CBCS Phase 1 & Phase 2 (invasive and CIS) Genotyping Data Summary

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For Further Information on Specific Genotyping Protocols Please contact:

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Genotyping/List of CBCS 1 & 2 genotypes done at NIEHS and UNC labs (1996-2007) and collaboration with other labs (1996-2008)

Gene	Description	Comments
DNA Repair		
NER pathway		
XPD 312 rs1799793	G (Asp) → A (Asn)	Publication (15)
XPD 751 rs13181	A (Lys) → C (Gln)	Publication (15)
XPC 939 rs2228001	A (Lys) → C (Gln)	Publication (15)
HRAD23B codon 249 rs1805329	C (Ala) → T (Val)	Publication (15)
XPG 1104 rs17655	G (Asp) → C (His)	Publication (15)
XPF 415 rs1800067	G (Arg) → A (Gln)	Publication (15)
XPF 662 rs2020955	T (Ser) → C (Pro)	Mostly African American. Publication (15)
ERCC6 1213 rs2228527	A (Arg) → G (Gly)	Publication (15)
ERCC6 1230 rs4253211	G (Arg) → C (Pro)	Publication (15)
ERCC1 nt 8092 rs3212986		
BER pathway		
XRCC1 194 rs1799782	C (Arg) → T (Trp)	Publications (6, 16)

XRCC1 280 rs25489	G (Arg) → A (His)	Publication (16)
XRCC1 399 rs25487	G (Arg) → A (Gln)	Publications (6, 16)
APE1 148 rs3136820	G (Glu) → T (Asp)	
HOGG1 326 rs1052133	C (Ser) → G (Cys)	
MYH 324 rs3219489	G (Gln) → C (His)	
Direct repair		
MGMT 84 rs12917	C (Leu) → T (Phe)	
Double Strand Break Repair		
XRCC3 241 rs861539	C (Thr) → T (Met)	Publication (13)
NBS1 185 rs1805794	G (Glu) → C (Gln)	Publication (13)
XRCC2 188 rs3218536	G (Arg) → A (His)	Publication (13)
BRCA2 372 rs144848	A (Asn) → C (His)	Publication (13)
BRCA2 intron 24 rs206340	G → A	
XRCC4 T1394 G rs2075685	T → G	
DNAPK cs C 55966 T		Only 500 Ph2 samples.

Carcinogen Metabolism		
NAT1	Slow, Rapid (NAT1-non*10, NAT1*10)	Phase 1 only Publications (1, 5)
NAT2	Slow, Rapid	Phase 1 only Publication (1)
GSTM1	Null, Present	Phase 1 only Publication (7)
GSTT1	Null, Present	Phase 1 only Publication (7)
GSTP1 rs1695	A (Ile) → G (Val)	Phase 1 only Publication (7)
UGTIA1	5/5, 5/6, 6/6, Any 7 or Any 8 repeat	Only 400 Phase 1 AA (Collaboration with MIT – pilot study) Publication (4)

Estrogen Metabolism		
COMT rs4680	G (Val, H or high activity) → A (Met, L or low activity)	Phase 1 only Publication (2)
CYP 17 5' UTR T/C	0 = wildtype allele 1 = mutant allele	Phase 1 only
CYP 19 +268 C/T	C → T	Phase 1 only (Conway lab)
CYP 3A4 rs2740574	A → G	
CYPIA1	M1, WT M2, WT M3, WT M4, WT	Phase 1 only M2, M4 (mostly nonAA) M3 (mostly AA) Publication (10)
CYP1B1 codon 432 rs1056836	C (Leu) → G (Val)	

Oxidative Damage and Metabolism		
MnSOD -9 rs4880	T (Val) → C (Ala)	Publication (9)
PTGS2 (COX2) codon 511 rs5273	T (Val) → C (Ala)	AA only Publication (14)
PPARG2 codon 12 rs1801282	C (Pro) → G (Ala)	
*Mitochondrial genome nt 10398	A, G	Vanderbilt SPORE collaboration Publication (12)
MT genome Nt 4216	C, T	Vanderbilt collaboration
MT genome nt 12308	A, G	Vanderbilt collaboration AA only
MPO -463 rs2333227	G → A	
NQ01 codon 187 rs1800566	C (Pro) → T (Ser)	
HFE 282 (rs1800562) 63 (rs1799945)	 G → A G → C	Vanderbilt collaboration

Cellular Adhesion		
CDH1 (E-cadherin) -160 rs16260	C → A	

Cell cycle control		
MDM2 -309 rs2279744	G, T	

Signal Transduction		
HER2 655	A (Ile) → G (Val)	Publications (8, 11)
TGFB1 +9 (aa 10) rs1800470	T (Leu) → C (Pro)	
Herstatin Codon 357 Arg or Cys Codon 371 Arg or Ile Nucleotide (nt) 1279 C or T	 Arg, Cys Arg, Ile C, T	AA only

Cellular Proliferation		
STK15 / 6 Phe 31 Ile rs2273535	T (Phe) → A (Ile)	
MYBL2 Ser 427 Gly rs2070235	A (Ser) → G (Gly)	Publication (18)

Other genes		
P57 (KIP2) P57 PAPA-repeat deletion polymorphisms	wt, del	Phase 1 only (N=204) Publication (3)
BRCA1 promoter	wt = wildtype ACA = ACA insertion	
TGFBR1 Transforming growth factor beta receptor 1	alleles: 6, 8, 9	(Duke collaboration) Phase 2 only (N=456)
GCLC -nt 1384 (glutathione cycteine ligase)	C (Pro) → T (Ser) T allele not found in whites.	(Vanderbilt collaboration) AA only

Collaboration with Fred and Susan Kadlubar in 2007 (University of Arkansas)		
UCP2	C, T	Phase 1 pilot study
CYP39A1	A, T	Phase 1 pilot study
GSTM5	C, T	Phase 1 pilot study
SULT1C2	C, G	Phase 1 pilot study
UCP2 3'UTR	The variant is an insertion (i) or deletion (d). Alleles are **i** or **d**.	Phase 1 pilot study (SAS variable name is UCP23UTR, not to be confused with UCP2)

NCI collaboration from 2005
Phase I samples (N=1494)

Repeated using Illumina/Taqman assays in 2008-2010 for CBCS Phase 1 & Phase 2 (invasive and CIS).

Gene	SNP	rs number	Alleles	**Repeated in Illumina/Taqman assays**
GATA3 **N = 5 SNPs**				
5'	FLJ45983-03 Formerly known as GATA3-04	1149901	C / T (G / A)	Done
	GATA3-77	3802604	G / A	Done
	GATA3-14	3781092	G / A	Failed assay
	GATA3-22	570613	T / C	Done
3'	GATA3-27	422628	T / C	Done
TP53 **N = 15 SNPs**				
3'	TP53-71	17887200	A / G	Failed assay
	TP53-15	9894946	C / T	Done
	TP53-14	1614984	C / T	Done
	TP53-25	4968187	G / A	Done
	TP53-11	12951053	T / G	Done
	TP53-10	12947788	T / C	Failed assay
	TP53-52	17880604	G / C	Done
	TP53-16	1625895	A / G	Done
	TP53-64	35163653	G / A	Failed assay
	TP53-18	1800372	A / G	Done
	TP53-66	2909430	A / G	Done
	TP53-65	9895829	T / C	Failed assay
Pro72Arg	TP53-01	1042522	C / G	Done
	TP53-34	1642785	C / G	Failed assay
5'	TP53-09	8079544	G / A	Done
FOXA1 **N = 2 SNPs**				
	FOXA1-07	33984772	A / G	Failed assay
	C14orf25-05	?	C / A	Not done

NQO1 **N = 6 SNPs**				
3'	NQO1-14	34906225	A/ T	Failed assay
	NQO1-15	10517	C / T	Done
	NQO1-01	1800566	C / T	Done
	NQO1-05	34755915	G / A	Done
	NQO1-08	689453	G / A	Done
5'	NQO1-07	689452	C / G	Done
XBP1 **N = 4 SNPs**				
3'	XBP1-02	2267131	A / G	Done
	XBP1-01	2097461	A / G	Done
	XBP1-07	35873774	T / C	Failed assay
5'	XBP1-08	35771921	T / C	Done

Illumina/Taqman Data

A. Illumina assay completed in 2008 for 1373 SNPs
CBCS Phase 1 & Phase 2 (invasive and CIS) (N=3748)

SNP categories

1. Ancestry Informative Markers (AIMS)
2. DNA Repair
    a. Nucleotide Excision Repair and Transcription-coupled Repair
    b. Double-Strand Break Repair -- Homologous Recombination Repair
    c. Base Excision Repair
    d. Direct Repair
    e. Double-Strand Break Repair -- Non-Homologous End Joining
    f. Bypass Polymerases
3. Damage Recognition, Cell Cycle Control, Cellular Proliferation and Cellular Adhesion
4. Hormone Metabolism
5. Oxidative Metabolism
6. Additional Genotypes from NCI Collaboration
7. Drug Metabolizing Enzymes (DMEs)
8. Hypothalamic-Pituitary-Adrenal (HPA) Axis
9. Hypothalamic-Pituitary-Ovarian (HPO) Axis
10. Inflammation
11. miRNA associated Genes
12. Obesity/Insulin Resistance Pathway Genes
13. Additional known candidate genes
14. Chuck Perou's candidates, including subtype specific genes
15. Replication of GWAS results
16. Additional genes in the FGFR2 and other pathways identified by GWAS
17. Additional SNPs

For detailed description of SNPs in each category, please see document "**List of SNPs using Illumina or Taqman Assay.docx**".

B. Taqman assay completed in (April and July) 2010 for 78 SNPs
CBCS Phase 1 & Phase 2 (invasive and CIS) (N=3851)

The SNPs either failed Illumina or were chosen after the Illumina run.

Please see document "**List of SNPs using Illumina or Taqman Assay.docx**" for SNPs description.

Publications From CBCS Genotyping Projects

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3. Li Y, Millikan R, Tse C-KJ, Newman B, Conway K, Liu ET. **Germline P57 polymorphisms and risk of breast cancer.** Human Genetics 104: 83-88, 1999.
4. Guillemette C, Millikan R, Newman B, Housman D. **Genetic Polymorphisms in uridine diphospho-glucuronosyltransferase 1A1 and association with breast cancer among African-Americans.** Cancer Research 60(4): 950-6, 2000.
5. Millikan RC. **NAT1*10 and NAT1*11 polymorphisms and breast cancer risk.** Cancer Epidemiology, Biomarkers, and Prevention 9(2): 217-9, 2000.
6. Duell E, Millikan R, Pittman G, Winkel S, Lunn R, Tse C-K, Eaton A, Mohrenweiser H, Newman B, Bell D. **XRCC1 polymorphisms and breast cancer risk.** Cancer Epidemiology, Biomarkers and Prevention 10: 567-573, 2000.
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8. Millikan R, Eaton A, Worley K, Biscocho L, Hodgson E, Huang W-Y, Geradts J, Iacocca M, Cowan D, Conway K, Dressler L. **HER2 codon 655 polymorphism and risk of breast cancer in African Americans and whites.** Breast Cancer Research and Treatment 79: 355-64, 2003.
9. Millikan R, Player J, de Cotret AR, Moorman P, Pittman G, Vannappagari V, Tse C-K, Keku T. **Manganese Superoxide Dismutase (MnSOD) Ala-9Val polymorphism and risk of breast cancer in a population-based case-control study of African Americans and whites.** Breast Cancer Research 6: 264-274, 2004.
10. Li Y, Millikan R, Bell D, Cui L, Tse C-K, Newman B, Conway K. **Cigarette smoking, cytochrome P4501A1 (CYP1A1) polymorphisms, and breast cancer among African Americans and white women.** Breast Cancer Research 6: 460-473, 2004.
11. Millikan R, Hummer A, Wolff M, Begg C. **HER2 codon 655 polymorphism and breast cancer: Results from kin-cohort and case-control analyses.** Breast Cancer Research and Treatment. 89: 309-12, 2005.
12. Canter J, Kallianpur A, Parl F, Millikan R. **Mitochondrial DNA G10398A polymorphism and invasive breast cancer in African-American women.** Cancer Research 65: 8028-33, 2005.
13. Millikan R, Player J, deCotret A, Tse C-K, Keku T. **Polymorphisms in DNA repair genes, medical exposure to ionizing radiation and breast cancer risk.** Cancer Epidemiology, Biomarkers and Prevention 14: 2326-34, 2005.
14. Moorman P, Sesay J, Nwosu V, Kane J, de Cotret A, Worley K, Millikan R. **COXR Polymorphism (Val^{511}Ala), NSAID Use and Breast Cancer in African-American Women.** Cancer Epidemiology, Biomarkers and Prevention 14: 3013-14, 2005.
15. Mechanic L, Millikan R, Player J, Rene de Cotret A, Winkel S, Worley K, Heard K, Tse C-K, Keku T. **Polymorphisms in Nucleotide Excision Repair Genes, Smoking and Breast Cancer in African Americans and Whites: A Population-Based Case-Control Study**. Carcinogenesis 27: 1377-85, 2006.
16. Pachkowski B, Winkel S, Kubota Y, Swenberg J, Millikan R, Nakamura J. **XRCC1 genotype and breast cancer: Functional studies and epidemiologic data demonstrate interactions between XRCC1 codon 280 His and smoking.** Cancer Research 66: 2876-77, 2006.

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18. Thorner A, Hoadley K, Parker J, Winkel S, Millikan R, and Perou C. **In vitro and in vivo analysis of B-Myb in basal-like breast cancer** Oncogene 28: 742-51, 2009
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