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Search for new breast cancer susceptibility genes

Oldenburg, R.A.

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CHAPTER 9

PUBLICATION LIST

1

A genome wide linkage search for breast cancer susceptibility genes.

Genes Chromosomes Cancer. 2006 Jul;45(7):646-55

Smith P, McGuffog L, Easton DF, Mann GJ, Pupo GM, Newman B, Chenevix-Trench G; kConFab Investigators; Szabo C, Southey M, Renard H, Odefrey F, Lynch H, Stoppa-Lyonnet D, Couch F, Hopper JL, Giles GG, McCredie MR, Buys S, Andrulis I, Senie R; BCFS, BRCAX Collaborators Group; Goldgar DE, **Oldenburg R**, Kroeze-Jansema K, Kraan J, Meijers-Heijboer H, Klijn JG, van Asperen C, van Leeuwen I, Vasen HF, Cornelisse CJ, Devilee P, Baskcomb L, Seal S, Barfoot R, Mangion J, Hall A, Edkins S, Rapley E, Wooster R, Chang-Claude J, Eccles D, Evans DG, Futreal PA, Nathanson KL, Weber BL; Breast Cancer Susceptibility Collaboration (UK); Rahman N, Stratton MR.

2

Characterization of familial non-BRCA1/2 breast tumors by loss of heterozygosity and immunophenotyping.

Clin Cancer Res. 2006 Mar 15;12(6):1693-700.

Oldenburg RA, Kroeze-Jansema K, Meijers-Heijboer H, van Asperen CJ, Hoogerbrugge N, van Leeuwen I, Vasen HF, Cleton-Jansen AM, Kraan J, Houwing-Duistermaat JJ, Morreau H, Cornelisse CJ, Devilee P.

3

Comparative genomic hybridization profiles in human BRCA1 and BRCA2 breast tumors highlight differential sets of genomic aberrations.

Cancer Res. 2005 Feb 1;65(3):822-7.

van Beers EH, van Welsem T, Wessels LF, Li Y, **Oldenburg RA**, Devilee P, Cornelisse CJ, Verhoef S, Hogervorst FB, van't Veer LJ, Nederlof PM.

4

Extending the p16-Leiden tumour spectrum by respiratory tract tumours.

J Med Genet. 2004 Mar;41(3):e31.

Oldenburg RA, de Vos tot Nederveen Cappel WH, van Puijenbroek M, van den Ouweland A, Bakker E, Griffioen G, Devilee P, Cornelisse CJ, Meijers-Heijboer H, Vasen HF, Morreau H.

5

Are ATM mutations 7271T->G and IVS10-6T->G really high-risk breast cancer-susceptibility alleles?

Cancer Res. 2004 Feb 1;64(3):840-3.

Szabo CI, Schutte M, Broeks A, Houwing-Duistermaat JJ, Thorstenson YR, Durocher F, **Oldenburg RA**, Wasielewski M, Odefrey F, Thompson D, Floore AN, Kraan J, Klijn JG, van den Ouweland AM, Wagner TM, Devilee P, Simard J, van't Veer LJ, Goldgar DE, Meijers-Heijboer H.

6

The CHEK2*110delC variant acts as a breast cancer risk modifier in non-BRCA1/BRCA2 multiple-case families.

Cancer Res. 2003 Dec 1;63(23):8153-7.

Oldenburg RA, Kroeze-Jansema K, Kraan J, Morreau H, Klijn JG, Hoogerbrugge N, Ligtenberg MJ, van Asperen CJ, Vasen HF, Meijers C, Meijers-Heijboer H, de Bock TH, Cornelisse CJ, Devilee P.

7

Low-penetrance susceptibility to breast cancer due to CHEK2(*)110delC in noncarriers of BRCA1 or BRCA2 mutations. *Nat Genet.* 2002 May;31(1):55-9.

Meijers-Heijboer H, van den Ouweland A, Klijn J, Wasielewski M, de Snoo A, **Oldenburg R**, Hollestelle A, Houben M, Crepin E, van Veghel-Plandsoen M, Elstrodt F, van Duijn C, Bartels C, Meijers C, Schutte M, McGuffog L, Thompson D, Easton D, Sodha N, Seal S, Barfoot R, Mangion J, Chang-Claude J, Eccles D, Eeles R, Evans DG, Houlston R, Murday V, Narod S, Peretz T, Peto J, Phelan C, Zhang HX, Szabo C, Devilee P, Goldgar D, Futreal PA, Nathanson KL, Weber B, Rahman N, Stratton MR; CHEK2-Breast Cancer Consortium.

8

Evaluation of linkage of breast cancer to the putative BRCA3 locus on chromosome 13q21 in 128 multiple case families from the Breast Cancer Linkage Consortium.

Proc Natl Acad Sci U S A. 2002 Jan 22;99(2):827-31.

Thompson D, Szabo CI, Mangion J, **Oldenburg RA**, Odefrey F, Seal S, Barfoot R, Kroeze-Jansema K, Teare D, Rahman N, Renard H, Mann G, Hopper JL, Buys SS, Andrulis IL, Senie R, Daly MB, West D, Ostrander EA, Offit K, Peretz T, Osorio A, Benitez J, Nathanson KL, Sinilnikova OM, Olah E, Bignon YJ, Ruiz P, Badzioch MD, Vasen HF, Futreal AP, Phelan CM, Narod SA, Lynch HT, Ponder BA, Eeles RA, Meijers-Heijboer H, Stoppa-Lyonnet D, Couch FJ, Eccles DM, Evans DG, Chang-Claude J, Lenoir G, Weber BL, Devilee P, Easton DF, Goldgar DE, Stratton MR; KConFab Consortium.

9

Genetic susceptibility for breast cancer: How many more genes to be found?

Crit Rev Oncol Hematol. 2007 May 9.

Oldenburg RA, Meijers-Heijboer H, Cornelisse CJ, Devilee P.

10

BRCAx breast tumors are distinct from sporadic and BRCA1 tumors by array-CGH but still heterogeneous supporting the possibility for multiple etiologies. *Submitted*

EH van Beers, **RA Oldenburg**, SA Joosse, MJ Ligtenberg, N Hoogerbrugge, K Kroeze-Jansema, H Meijers-Heijboer, FB Hogervorst, S Verhoef, P Devilee, PM Nederlof.

11

Genome-wide linkage scan in Dutch hereditary non-BRCA1/2 breast cancer families identifies 9q21-22 as a putative breast cancer susceptibility locus. *Submitted*

R.A. Oldenburg, K.H.G. Kroeze, J.J. Houwing-Duistermaat, C.J. van Asperen, A. van den Ouweland, E. Bakker, E.H. van Beers, P.M. Nederlof, H. Vasen, N. Hoogerbrugge, C.J. Cornelisse, H. Meijers-Heijboer, P. Devilee.

12

Genomewide high-density SNP linkage analysis of non-BRCA1/2 breast cancer families identifies various candidate regions and has greater power than microsatellite studies.

BMC Genomics. 2007 Aug 30;8:299.

Gonzalez-Neira A, Rosa-Rosa JM, Osorio A, Gonzalez E, Southey M, Sinilnikova O, Lynch H, **Oldenburg RA**, van Asperen CJ, Hoogerbrugge N, Pita G, Devilee P, Goldgar D, Benitez J.

CURRICULUM VITAE

The author of this thesis was born on 6th of October 1968 in Lower Hutt, Wellington, New Zealand, as the third son of Hans Oldenburg en Nibs Bloem. He passed his VWO exam in 1987 at the 'Montessori School' in The Hague. After finishing his introductory exam Computer Science in 1990 he started his medical career at the University in Gent, Belgium. He obtained his MD degree from the Leiden University in 1997. He started working as a junior resident for the department of Clinical Genetics at the Erasmus University Rotterdam in 1998. In 1999 he was offered an 'AGIKO' position in which the training for clinical genetics is combined with the research project (group leader Prof. P. Devilee) involving familial breast cancer, of which this thesis is the end product. He has finished his training for clinical genetics in October 2007 and he has received a staff position at the Department of Clinical Genetics, Erasmus Medical Centre Rotterdam. His main focus will be oncogenetics. He lives with Mariëtte van Pelt since 1992. They have two daughters; Michelle (1999) and Cathelijne (2002).

REFERENCE LIST CHAPTER 2 AND 6

1. **Breasted, J. H.** The Edwin Smith Surgical Papyrus 403-406 *University of Chicago Press, Chicago (1930)*
2. Tumours of the breast in World Health Organization: Tumours of the Breast and Female Genital Organs 9-110. *IARC Press, Lyon (2003)*
3. **Parkin, D. M., Pisani, P., & Ferlay, J.** Global cancer statistics. *CA Cancer J.Clin.* 49, 33-64, 1 (1999)
4. **Parkin, D. M.** International variation. *Oncogene* 23, 6329-6340 (2004)
5. **Ziegler, R. G. et al.** Migration patterns and breast cancer risk in Asian-American women. *J Natl.Cancer Inst.* 85, 1819-1827 (1993)
6. **Kliwer, E. V. & Smith, K. R.** Breast cancer mortality among immigrants in Australia and Canada. *J Natl.Cancer Inst.* 87, 1154-1161 (1995)
7. **Hill, T. D., Khamis, H. J., Tyczynski, J. E., & Berkel, H. J.** Comparison of male and female breast cancer incidence trends, tumor characteristics, and survival. *Ann.Epidemiol.* 15, 773-780 (2005)
8. **Hulka, B. S. & Moorman, P. G.** Breast cancer: hormones and other risk factors. *Maturitas.* 38, 103-113 (2001)
9. **Garfinkel, L., Boring, C. C., & Heath, C. W., Jr.** Changing trends. An overview of breast cancer incidence and mortality. *Cancer.* 74, 222-227 (1994).
10. **Bernstein, L., Teal, C. R., Joslyn, S., & Wilson, J.** Ethnicity-related variation in breast cancer risk factors. *Cancer.* 97, 222-229 (2003)
11. **Dumitrescu, R. G. & Cotarla, I.** Understanding breast cancer risk -- where do we stand in 2005? *J Cell Mol.Med.* 9, 208-221 (2005)
12. **Russo, J., Hu, Y. F., Yang, X., & Russo, I. H.** Developmental, cellular, and molecular basis of human breast cancer. *J.Natl.Cancer Inst.Monogr.* 17-37 (2000).
13. **Cavalieri, E., Frenkel, K., Liehr, J. G., Rogan, E., & Roy, D.** Estrogens as endogenous genotoxic agents--DNA adducts and mutations. *J.Natl.Cancer Inst.Monogr.* 75-93 (2000).
14. **Berkey, C. S., Frazier, A. L., Gardner, J. D., & Colditz, G. A.** Adolescence and breast carcinoma risk. *Cancer* 85, 2400-2409 (1999)
15. **Kelsey, J. L. & Horn-Ross, P. L.** Breast cancer: magnitude of the problem and descriptive epidemiology. *Epidemiol.Rev.* 15, 7-16 (1993)
16. **Collaborative Group on Hormonal Factors in Breast Cancer.** Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet.* 347, 1713-1727 (1996)
17. **McPherson, K., Steel, C. M., & Dixon, J. M.** ABC of breast diseases. Breast cancer-epidemiology, risk factors, and genetics. *Br.Med.J.* 321, 624-628 (2000)
18. **Gikas, P. D. & Mokbel, K.** Phytoestrogens and the risk of breast cancer: a review of the literature. *Int.J Fertil.Womens Med.* 50, 250-258 (2005)
19. **Huang, Z. et al.** Dual effects of weight and weight gain on breast cancer risk. *JAMA.* 278, 1407-1411 (1997)
20. **Lahmann, P. H. et al.** Body size and breast cancer risk: findings from the European Prospective Investigation into Cancer And Nutrition (EPIC). *Int.J Cancer.* %20;111, 762-771 (2004).
21. **Trentham-Dietz, A. et al.** Weight change and risk of postmenopausal breast cancer (United States). *Cancer Causes Control.* 11, 533-542 (2000)

22. **McTiernan, A. et al.** Adiposity and sex hormones in postmenopausal breast cancer survivors. *J Clin Oncol.* 21, 1961-1966 (2003)
23. **Biglia, N. et al.** Management of risk of breast carcinoma in postmenopausal women. *Endocr.Relat Cancer.* 11, 69-83 (2004)
24. **Lagerros, Y. T., Hsieh, S. F., & Hsieh, C. C.** Physical activity in adolescence and young adulthood and breast cancer risk: a quantitative review. *Eur.J Cancer Prev.* 13, 5-12 (2004)
25. **Hankinson, S. E., Colditz, G. A., & Willett, W. C.** Towards an integrated model for breast cancer etiology - The lifelong interplay of genes, lifestyle, and hormones. *Breast Cancer Res.* 6, 213-218 (2004)
26. **Byrne, C. et al.** Effects of mammographic density and benign breast disease on breast cancer risk (United States). *Cancer Causes Control.* 12, 103-110 (2001)
27. **Boyd, N. F. et al.** Heritability of mammographic density, a risk factor for breast cancer. *N.Engl.J.Med.* 347, 886-894 (2002)
28. **van Gils, C. H., Hendriks, J. H., Otten, J. D., Holland, R., & Verbeek, A. L.** Parity and mammographic breast density in relation to breast cancer risk: indication of interaction. *Eur.J Cancer Prev.* 9, 105-111 (2000)
29. **Stone, J. et al.** The heritability of mammographically dense and nondense breast tissue. *Cancer Epidemiol.Biomarkers Prev.* 15, 612-617 (2006)
30. **Tokunaga, M. et al.** Incidence of female breast cancer among atomic bomb survivors, Hiroshima and Nagasaki, 1950-1980. *Radiat.Res.* 112, 243-272 (1987)
31. **Butel, J. S.** Viral carcinogenesis: revelation of molecular mechanisms and etiology of human disease. *Carcinogenesis.* 21, 405-426 (2000)
32. **zur, H. H.** Cervical carcinoma and human papillomavirus: on the road to preventing a major human cancer. *J Natl.Cancer Inst.* 93, 252-253 (2001)
33. **Stuver, S. O., Boschi-Pinto, C., & Trichopoulos, D.** Infection with hepatitis B and C viruses, social class and cancer. *IARC Sci.Publ.* 319-324 (1997)
34. **Iscovich, J., Boffetta, P., Franceschi, S., Azizi, E., & Sarid, R.** Classic kaposi sarcoma: epidemiology and risk factors. *Cancer.* 88, 500-517 (2000)
35. **Bangham, C. R.** HTLV-1 infections. *J Clin Pathol.* 53, 581-586 (2000)
36. **Feller, W. F. & Chopra, H. C.** A small virus-like particle observed in human breast cancer by means of electron microscopy. *J Natl.Cancer Inst.* 40, 1359-1373 (1968)
37. **Segev, N., Hizi, A., Kirenberg, F., & Keydar, I.** Characterization of a protein, released by the T47D cell line, immunologically related to the major envelope protein of mouse mammary tumor virus. *Proc.Natl.Acad.Sci.U.S.A.* 82, 1531-1535 (1985)
38. **Dion, A. S.** Virus-like particles and macromolecules in human milk and breast tumors. *CRC Crit Rev.Clin Lab Sci.* 11, 245-270 (1979)
39. **Wang, Y. et al.** Detection of mammary tumor virus ENV gene-like sequences in human breast cancer. *Cancer Res.* 55, 5173-5179 (1995)
40. **Etkind, P., Du, J., Khan, A., Pillitteri, J., & Wiernik, P. H.** Mouse mammary tumor virus-like ENV gene sequences in human breast tumors and in a lymphoma of a breast cancer patient. *Clin Cancer Res.* 6, 1273-1278 (2000)
41. **Pogo, B. G. et al.** Sequences homologous to the mouse mammary tumor virus env gene in human breast carcinoma correlate with overexpression of laminin receptor. *Clin Cancer Res.* 5, 2108-2111 (1999)
42. **Van 't Veer, L. J. et al.** Gene expression profiling predicts clinical outcome of breast cancer. *Nature* 415, 530-536 (2002)

43. **Einav, U. et al.** Gene expression analysis reveals a strong signature of an interferon-induced pathway in childhood lymphoblastic leukemia as well as in breast and ovarian cancer. *Oncogene*. 24, 6367-6375 (2005)
44. **Yin, H. et al.** Transcription of human endogenous retroviral sequences related to mouse mammary tumor virus in human breast and placenta: similar pattern in most malignant and nonmalignant breast tissues. *AIDS Res.Hum.Retroviruses*. 13, 507-516 (1997)
45. **Witt, A. et al.** The mouse mammary tumor virus-like env gene sequence is not detectable in breast cancer tissue of Austrian patients. *Oncol Rep*. 10, 1025-1029 (2003)
46. **Mant, C., Gillett, C., D'Arrigo, C., & Cason, J.** Human murine mammary tumour virus-like agents are genetically distinct from endogenous retroviruses and are not detectable in breast cancer cell lines or biopsies. *Virology*. 318, 393-404 (2004)
47. **Titus-Ernstoff, L. et al.** Exposure to breast milk in infancy and adult breast cancer risk. *J Natl.Cancer Inst*. 90, 921-924 (1998)
48. **Stewart, T., Tsai, S. C., Grayson, H., Henderson, R., & Opelz, G.** Incidence of de-novo breast cancer in women chronically immunosuppressed after organ transplantation. *Lancet*. 346, 796-798 (1995)
49. **Frisch, M., Biggar, R. J., Engels, E. A., & Goedert, J. J.** Association of cancer with AIDS-related immunosuppression in adults. *JAMA*. 285, 1736-1745 (2001)
50. **Ross, S. R., Schofield, J. J., Farr, C. J., & Bucan, M.** Mouse transferrin receptor 1 is the cell entry receptor for mouse mammary tumor virus. *Proc.Natl.Acad.Sci.U.S.A.* 99, 12386-12390 (2002)
51. **Steel, M., Thompson, A., & Clayton, J.** Genetic aspects of breast cancer. *Br.Med Bull*. 47, 504-518 (1991)
52. **Eisinger, F., Sobol, H., Serin, D., & Whorton, J. C.** Hereditary breast cancer, circa 1750. *Lancet*. 351, 1366 (1998)
53. **Collaborative Group on Hormonal Factors in Breast Cancer.** Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58209 women with breast cancer and 101986 women without the disease. *Lancet* 358, 1389-1399 (2001)
54. **Thompson, D. & Easton, D.** The genetic epidemiology of breast cancer genes. *Journal of Mammary Gland Biology and Neoplasia* 9, 221-236 (2004)
55. **Amundadottir, L. T. et al.** Cancer as a complex phenotype: pattern of cancer distribution within and beyond the nuclear family. *PLoS.Med.* 1, e65 (2004)
56. **Claus, E. B., Risch, N., & Thompson, W. D.** Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. *Cancer*. 73, 643-651 (1994)
57. **Dunning, A. M. et al.** A systematic review of genetic polymorphisms and breast cancer risk. *Cancer Epidemiol.Biomarkers Prev*. 8, 843-854 (1999)
58. **de Jong, M. M. et al.** Genes other than *BRCA1* and *BRCA2* involved in breast cancer susceptibility. *J.Med.Genet*. 39, 225-242 (2002)
59. **Tavtigian, S. V. et al.** The complete *BRCA2* gene and mutations in chromosome 13q-linked kindreds. *Nature Genet* 12, 333-337 (1996)
60. **Kinzler, K. W. & Vogelstein, B.** Cancer-susceptibility genes. Gatekeepers and caretakers. *Nature* 386, 761-763 (1997)
61. **Breivik, J.** The evolutionary origin of genetic instability in cancer development. *Semin.Cancer Biol*. 15, 51-60 (2005)
62. **Scully, R. & Livingston, D.** In search of the tumour-suppressor functions of *BRCA1* and *BRCA2*. *Nature* 408, 429-433 (2000)

63. **Venkitaraman, A. R.** Cancer susceptibility and the functions of BRCA1 and BRCA2. *Cell* 108, 171-182 (2002)
64. **Venkitaraman, A. R.** Tracing the network connecting BRCA and Fanconi anaemia proteins. *Nature Reviews Cancer* 4, 266-276 (2004)
65. **Narod, S. A. & Foulkes, W. D.** BRCA1 and BRCA2: 1994 and beyond. *Nature Reviews Cancer* 4, 665-676 (2004)
66. **Howlett, N. G. et al.** Biallelic inactivation of BRCA2 in Fanconi anemia. *Science* 297, 606-609 (2002)
67. **Patel, K. J. et al.** Involvement of BRCA2 in DNA repair. *Mol. Cell* 1, 347-357 (1998)
68. **Seal, S. et al.** Evaluation of Fanconi anemia genes in familial breast cancer predisposition. *Cancer Res.* 63, 8596-8599 (2003)
69. **Thompson, E. et al.** A novel duplication polymorphism in the FANCA promoter and its association with breast and ovarian cancer. *BMC.Cancer.* 5, 43 (2005)
70. **Offit, K. et al.** Shared genetic susceptibility to breast cancer, brain tumors, and Fanconi anemia. *J.Natl.Cancer Inst.* 95, 1548-1551 (2003)
71. **Antoniou, A. C. et al.** A comprehensive model for familial breast cancer incorporating BRCA1, BRCA2 and other genes. *Br.J.Cancer* 86, 76-83 (2002)
72. **Roa, B. B., Boyd, A. A., Volcik, K., & Richards, C. S.** Ashkenazi Jewish population frequencies for common mutations in BRCA1 and BRCA2. *Nature Genet* 14, 185-187 (1996)
73. **Berman, D. B. et al.** A common mutation in BRCA2 that predisposes to a variety of cancers is found in both Jewish Ashkenazi and non-Jewish individuals. *Cancer Res.* 56, 3409-3414 (1996)
74. **Antoniou, A. et al.** Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: A combined analysis of 22 studies. *Am.J.Hum.Genet.* 72, 1117-1130 (2003)
75. **Ford, D. et al.** Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. *Am J Hum Genet* 62, 676-689 (1998)
76. **Chen, S. et al.** Characterization of BRCA1 and BRCA2 mutations in a large United States sample. *J.Clin.Oncol.* 24, 863-871 (2006)
77. **Wang, W. W. et al.** A single nucleotide polymorphism in the 5' untranslated region of RAD51 and risk of cancer among BRCA1/2 mutation carriers. *Cancer Epidemiol.Biomarkers Prev.* 10, 955-960 (2001)
78. **Kadouri, L. et al.** A single-nucleotide polymorphism in the RAD51 gene modifies breast cancer risk in BRCA2 carriers, but not in BRCA1 carriers or noncarriers. *Br.J.Cancer* 90, 2002-2005 (2004)
79. **Rebbeck, T. R. et al.** Modification of BRCA1-associated breast cancer risk by the polymorphic androgen-receptor cag repeat. *Am J Hum Genet* 64, 1371-1377 (1999)
80. **Rebbeck, T. R. et al.** Modification of BRCA1- and BRCA2-associated breast cancer risk by AIB1 genotype and reproductive history. *Cancer Res.* 61, 5420-5424 (2001)
81. **Spurdle, A. B. et al.** The androgen receptor CAG repeat polymorphism and modification of breast cancer risk in BRCA1 and BRCA2 mutation carriers. *Breast Cancer Res.* 7, R176-R183 (2005)
82. **Kadouri, L. et al.** CAG and GGC repeat polymorphisms in the androgen receptor gene and breast cancer susceptibility in BRCA1/2 carriers and non-carriers. *Br J Cancer* 85, 36-40 (2001)
83. **Phelan, C. M. et al.** Ovarian cancer risk in BRCA1 carriers is modified by the HRAS1 variable number of tandem repeat (VNTR) locus. *Nature Genet* 12, 309-311 (1996)
84. **Runnebaum, I. B. et al.** Progesterone receptor variant increases ovarian cancer risk in BRCA1 and BRCA2 mutation carriers who were never exposed to oral contraceptives. *Pharmacogenetics* 11, 635-638 (2001)

85. **Thompson, D., Easton, D., & Breast Cancer Linkage Consortium.** Variation in cancer risks, by mutation position, in BRCA2 mutation carriers. *Am J Hum Genet* 68, 410-419 (2001)
86. **Thompson, D., Easton, D., & Breast Cancer Linkage Consortium.** Variation in BRCA1 cancer risks by mutation position. *Cancer Epidemiol.Biomarkers Prev.* 11, 329-336 (2002)
87. **Van Asperen, C. J. et al.** Cancer risks in BRCA2 families Estimates for sites other than breast and ovary. *J Med Genet* 42, 711-719 (2005)
88. **Easton, D.** Breast cancer genes - What are the real risks? *Nature Genet* 16, 210-211 (1997)
89. **Breast Cancer Linkage Consortium.** Cancer Risks in BRCA2 Mutation Carriers. *J.Natl.Cancer Inst.* 91, 1310-1316 (1999)
90. **Thompson, D., Easton, D. F., & Breast Cancer Linkage Consortium.** Cancer incidence in BRCA1 mutation carriers. *J.Natl.Cancer Inst.* 94, 1358-1365 (2002)
91. **Pluquet, O. & Hainaut, P.** Genotoxic and non-genotoxic pathways of p53 induction. *Cancer Lett.* 174, 1-15 (2001)
92. **Malkin, D. et al.** Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms. *Science* 250, 1233-1238 (1990)
93. **Frebourg, T. et al.** Germ-line p53 mutations in 15 families with Li-Fraumeni syndrome. *Am.J.Hum.Genet.* 56, 608-615 (1995)
94. **Birch, J. et al.** Prevalence and diversity of constitutional mutations in the p53 gene among 21 Li-Fraumeni families. *Cancer Res.* 54, 1298-1304 (1994)
95. **Varley, J. M. et al.** Germ-line mutations of TP53 in Li-Fraumeni families: An extended study of 39 families. *Cancer Res.* 57, 3245-3252 (1997)
96. **Evans, D. G. et al.** Low rate of TP53 germline mutations in breast cancer/sarcoma families not fulfilling classical criteria for Li-Fraumeni syndrome. *J Med Genet.* 39, 941-944 (2002)
97. **Strong, L. C., Williams, W. R., & Tainsky, M. A.** The Li-Fraumeni syndrome: from clinical epidemiology to molecular genetics. *Am.J Epidemiol.* 135, 190-199 (1992)
98. **Chompret, A. et al.** p53 germline mutations in childhood cancers and cancer risk for carrier individuals. *Br J Cancer* 82, 1932-1937 (2000)
99. **Garber, J. E. et al.** Follow-up study of twenty-four families with Li-Fraumeni syndrome. *Cancer Res.* 51, 6094-6097 (1991)
100. **Cornelis, R. et al.** Evidence for a gene on 17p13.3, distal to TP53, as a target for allele loss in breast tumors without p53 mutations. *Cancer Res.* 54, 4200-4206 (1994)
101. **Nayak, B. K. & Das, B. R.** Mutation and methylation status of p53 gene promoter in human breast tumours. *Tumour.Biol.* 20, 341-346 (1999)
102. **Rapakko, K. et al.** Germline TP53 alterations in Finnish breast cancer families are rare and occur at conserved mutation-prone sites. *Br.J.Cancer* 84, 116-119 (2001)
103. **Borresen, A. L. et al.** Screening for germ line TP53 mutations in breast cancer patients. *Cancer Res.* 52, 3234-3236 (1992).
104. **Nelen, M. R. et al.** Localization of the gene for Cowden disease to chromosome 10q22-23. *Nature Genet* 13, 114-116 (1996)
105. **Liaw, D. et al.** Germline mutations of the PTEN gene in Cowden disease, an inherited breast and thyroid cancer syndrome. *Nature Genet* 16[1], 64-67. (1997)
106. **Lindor, N. M. & Greene, M. H.** The concise handbook of family cancer syndromes. Mayo Familial Cancer Program. *J Natl.Cancer Inst.* 90, 1039-1071 (1998)
107. **Mallory, S. B.** Cowden syndrome (multiple hamartoma syndrome). *Dermatol.Clin.* 13, 27-31 (1995)

108. **Schweitzer, S., Hogge, J. P., Grimes, M., Bear, H. D., & de Paredes, E. S.** Cowden disease: a cutaneous marker for increased risk of breast cancer. *AJR Am.J Roentgenol.* 172, 349-351 (1999)
109. **Marsh, D. J. et al.** Mutation spectrum and genotype-phenotype analyses in Cowden disease and Bannayan-Zonana syndrome, two hamartoma syndromes with germline PTEN mutation. *Hum.Mol.Genet.* 7, 507-515 (1998)
110. **Eng, C.** Genetics of Cowden syndrome: through the looking glass of oncology. *Int.J Oncol.* 12, 701-710 (1998)
111. **Starink, T. M. et al.** The Cowden syndrome: a clinical and genetic study in 21 patients. *Clin Genet.* 29, 222-233 (1986)
112. **Fackenthal, J. D. et al.** Male breast cancer in Cowden syndrome patients with germline PTEN mutations. *J.Med.Genet.* 38, 159-164 (2001)
113. **Chen, J. D., Lindblom, P., & Lindblom, A.** A study of the PTEN/MMAC1 gene in 136 breast cancer families. *Hum Genet* 102, 124-125 (1998)
114. **Carroll, B. T., Couch, F. J., Rebbeck, T. R., & Weber, B. L.** Polymorphisms in PTEN in breast cancer families. *J Med Genet.* 36, 94-96 (1999)
115. **Rhei, E. et al.** Mutation analysis of the putative tumor suppressor gene PTEN/MMAC1 in primary breast carcinomas. *Cancer Res.* 57, 3657-3659 (1997)
116. **Freihoff, D. et al.** Exclusion of a major role for the PTEN tumour-suppressor gene in breast carcinomas. *Br.J.Cancer* 79, 754-758 (1999)
117. **Feilotter, H. E. et al.** Analysis of the 10q23 chromosomal region and the PTEN gene in human sporadic breast carcinoma. *Br J Cancer* 79, 718-723 (1999)
118. **Hemminki, A. et al.** Localization of a susceptibility locus for Peutz-Jeghers syndrome to 19p using comparative genomic hybridization and targeted linkage analysis. *Nat.Genet.* 15, 87-90 (1997)
119. **Kallioniemi, O. P. et al.** Comparative genomic hybridization: a rapid new method for detecting and mapping DNA amplification in tumors. *Semin.Cancer Biol.* 4, 41-46 (1993)
120. **Jenne, D. E. et al.** Peutz-Jeghers syndrome is caused by mutations in a novel serine threonine kinase. *Nature Genet* 18, 38-43 (1998)
121. **Wada, K., Tanaka, M., Yamaguchi, K., & Wada, K.** Carcinoma and polyps of the gallbladder associated with Peutz-Jeghers syndrome. *Dig.Dis.Sci.* 32, 943-946 (1987)
122. **Westerman, A. M. et al.** Peutz-Jeghers syndrome: 78-year follow-up of the original family. *Lancet.* 353, 1211-1215 (1999)
123. **Giardiello, F. M. et al.** Increased risk of cancer in the Peutz-Jeghers syndrome. *N.Engl.J Med.* 316, 1511-1514 (1987)
124. **Spigelman, A. D., Murday, V., & Phillips, R. K.** Cancer and the Peutz-Jeghers syndrome. *Gut.* 30, 1588-1590 (1989)
125. **Boardman, L. A. et al.** Increased risk for cancer in patients with the Peutz-Jeghers syndrome. *Ann.Intern.Med.* 128, 896-899 (1998)
126. **Lim, W. et al.** Further observations on LKB1/STK11 status and cancer risk in Peutz-Jeghers syndrome. *Br.J Cancer.* 89, 308-313 (2003)
127. **Giardiello, F. M. et al.** Very high risk of cancer in familial Peutz-Jeghers syndrome. *Gastroenterology.* 119, 1447-1453 (2000)
128. **Shen, Z., Wen, X. F., Lan, F., Shen, Z. Z., & Shao, Z. M.** The tumor suppressor gene LKB1 is associated with prognosis in human breast carcinoma. *Clin Cancer Res.* 8, 2085-2090 (2002)
129. **Bignell, G. R. et al.** Low frequency of somatic mutations in the LKB1/Peutz- Jeghers syndrome gene in sporadic breast cancer. *Cancer Res.* 58, 1384-1386 (1998)

130. **Guilford, P. et al.** E-cadherin germline mutations in familial gastric cancer. *Nature* 392, 402-405 (1998)
131. **Pharoah, P. D., Guilford, P., & Caldas, C.** Incidence of gastric cancer and breast cancer in CDH1 (E-cadherin) mutation carriers from hereditary diffuse gastric cancer families. *Gastroenterology*. 121, 1348-1353 (2001)
132. **Berx, G. et al.** E-cadherin is inactivated in a majority of invasive human lobular breast cancers by truncation mutations throughout its extracellular domain. *Oncogene* 13, 1919-1925 (1996)
133. **Chan, J. K. & Wong, C. S.** Loss of E-cadherin is the fundamental defect in diffuse-type gastric carcinoma and infiltrating lobular carcinoma of the breast. *Adv.Anat.Pathol.* 8, 165-172 (2001)
134. **Graziano, F., Humar, B., & Guilford, P.** The role of the E-cadherin gene (CDH1) in diffuse gastric cancer susceptibility: from the laboratory to clinical practice. *Ann.Oncol.* 14, 1705-1713 (2003)
135. **Mastracci, T. L., Tjan, S., Bane, A. L., O'Malley, F. P., & Andrusis, I. L.** E-cadherin alterations in atypical lobular hyperplasia and lobular carcinoma in situ of the breast. *Mod.Pathol.* 18, 741-751 (2005)
136. **Sarriso, D. et al.** Epigenetic and genetic alterations of APC and CDH1 genes in lobular breast cancer: relationships with abnormal E-cadherin and catenin expression and microsatellite instability. *Int.J.Cancer.* %20;106, 208-215 (2003)
137. **Suriano, G. et al.** Characterization of a recurrent germ line mutation of the E-cadherin gene: implications for genetic testing and clinical management. *Clin Cancer Res.* 11, 5401-5409 (2005)
138. **Keller, G. et al.** Diffuse type gastric and lobular breast carcinoma in a familial gastric cancer patient with an E-cadherin germline mutation. *Am.J.Pathol.* 155, 337-342 (1999)
139. **Jonsson, B. A., Bergh, A., Stattin, P., Emmanuëlsson, M., & Gronberg, H.** Germline mutations in E-cadherin do not explain association of hereditary prostate cancer, gastric cancer and breast cancer. *Int.J.Cancer.* %20;98, 838-843 (2002)
140. **Salahshor, S. et al.** Low frequency of E-cadherin alterations in familial breast cancer. *Breast Cancer Res.* 3, 199-207 (2001)
141. **Bakkenist, C. J. & Kastan, M. B.** DNA damage activates ATM through intermolecular autophosphorylation and dimer dissociation. *Nature.* 421, 499-506 (2003)
142. **Pippard, E. C., Hall, A. J., Barker, D. J., & Bridges, B. A.** Cancer in homozygotes and heterozygotes of ataxia-telangiectasia and xeroderma pigmentosum in Britain. *Cancer Res.* 48, 2929-2932 (1988)
143. **Swift, M., Chase, C., & Morrell, D.** Cancer predisposition of Ataxia-Telangiectasia heterozygotes. *Cancer Genet.Cytogenet.* 46, 21-27 (1990)
144. **Easton, D. F.** Cancer risks in A-T heterozygotes. *Int J Radiat Biol* 66, S177-S182 (1994)
145. **Hall, J.** The Ataxia-telangiectasia mutated gene and breast cancer: gene expression profiles and sequence variants. *Cancer Lett.* 227, 105-114 (2005)
146. **Thompson, D. et al.** Cancer risks and mortality in heterozygous ATM mutation carriers. *J.Natl.Cancer Inst.* 97, 813-822 (2005)
147. **Renwick, A. et al.** ATM mutations that cause ataxia-telangiectasia are breast cancer susceptibility alleles. *Nat Genet* 38, 873-875 (2006)
148. **Vorechovsky, I. et al.** The ATM gene and susceptibility to breast cancer: analysis of 38 breast tumors reveals no evidence for mutation. *Cancer Res.* 56, 2726-2732 (1996)
149. **FitzGerald, M. G. et al.** Heterozygous ATM mutations do not contribute to early onset of breast cancer. *Nature Genet.* 15, 307-310 (1997)
150. **Broeks, A. et al.** ATM-heterozygous germline mutations contribute to breast cancer-susceptibility. *Am J Hum Genet* 66, 494-500 (2000)
151. **Chenevix-Trench, G. et al.** Dominant Negative ATM Mutations in Breast Cancer Families. *J.Natl.Cancer Inst.* 94, 205-215 (2002)

152. **Szabo, C. I. et al.** Are ATM mutations 7271T->G and IVS10-6T->G really high-risk breast cancer-susceptibility alleles? *Cancer Res.* 64, 840-843 (2004)
153. **Thompson, D. et al.** Two ATM variants and breast cancer risk. *Hum.Mutat.* 25, 594-595 (2005)
154. **Gatti, R. A., Tward, A., & Concannon, P.** Cancer risk in ATM heterozygotes: a model of phenotypic and mechanistic differences between missense and truncating mutations. *Mol.Genet Metab.* 68, 419-423 (1999)
155. **Meyn, M. S.** Ataxia-telangiectasia, cancer and the pathobiology of the ATM gene. *Clin Genet.* 55, 289-304 (1999)
156. **Bretsky, P. et al.** The relationship between twenty missense ATM variants and breast cancer risk: The multiethnic cohort. *Cancer Epidemiol.Biomarkers Prev.* 12, 733-738 (2003)
157. **Tamimi, R. M. et al.** Common ataxia telangiectasia mutated haplotypes and risk of breast cancer: a nested case-control study. *Breast Cancer Res.* 6, R416-R422 (2004)
158. **Bernstein, J. L. et al.** Population-based estimates of breast cancer risks associated with ATM gene variants c.7271T>G and c.1066-6T>G (IVS10-6T>G) from the Breast Cancer Family Registry. *Hum.Mutat.* 27, 1122-1128 (2006)
159. **Rosfjord, E. C. & Dickson, R. B.** Growth factors, apoptosis, and survival of mammary epithelial cells. *J Mammary.Gland.Biol.Neoplasia.* 4, 229-237 (1999)
160. **Janda, E. et al.** Ras and TGF[beta] cooperatively regulate epithelial cell plasticity and metastasis: dissection of Ras signaling pathways. *J Cell Biol.* 156, 299-313 (2002)
161. **Lehmann, K. et al.** Raf induces TGFbeta production while blocking its apoptotic but not invasive responses: a mechanism leading to increased malignancy in epithelial cells. *Genes Dev.* 14, 2610-2622 (2000)
162. **Oft, M., Akhurst, R. J., & Balmain, A.** Metastasis is driven by sequential elevation of H-ras and Smad2 levels. *Nat.Cell Biol.* 4, 487-494 (2002)
163. **Schulze, A., Lehmann, K., Jefferies, H. B., McMahon, M., & Downward, J.** Analysis of the transcriptional program induced by Raf in epithelial cells. *Genes Dev.* 15, 981-994 (2001)
164. **Goumans, M. J. et al.** Balancing the activation state of the endothelium via two distinct TGF-beta type I receptors. *EMBO J.* 21, 1743-1753 (2002)
165. **Derynck, R., Akhurst, R. J., & Balmain, A.** TGF-beta signaling in tumor suppression and cancer progression. *Nat.Genet.* 29, 117-129 (2001)
166. **Lucke, C. D. et al.** Inhibiting mutations in the transforming growth factor beta type 2 receptor in recurrent human breast cancer. *Cancer Res.* 61, 482-485 (2001)
167. **Chen, T., Carter, D., Garrigue-Antar, L., & Reiss, M.** Transforming growth factor beta type I receptor kinase mutant associated with metastatic breast cancer. *Cancer Res.* 58, 4805-4810 (1998)
168. **Xie, W. et al.** Alterations of Smad signaling in human breast carcinoma are associated with poor outcome: a tissue microarray study. *Cancer Res.* 62, 497-505 (2002)
169. **Dunning, A. M. et al.** A transforming growth factorbeta1 signal peptide variant increases secretion in vitro and is associated with increased incidence of invasive breast cancer. *Cancer Res.* 63, 2610-2615 (2003)
170. **Chun, H. J. et al.** Pleiotropic defects in lymphocyte activation caused by caspase-8 mutations lead to human immunodeficiency. *Nature.* 419, 395-399 (2002)
171. **MacPherson, G. et al.** Association of a common variant of the CASP8 gene with reduced risk of breast cancer. *J.Natl.Cancer Inst.* 96, 1866-1869 (2004)
172. **Cox, A. et al.** A common coding variant in CASP8 is associated with breast cancer risk. *Nat Genet.* 39, 352-358 (2007)

173. **Frank, B. et al.** Association of the CASP10 V410I variant with reduced familial breast cancer risk and interaction with the CASP8 D302H variant. *Carcinogenesis* 27, 606-609 (2006)
174. **Sodha, N. et al.** Increasing evidence that germline mutations in CHEK2 do not cause Li- Fraumeni syndrome. *Hum.Mutat.* 20, 460-462 (2002)
175. **Meijers-Heijboer, H. et al.** Low-penetrance susceptibility to breast cancer due to CHEK2*1100delC in noncarriers of BRCA1 or BRCA2 mutations. *Nature Genet.* 31, 55-59 (2002)
176. **Vahteristo, P. et al.** A CHEK2 genetic variant contributing to a substantial fraction of familial breast cancer. *Am.J.Hum.Genet.* 71, 432-438 (2002).
177. **Oldenburg, R. A. et al.** The CHEK2*1100delC variant acts as a breast cancer risk modifier in non-BRCA1/BRCA2 multiple-case families. *Cancer Res.* 63, 8153-8157 (2003)
178. **Meijers-Heijboer, H. et al.** The CHEK2 1100delC Mutation Identifies Families with a Hereditary Breast and Colorectal Cancer Phenotype. *Am.J.Hum.Genet.* 72, 1308-1314 (2003)
179. **The CHEK2 Breast Cancer Case-Control Consortium.** CHEK2*1100delC and susceptibility to breast cancer: a collaborative analysis involving 10,860 breast cancer cases and 9,065 controls from ten studies. *Am.J.Hum.Genet.* 74, 1175-1182 (2004)
180. **Schutte, M. et al.** Variants in CHEK2 other than 1100delC do not make a major contribution to breast cancer susceptibility. *Am J Hum Genet* 72, 1023-1028 (2003)
181. **Dufault, M. R. et al.** Limited relevance of the CHEK2 gene in hereditary breast cancer. *Int.J.Cancer* 110, 320-325 (2004).
182. **Bogdanova, N. et al.** Association of two mutations in the CHEK2 gene with breast cancer. | *Int.J.Cancer* 116, 263-266 (2005)
183. **Kilpivaara, O. et al.** CHEK2 variant 1157T may be associated with increased breast cancer risk. *Int.J.Cancer* 111, 543-547 (2004)
184. **de Bock, G. H. et al.** Tumour characteristics and prognosis of breast cancer patients carrying the germline CHEK2*1100delC variant. *J.Med.Genet.* 41, 731-735 (2004)
185. **Johnson, N. et al.** Interaction between CHEK2*1100delC and other low-penetrance breast-cancer susceptibility genes: a familial study. *Lancet* 366, 1554-1557 (2005)
186. **Huzarski, T. et al.** Pathology of breast cancer in women with constitutional CHEK2 mutations. *Breast Cancer Res Treatm* 90, 187-189 (2005)
187. **Oldenburg, R. A. et al.** Characterization of familial non-BRCA1/2 breast tumors by loss of heterozygosity and immunophenotyping. *Clin.Cancer Res.* 12, 1693-1700 (2006)
188. **Wu, L. J. C. et al.** Identification of a ring protein that can interact in vivo with the BRCA1 gene product. *Nature Genet* 14, 430-440 (1996)
189. **Meza, J. E., Brzovic, P. S., King, M. C., & Klevit, R. E.** Mapping the functional domains of BRCA1 - Interaction of the ring finger domains of BRCA1 and BARD1. *J.Biol.Chem.* 274, 5659-5665 (1999)
190. **Joukov, V., Chen, J., Fox, E. A., Green, J. B. A., & Livingston, D. M.** Functional communication between endogenous BRCA1 and its partner, BARD1, during *Xenopus laevis* development. *Proc.Natl.Acad.Sci.USA* 98, 12078-12083 (2001)
191. **Irminger, F, I et al.** Identification of BARD1 as mediator between proapoptotic stress and p53-dependent apoptosis. *Mol.Cell* 8, 1255-1266 (2001)
192. **Thai, T. H. et al.** Mutations in the BRCA1-associated RING domain (BARD1) gene in primary breast, ovarian and uterine cancers. *Hum.Mol.Genet.* 7, 195-202 (1998)
193. **Ghimenti, C. et al.** Germline mutations of the BRCA1-associated ring domain (BARD1) gene in breast and breast/ovarian families negative for BRCA1 and BRCA2 alterations. *Genes Chrom.Cancer* 33, 235-242 (2002)

194. **Karpinen, S. M. et al.** Nordic collaborative study of the *BARD1* Cys557Ser allele in 3956 patients with cancer: enrichment in familial *BRCA1/BRCA2* mutation-negative breast cancer but not in other malignancies. *J.Med.Genet.* 43, 856-862 (2006)
195. **Mathew, C. G.** Fanconi anaemia genes and susceptibility to cancer. *Oncogene* 25, 5875-5884 (2006)
196. **Hirsch, B. et al.** Association of biallelic *BRCA2/FANCD1* mutations with spontaneous chromosomal instability and solid tumors of childhood. *Blood* 103, 2554-2559 (2004)
197. **Reid, S. et al.** Biallelic *BRCA2* mutations are associated with multiple malignancies in childhood including familial Wilms tumour. *J Med Genet* 42, 147-151 (2005)
198. **Lewis, A. G. et al.** Mutation analysis of *FANCD2*, *BRIP1/BACH1*, *LMO4* and *SFN* in familial breast cancer. *Breast Cancer Res.* 7, R1005-R1016 (2005)
199. **Barroso, E. et al.** *FANCD2* associated with sporadic breast cancer risk. *Carcinogenesis* 27, 1930-1937 (2006)
200. **Cantor, S. B. et al.** *BACH1*, a novel helicase-like protein, interacts directly with *BRCA1* and contributes to its DNA repair function. *Cell* 105, 149-160 (2001)
201. **Cantor, S. et al.** The *BRCA1*-associated protein *BACH1* is a DNA helicase targeted by clinically relevant inactivating mutations. *Proceedings of the National Academy of Sciences of the United States of America* 101, 2357-2362 (2004)
202. **Peng, M., Litman, R., Jin, Z., Fong, G., & Cantor, S. B.** *BACH1* is a DNA repair protein supporting *BRCA1* damage response. *Oncogene* 25, 2245-2253 (2006)
203. **Luo, L. P. et al.** No mutations in the *BACH1* gene in *BRCA1* and *BRCA2* negative breast-cancer families linked to 17q22. *Int.J.Cancer* 98, 638-639 (2002)
204. **Karpinen, S. M., Vuosku, J., Heikkinen, K., Allinen, M., & Winqvist, R.** No evidence of involvement of germline *BACH1* mutations in Finnish breast and ovarian cancer families. *Eur.J.Cancer* 39, 366-371 (2003)
205. **Rutter, J. L. et al.** Mutational analysis of the *BRCA1*-interacting genes *ZNF350/ZBRK1* and *BRIP1/BACH1* among *BRCA1* and *BRCA2*-negative probands from breast-ovarian cancer families and among early-onset breast cancer cases and reference individuals. *Hum Mutat* 22, 121-128 (2003)
206. **Vahteristo, P. et al.** *BACH1* Ser919Pro variant and breast cancer risk. *BMC. Cancer* 1-7 (2005)
207. **Vahteristo, P. et al.** *BARD1* variants Cys557Ser and Val507Met in breast cancer predisposition. *Eur J Hum Genet* 14, 167-172 (2006)
208. **Seal, S. et al.** Truncating mutations in the Fanconi anemia J gene *BRIP1* are low-penetrance breast cancer susceptibility alleles. *Nat Genet.* 38, 1239-1241 (2006)
209. **Xia, B. et al.** Control of *BRCA2* cellular and clinical functions by a nuclear partner, *PALB2*. *Mol.Cell* 22, 719-729 (2006)
210. **Reid, S. et al.** Biallelic mutations in *PALB2* cause Fanconi anemia subtype FA-N and predispose to childhood cancer. *Nat.Genet* 39, 162-164 (2007)
211. **Rahman, N. et al.** *PALB2*, which encodes a *BRCA2*-interacting protein, is a breast cancer susceptibility gene. *Nat Genet.* 39, 165-167 (2007)
212. **Shih, H. A. et al.** *BRCA1* and *BRCA2* mutation frequency in women evaluated in a breast cancer risk evaluation clinic. *J Clin Oncol* 20, 994-999 (2002)
213. **Verhoog, L. C. et al.** Large regional differences in the frequency of distinct *BRCA1/BRCA2* mutations in 517 Dutch breast and/or ovarian cancer families. *Eur J Cancer* 37, 2082-2090 (2001)
214. **FitzGerald, M. G. et al.** Germline mutations in *PTEN* are an infrequent cause of genetic predisposition to breast cancer. *Oncogene* 17, 727-731 (1998)

215. **Claus, E. B., Risch, N., & Douglas, W.** Genetic analysis of breast cancer in the cancer and steroid hormone study. *Am.J.Hum.Genet.* 48, 232-242 (1991)
216. **Go, R. C., King, M. C., Bailey-Wilson, J., Elston, R. C., & Lynch, H. T.** Genetic epidemiology of breast cancer and associated cancers in high-risk families. I. Segregation analysis. *J Natl.Cancer Inst.* 71, 455-461 (1983)
217. **Eccles, D., Marlow, A., Royle, G., Collins, A., & Morton, N. E.** Genetic epidemiology of early onset breast cancer. *J Med Genet.* 31, 944-949 (1994)
218. **Miki, Y. et al.** A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. *Science* 266, 66-71 (1994)
219. **Wooster, R. et al.** Identification of the breast cancer susceptibility gene BRCA2. *Nature* 378, 789-792 (1995)
220. **Cui, J. & Hopper, J. L.** Distribution of family history of a disease as a function of mode of inheritance, genetic relative hazard, allele frequency and disease status of the proband, with application to female breast cancer. *J Epidemiol.Biostat.* 6, 331-342 (2001)
221. **Antoniou, A. C. et al.** Evidence for further breast cancer susceptibility genes in addition to BRCA1 and BRCA2 in a population-based study. *Genet.Epidemiol.* 21, 1-18 (2001)
222. **Hall, J. et al.** Linkage of early-onset familial breast cancer to chromosome 17q21. *Science* 250, 1684-1689 (1990)
223. **Narod, S. et al.** An evaluation of genetic heterogeneity in 145 breast-ovarian cancer families. *Am J Hum Genet* 56, 254-264 (1995)
224. **Easton, D., Bishop, D., Ford, D., Crockford, G., & Breast Cancer Linkage Consortium.** Genetic linkage analysis in familial breast and ovarian cancer: Results from 214 families. *Am.J.Hum.Genet.* 52, 678-701 (1993)
225. **Stratton, M. et al.** Familial male breast cancer is not linked to the BRCA1 locus on chromosome 17q. *Nature Genet* 7, 103-107 (1994)
226. **Wooster, R. et al.** Localization of a breast cancer susceptibility gene BRCA2 to chromosome 13q12-13. *Science* 265, 2088-2090 (1994)
227. **Miller, B. J., Wang, D., Krahe, R., & Wright, F. A.** Pooled analysis of loss of heterozygosity in breast cancer: a genome scan provides comparative evidence for multiple tumor suppressors and identifies novel candidate regions. *Am J Hum Genet* 73, 748-767 (2003)
228. **Kainu, T. et al.** Somatic deletions in hereditary breast cancers implicate 13q21 as a putative novel breast cancer susceptibility locus. *Proc.Natl.Acad.Sci.USA* 97, 9603-9608 (2000)
229. **Kerangueven, F. et al.** Loss of heterozygosity and linkage analysis in breast carcinoma: Indication for a putative third susceptibility gene on the short arm of chromosome 8. *Oncogene* 10, 1023-1026 (1995)
230. **Eisinger, F. et al.** Germ line mutation at BRCA1 affects the histoprognotic grade in hereditary breast cancer. *Cancer Res.* 56, 471-474 (1996)
231. **Seitz, S. et al.** Strong indication for a breast cancer susceptibility gene on chromosome 8p12-p22: linkage analysis in German breast cancer families. *Oncogene* 14, 741-743 (1997)
232. **Seitz, S. et al.** Deletion mapping and linkage analysis provide strong indication for the involvement of the human chromosome region 8p12-p22 in breast carcinogenesis. *Br J Cancer* 76, 983-991 (1997)
233. **Rahman, N. et al.** Absence of evidence for a familial breast cancer susceptibility gene at chromosome 8p12-p22. *Oncogene* 19, 4170-4173 (2000)
234. **Thompson, D. et al.** Evaluation of linkage of breast cancer to the putative BRCA3 locus on chromosome 13q21 in 128 multiple case families from the Breast Cancer Linkage Consortium. *Proc.Natl.Acad.Sci.USA* 99, 827-831 (2002)

235. **Smith, P. et al.** A genome wide linkage search for breast cancer susceptibility genes. *Genes Chrom.Cancer* 45, 646-655 (2006)
236. **Huusko, P. et al.** Genome-wide scanning for linkage in Finnish breast cancer families. *Eur.J.Hum.Genet.* 12, 98-104 (2004)
237. **Lakhani, S. R. et al.** Multifactorial analysis of differences between sporadic breast cancers and cancers involving BRCA1 and BRCA2 mutations. *J.Natl.Cancer Inst.* 90, 1138-1145 (1998)
238. **Lakhani, S. R. et al.** The pathology of familial breast cancer: histological features of cancers in families not attributable to mutations in BRCA1 or BRCA2. *Clin.Cancer Res.* 6, 782-789 (2000)
239. **Lakhani, S. R.** The pathology of familial breast cancer: Morphological aspects. *Breast Cancer Res.* 1, 31-35 (1999)
240. **Catteau, A., Harris, W. H., Xu, C. F., & Solomon, E.** Methylation of the BRCA1 promotor region in sporadic breast and ovarian cancer: correlation with disease characteristics. *Oncogene* 18, 1957-1965 (1999)
241. **Esteller, M. et al.** Promoter hypermethylation and BRCA1 inactivation in sporadic breast and ovarian tumors. *J.Natl.Cancer Inst.* 92, 564-569 (2000)
242. **Hamann, U. & Sinn, H. P.** Survival and tumor characteristics of German hereditary breast cancer patients. *Breast Cancer Res.Treat.* 59, 185-192 (2000)
243. **Stoppa-Lyonnet, D. et al.** Familial invasive breast cancers: worse outcome related to BRCA1 mutations. *J Clin Oncol.* 18, 4053-4059 (2000)
244. **Robson, M. et al.** BRCA-associated breast cancer in young women. *J Clin Oncol* 16, 1642-1649 (1998)
245. **Breast Cancer Linkage Consortium.** Pathology of familial breast cancer: Differences between breast cancers in carriers of BRCA1 or BRCA2 mutations and sporadic cases. *Lancet* 349, 1505-1510 (1997)
246. **Callahan, R. et al.** Genetic and molecular heterogeneity of breast cancer cells. *Clin.Chim.Acta* 217, 63-73 (1993)
247. **Lasko, D., Cavenee, W., & Nordenskjöld, M.** Loss of constitutional heterozygosity in human cancer. *Annu.Rev.Genet.* 25, 281-314 (1991)
248. **Newton, M. A., Gould, M. N., Reznikoff, C. A., & Haag, J. D.** On the statistical analysis of allelic-loss data. *Stat.Med.* 17, 1425-1445 (1998)
249. **Newton, M. A. & Lee, Y.** Inferring the location and effect of tumor suppressor genes by instability-selection modeling of allelic-loss data. *Biometrics.* 56, 1088-1097 (2000).
250. **Osorio, A. et al.** Loss of heterozygosity analysis at the BRCA loci in tumor samples from patients with familial breast cancer. *Int.J.Cancer* 99, 305-309 (2002).
251. **Tirkkonen, M. et al.** Distinct somatic genetic changes associated with tumor progression in carriers of BRCA1 and BRCA2 germ-line mutations. *Cancer Res.* 57, 1222-1227 (1997).
252. **Tirkkonen, M. et al.** Somatic genetic alterations in BRCA2-associated and sporadic male breast cancer. *Genes Chrom Cancer* 24, 56-61 (1999)
253. **Devilee, P., Cleton-Jansen, A. M., & Cornelisse, C. J.** Ever since Knudson. *Trends Genet* 17, 569-573 (2001)
254. **Zhuang, Z. et al.** Trisomy 7-harboring non-random duplication of the mutant MET allele in hereditary papillary renal carcinomas. *Nature Genet.* 20, 66-69 (1998)
255. **Wessels, L. F. A. et al.** Molecular classification of breast carcinomas by comparative genomic hybridization: a specific somatic genetic profile for BRCA1 tumors. *Cancer Res.* 62, 7110-7117 (2002)
256. **van Beers, E. H. et al.** Comparative genomic hybridization profiles in human BRCA1 and BRCA2 breast tumors highlight differential sets of genomic aberrations. *Cancer Res.* 65, 822-827 (2005)

257. **Jonsson, G. et al.** Distinct Genomic Profiles in Hereditary Breast Tumors Identified by Array-Based Comparative Genomic Hybridization. *Cancer Res.* 65, 7612-7621 (2005)
258. **Gronwald, J. et al.** Comparison of genomic abnormalities between BRCA1 and sporadic breast cancers studied by comparative genomic hybridization. *Int.J.Cancer* 114, 230-236 (2005)
259. **Lakhani, S. R. et al.** The pathology of familial breast cancer: Predictive value of immunohistochemical markers estrogen receptor, progesterone receptor, HER-2, and p53 in patients with mutations in BRCA1 and BRCA2. *J Clin Oncol* 20, 2310-2318 (2002)
260. **Palacios, J. et al.** Immunohistochemical characteristics defined by tissue microarray of hereditary breast cancer not attributable to BRCA1 or BRCA2 mutations: Differences from breast carcinomas arising in BRCA1 and BRCA2 mutation carriers. *Clinical Cancer Research* 9, 3606-3614 (2003)
261. **Sorlie, T. et al.** Repeated observation of breast tumor subtypes in independent gene expression data sets. *Proc.Natl.Acad.Sci.USA* 100, 8418-8423 (2003)
262. **Hedenfalk, I. et al.** Molecular classification of familial non-BRCA1/BRCA2 breast cancer. *Proc.Natl.Acad.Sci.USA* 100, 2532-2537 (2003)
263. **Abd El-Rehim, D. M. et al.** Expression of luminal and basal cytokeratins in human breast carcinoma. *J.Pathol.* 203, 661-671 (2004)
264. **Bergman, A. et al.** Genome-wide linkage scan for breast cancer susceptibility loci in Swedish hereditary non-BRCA1/2 families: suggestive linkage to 10q23.32-q25.3. *Genes Chrom.Cancer* 46, 302-309 (2007)
265. **Schadt, E. E.** Exploiting naturally occurring Dna variation and molecular profiling data to dissect disease and drug response traits. *Current Opinion in Biotechnology* 16, 647-654 (2005)
266. **Sorlie, T. et al.** Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proc.Natl.Acad.Sci.USA* 98, 10869-10874 (2001)
267. **Hedenfalk, I. et al.** Gene-expression profiles in hereditary breast cancer. *N.Engl.J.Med.* 344, 539-548 (2001)
268. **Vierimaa, O. et al.** Pituitary adenoma predisposition caused by germline mutations in the AIP gene. *Science* 312, 1228-1230 (2006)
269. **Calin, G. A. & Croce, C. M.** MicroRNA signatures in human cancers. *Nat Rev.Cancer* 6, 857-866 (2006)
270. **Pharoah, P. D., Dunning, A. M., Ponder, B. A., & Easton, D. F.** Association studies for finding cancer-susceptibility genetic variants. *Nat.Rev.Cancer* 4, 850-860 (2004)
271. **Risch, N. J.** Searching for genetic determinants in the new millennium. *Nature.* 405, 847-856 (2000)
272. **Cardon, L. R. & Bell, J. I.** Association study designs for complex diseases. *Nat.Rev.Genet.* 2, 91-99 (2001)
273. **Wang, W. Y., Barratt, B. J., Clayton, D. G., & Todd, J. A.** Genome-wide association studies: theoretical and practical concerns. *Nat Rev.Genet.* 6, 109-118 (2005)
274. **Hirschhorn, J. N. & Daly, M. J.** Genome-wide association studies for common diseases and complex traits. *Nat Rev.Genet.* 6, 95-108 (2005)
275. **Rioux, J. D. et al.** Genetic variation in the 5q31 cytokine gene cluster confers susceptibility to Crohn disease. *Nat.Genet.* 29, 223-228 (2001)
276. **Stefansson, H. et al.** Neuregulin 1 and susceptibility to schizophrenia. *Am.J Hum.Genet.* 71, 877-892 (2002)
277. **Altshuler, D. et al.** The common PPARgamma Pro12Ala polymorphism is associated with decreased risk of type 2 diabetes. *Nat.Genet.* 26, 76-80 (2000)

278. **Peto, J. et al.** Prevalence of BRCA1 and BRCA2 gene mutations in patients with early-onset breast cancer. *J.Natl.Cancer Inst.* 91, 943-949 (1999)
279. **Lichtenstein, P. et al.** Environmental and heritable factors in the causation of cancer--analyses of cohorts of twins from Sweden, Denmark, and Finland. *N.Engl.J.Med.* 343, 78-85 (2000)
280. **Peto, J. & Mack, T. M.** High constant incidence in twins and other relatives of women with breast cancer. *Nature Genet* 26, 411-414 (2000)
281. **Johnson, N. et al.** Counting potentially functional variants in BRCA1, BRCA2 and ATM predicts breast cancer susceptibility. *Hum.Mol.Genet.* 16, 1051-1057 (2007)
282. **Baynes, C. et al.** Common variants in the ATM, BRCA1, BRCA2, CHEK2 and TP53 cancer susceptibility genes are unlikely to increase breast cancer risk. *Breast Cancer Res.* 9, R27 (2007)
283. **Patil, N. et al.** Blocks of limited haplotype diversity revealed by high-resolution scanning of human chromosome 21. *Science.* 294, 1719-1723 (2001)
284. **Johnson, G. C. et al.** Haplotype tagging for the identification of common disease genes. *Nat.Genet.* 29, 233-237 (2001)
285. **Gabriel, S. B. et al.** The structure of haplotype blocks in the human genome. *Science.* 296, 2225-2229 (2002)
286. **Kruglyak, L.** Prospects for whole-genome linkage disequilibrium mapping of common disease genes. *Nature Genet.* 22, 139-144 (1999)
287. **Hinds, D. A. et al.** Whole-genome patterns of common DNA variation in three human populations. *Science* 307, 1072-1079 (2005)
288. **Altshuler, D. et al.** A haplotype map of the human genome. *Nature* 437, 1299-1320 (2005)
289. **Haiman, C. A. et al.** A comprehensive haplotype analysis of CYP19 and breast cancer risk: the Multiethnic Cohort. *Hum.Mol.Genet.* 12, 2679-2692 (2003)
290. **Freedman, M. L. et al.** Common variation in BRCA2 and breast cancer risk: a haplotype-based analysis in the Multiethnic Cohort. *Hum.Mol.Genet.* 13, 2431-2441 (2004)
291. **Antoniou, A. C. & Easton, D. F.** Polygenic inheritance of breast cancer: Implications for design of association studies. *Genet.Epidemiol.* 25, 190-202 (2003)
292. **Houlston, R. S. & Peto, J.** The future of association studies of common cancers. *Hum.Genet.* 112, 434-435 (2003)
293. **Roberts, S. A. et al.** Heritability of cellular radiosensitivity: a marker of low-penetrance predisposition genes in breast cancer? *Am J Hum Genet* 65, 784-794 (1999)
294. **Easton, D. F. et al.** Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature* 447, 1087-1095 (2007)
295. **Wright, A., Charlesworth, B., Rudan, I., Carothers, A., & Campbell, H.** A polygenic basis for late-onset disease. *Trends Genet.* 19, 97-106 (2003)
296. **Pharoah, P. D. P. et al.** Polygenic susceptibility to breast cancer and implications for prevention. *Nature Genet.* 31, 33-36 (2002)
297. **Munoz-Gamez, J. A. et al.** PARP inhibition sensitizes p53-deficient breast cancer cells to doxorubicin-induced apoptosis. *Biochem.J.* 386, 119-125 (2005)
298. **Hay, T. et al.** Efficient deletion of normal Brca2-deficient intestinal epithelium by poly(ADP-ribose) polymerase inhibition models potential prophylactic therapy. *Cancer Res.* 65, 10145-10148 (2005)
299. **Farmer, H. et al.** Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. *Nature* 434, 917-921 (2005)
300. **Bryant, H. E. et al.** Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase. *Nature* 434, 913-917 (2005)

301. **Ford, D. et al.** Risks of cancer in BRCA1-mutation carriers. *Lancet* 343, 692-695 (1994)
302. **King, M. C., Go, R. C., Elston, R. C., Lynch, H. T., & Petrakis, N. L.** Allele increasing susceptibility to human breast cancer may be linked to the glutamate-pyruvate transaminase locus. *Science*. 208, 406-408 (1980)
303. **Skolnick, M. H., Thompson, E. A., Bishop, D. T., & Cannon, L. A.** Possible linkage of a breast cancer-susceptibility locus to the ABO locus: sensitivity of LOD scores to a single new recombinant observation. *Genet Epidemiol.* 1, 363-373 (1984).
304. **Zuppan, P., Hall, J., Lee, M., Ponglikitmongkol, M., & King, M.-C.** Possible linkage of the estrogen receptor gene to breast cancer in a family with late-onset disease. *Am.J.Hum.Genet.* 48, 1065-1068 (1991)
305. **Ellis, N. A. et al.** Localization of breast cancer susceptibility loci by genome-wide SNP linkage disequilibrium mapping. *Genet.Epidemiol.* 30, 48-61 (2006)
306. **Honrado, E. et al.** Immunohistochemical expression of DNA repair proteins in familial breast cancer differentiate BRCA2-associated tumors. *J Clin Oncol.* %20;23, 7503-7511 (2005)
307. **Eerola, H. et al.** Histopathological features of breast tumours in BRCA1, BRCA2 and mutation-negative breast cancer families. *Breast Cancer Res* 7, R93-R100 (2004)
308. **Easton, D., Ford, D., Bishop, D., & Breast Cancer Linkage Consortium.** Breast and ovarian cancer incidence in BRCA1-mutation carriers. *Am J Hum Genet* 56, 265-271 (1995)

