitis B virus resembles a serine protease inhibitor. *Jpn J Cancer Res* **81**, 1191-4.
258. Takahashi, K., Akahane, Y., Hino, K., Ohta, Y. and Mishiro, S. (1998). Hepatitis B virus genomic sequence in the circulation of hepatocellular carcinoma patients: comparative analysis of 40 full-length isolates. *Arch Virol* **143**, 2313-26.
259. Testut, P., Renard, C. A., Terradillos, O., Vitvitski-Trepo L, Tekaiia F, Degott C, Blake J, Boyer B, and Buendia MA. (1996). A new hepadnavirus endemic in arctic ground squirrels in Alaska. *J Virol* **70**, 4210-9.

-
260. Thakur, V., Guptan, R. C., Kazim, S. N., Malhotra, V. and Sarin, S. K. (2002). Profile, spectrum and significance of HBV genotypes in chronic liver disease patients in the Indian subcontinent. *J Gastroenterol Hepatol* **17**, 165-70.
261. Tiollais, P., Pourcel, C. and Dejean, A. (1985). The hepatitis B virus. *Nature* **317**, 489-95.
262. Tokino, T. & Matsubara, K. (1991). Chromosomal sites for hepatitis B virus integration in human hepatocellular carcinoma. *J Virol* **65**, 6761-4.
263. Toukan, A. U., Sharaiha, Z. K., Abu-el-Rub, O. A., Hmoud, M. K., Dahbour, S. S., Abu-Hassan, H., Yacoub, S. M., Hadler, S. C., Margolis, H. S., Coleman, P. J. and et al. (1990). The epidemiology of hepatitis B virus among family members in the Middle East. *Am J Epidemiol* **132**, 220-32.
264. Transy, C., Fourel, G., Robinson, W. S., Tiollais, P., Marion, P. L. and Buendia, M. A. (1992). Frequent amplification of c-myc in ground squirrel liver tumors associated with past or ongoing infection with a hepadnavirus. *Proc Natl Acad Sci U S A* **89**, 3874-8.
265. Tsuei, D. J., Hsu, T. Y., Chen, J. Y., Chang, M. H., Hsu, H. C. and Yang, C. S. (1994). Analysis of integrated hepatitis B virus DNA and flanking cellular sequences in a childhood hepatocellular carcinoma. *J Med Virol* **42**, 287-93.
266. Tur-Kaspa, R., Burk, R. D., Shaul, Y. & Shafritz, D. A. (1986). Hepatitis B virus DNA contains a glucocorticoid-responsive element. *Proc Natl Acad Sci U S A* **83**, 1627-31.

-
267. Tuttleman, J. S., Pourcel, C. and Summers, J. (1986). Formation of the pool of covalently closed circular viral DNA in hepadnavirus-infected cells. *Cell* **47**, 451-60.
268. Twu, J. S. & Schloemer, R. H. (1987). Transcriptional trans-activating function of hepatitis B virus. *J Virol* **61**, 3448-53.
269. Twu, J. S. and Schloemer, R. H. (1987). Transcriptional trans-activating function of hepatitis B virus. *J Virol* **61**, 3448-53.
270. Uchida, T., Gotoh, K. and Shikata, T. (1995). Complete nucleotide sequences and the characteristics of two hepatitis B virus mutants causing serologically negative acute or chronic hepatitis B. *J Med Virol* **45**, 247-52.
271. Unsal, H., Yakicier, C., Marcais, C., Kew, M., Volkmann, M., Zentgraf, H., Isselbacher, K. J. and Ozturk, M. (1994). Genetic heterogeneity of hepatocellular carcinoma. *Proc Natl Acad Sci U S A* **91**, 822-6.
272. Urban, S., Schwarz, C., Marx, U. C., Zentgraf, H., Schaller, H. & Multhaupt, G. (2000). Receptor recognition by a hepatitis B virus reveals a novel mode of high affinity virus-receptor interaction. *Embo J* **19**, 1217-27.
273. Uy, A., Wunderlich, G., Olsen, D. B., Heermann, K. H., Gerlich, W. H. and Thomssen, R. (1992). Genomic variability in the preS1 region and determination of routes of transmission of hepatitis B virus. *J Gen Virol* **73** (Pt 11), 3005-9.
274. Vaudin, M., Wolstenholme, A. J., Tsiquaye, K. N., Zuckerman A. J. and Harrison, T. J. (1988). The complete nucleotide sequence of the genome of a

- hepatitis B virus isolated from a naturally infected chimpanzee. *J Gen Virol* **69** (Pt 6), 1383-9.
275. Verschoor, E. J., Warren, K. S., Langenhuijzen, S., Heriyanto., Swan, R. A. and Heeney, J. L. (2001). Analysis of two genomic variants of orang-utan hepadnavirus and their relationship to other primate hepatitis B-like viruses. *J Gen Virol* **82**(Pt 4), 893-7.
276. Vieth, S., Manegold, C., Drosten, C., Nippraschk, T. & Gunther, S. (2002). Sequence and phylogenetic analysis of hepatitis B virus genotype G isolated in Germany. *Virus Genes* **24**, 153-6.
277. von Heijne, G. (1983). Patterns of amino acids near signal-sequence cleavage sites. *Eur J Biochem* **133**, 17-21.
278. von Heijne, G. (1984). Analysis of the distribution of charged residues in the N-terminal region of signal sequences: implications for protein export in prokaryotic and eukaryotic cells. *Embo J* **3**, 2315-8.
279. Vos, G. H., Rose, E. F. and Marimuthu, T. (1980). Hepatitis B antigen and antibodies in rural and urban Southern African blacks. *S Afr Med J.* **57**, 868-70.
280. Wang, G. H. and Seeger, C. (1992). The reverse transcriptase of hepatitis B virus acts as a protein primer for viral DNA synthesis. *Cell* **71**, 663-70.
281. Wang, G. H. and Seeger, C. (1993). Novel mechanism for reverse transcription in hepatitis B viruses. *J Virol* **67**, 6507-12.
282. Wang, H. P. and Rogler, C. E. (1991). Topoisomerase I-mediated integration of hepadnavirus DNA in vitro. *J Virol* **65**, 2381-92.

-
283. Wang, J., Chenivesse, X., Henglein, B. and Brechot, C. (1990). Hepatitis B virus integration in a cyclin A gene in a hepatocellular carcinoma. *Nature* **343**, 555-7.
284. Wang, Y., Cui, F., Lv, Y., Li, C., Xu, X., Deng, C., Wang, D., Sun, Y., Hu, G., Lang, Z., Huang, C. and Yang, X. (2004). HBsAg and HBx knocked into the p21 locus causes hepatocellular carcinoma in mice. *Hepatology* **39**, 318-24.
285. Warren, K. S., Heeney, J. L., Swan R. A., Heriyanto. and Verschoor, E. J. A new group of hepadnaviruses naturally infecting orangutans (*Pongo pygmaeus*). *J Virol* **73**, 7860-5.
286. Webster, G. J. and Bertoletti, A. (2002). Control or persistence of hepatitis B virus: the critical role of initial host-virus interactions. *Immunol Cell Biol* **80**, 101-5.
287. Webster, G. J., Reignat, S., Maini, M. K., Whalley, S. A., Ogg, G. S., King, A., Brown, D., Amlot, P. L., Williams, R., Vergani, D., Dusheiko, G. M. and Bertoletti, A. (2000). Incubation phase of acute hepatitis B in man: dynamic of cellular immune mechanisms. *Hepatology* **32**, 1117-24.
288. Westland, C., Delaney, W., Yang, H., Chen, S. S., Marcellin, P., Hadziyannis, S., Gish, R., Fry, J., Brosgart, C., Gibbs, C., Miller, M. and Xiong, S. Hepatitis B virus genotypes and virologic response in 694 patients in phase III studies of adefovir dipivoxil 1. *Gastroenterology* **125**, 107-116.
289. Whitten, T. M., Quets, A. T. & Schloemer, R. H. (1991). Identification of the hepatitis B virus factor that inhibits expression of the beta interferon gene. *J Virol* **65**, 4699-704.

-
290. Will, H., Reiser, W., Weimer, T., Pfaff, E., Buscher, M., Sprengel, R., Cattaneo, R. and Schaller H. (1987). Replication strategy of human hepatitis B virus. *J Virol* **61**,904-11.
291. Wong, D. K., Cheung, A. M., O'Rourke, K., Naylor, C. D., Detsky, A. S. and Heathcote, J. (1993). Effect of alpha-interferon treatment in patients with hepatitis B e antigen-positive chronic hepatitis B. A meta-analysis. *Ann Intern Med* **119**, 312-23.
292. www.invitrogen.com
293. www.virology-online.com
294. Xia, X. & Xie, Z. (2001). DAMBE: software package for data analysis in molecular biology and evolution. *J Hered* **92**, 371-3.
295. Yaginuma, K., Kobayashi, H., Kobayashi, M., Morishima, T., Matsuyama, K. and Koike, K. (1987). Multiple integration site of hepatitis B virus DNA in hepatocellular carcinoma and chronic active hepatitis tissues from children. *J Virol* **61**, 1808-13.
296. Yaginuma, K., Shirakata, Y., Kobayashi, M. and Koike, K. (1987a). Hepatitis B virus (HBV) particles are produced in a cell culture system by transient expression of transfected HBV DNA. *Proc Natl Acad Sci U S A* **84**, 2678-82.
297. Yamamoto, K., Horikita, M., Tsuda, F., Itoh, K., Akahane, Y., Yotsumoto, S., Okamoto, H., Miyakawa, Y. and Mayumi, M. (1994). Naturally occurring escape mutants of hepatitis B virus with various mutations in the S gene in carriers seropositive for antibody to hepatitis B surface antigen. *J Virol* **68**, 2671-6.

-
298. Yang, W. and Summers, J. (1995). Illegitimate replication of linear hepadnavirus DNA through nonhomologous recombination. *J Virol* **69**, 4029-36.
299. Yang, W. and Summers, J. (1995). Illegitimate replication of linear hepadnavirus DNA through nonhomologous recombination. *J Virol* **69**, 4029-36.
300. Yang, W. and Summers, J. (1999). Integration of hepadnavirus DNA in infected liver: evidence for a linear precursor. *J Virol* **73**, 9710-7.
301. Yu, X. and Mertz, J. E. (1996). Promoters for synthesis of the pre-C and pregenomic mRNAs of human hepatitis B virus are genetically distinct and differentially regulated. *J Virol* **70**, 8719-26.
302. Yuan, T. T., Lin, M. H., Chen, D. S. and Shih, C. (1998). A defective interference-like phenomenon of human hepatitis B virus in chronic carriers. *J Virol* **72**, 578-84.
303. Yuan, T. T., Lin, M. H., Qiu, S. M. and Shih, C. (1998b). Functional characterization of naturally occurring variants of human hepatitis B virus containing the core internal deletion mutation. *J Virol* **72**, 2168-76.
304. Yuen, M. F., Sablon, E., Tanaka, Y., Kato, T., Mizokami, M., Doutreloigne, J., Yuan, H. J., Wong, D. K., Sum, S. M. and Lai, C. L. (2004a). Epidemiological study of hepatitis B virus genotypes, core promoter and precore mutations of chronic hepatitis B infection in Hong Kong. *J Hepatol* **41**, 119-25.
305. Yuen, M. F., Tanaka, Y., Mizokami, M., Yuen, J. C., Wong, D. K., Yuan, H. J., Sum, S. M., Chan, A. O., Wong, B. C. and Lai, C. L. (2004b). Role of

-
- hepatitis B virus genotypes Ba and C, core promoter and precore mutations on hepatocellular carcinoma: a case control study. *Carcinogenesis* **25**, 1593-8.
306. Yuh, C. H. & Ting, L. P. (1990). The genome of hepatitis B virus contains a second enhancer: cooperation of two elements within this enhancer is required for its function. *J Virol* **64**, 4281-7.
307. Yuh, C. H. & Ting, L. P. (1993). Differentiated liver cell specificity of the second enhancer of hepatitis B virus. *J Virol* **67**, 142-9.
308. Yuh, C. H., Chang, Y. L. and Ting, L. P. (1992). Transcriptional regulation of precore and pregenomic RNAs of hepatitis B virus. *J Virol* **66**, 4073-84.
309. Zahm, P., Hofschneider, P. H. and Koshy, R. (1988). The HBV X-ORF encodes a transactivator: a potential factor in viral hepatocarcinogenesis. *Oncogene* **3**, 169-77.
310. Zhou, Y. J. (1980). A virus possibly associated with hepatitis and hepatoma in ducks. *Shanghai Medical Journal* **3**, 641-644.
311. Zuker, M. (2003). Mfold web server for nucleic acid folding and hybridization prediction. *Nucleic Acids Res* **31**, 3406-15.