

## Original Article

# Associations of plasma extracellular microRNAs with new-onset breast cancer in the Framingham heart study

Hannah Karlin<sup>1,2</sup>, Martin Larson<sup>1,3</sup>, Jian Rong<sup>1,4</sup>, Tianxiao Huan<sup>1,2,5</sup>, Paul Courchesne<sup>1,2</sup>, Jane E Freedman<sup>6</sup>, Jennifer E Ho<sup>1,7,8</sup>, Kahraman Tanriverdi<sup>6</sup>, Gregory P Mueller<sup>9</sup>, Daniel Levy<sup>1,2,10</sup>

<sup>1</sup>Framingham Heart Study, Framingham, MA, USA; <sup>2</sup>Population Sciences Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA; <sup>3</sup>Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA; <sup>4</sup>Department of Neurology, Boston University Chobanian and Avedisian School of Medicine, Boston, MA, USA; <sup>5</sup>Department of Ophthalmology and Visual Sciences, University of Massachusetts Medical School, Worcester, MA, USA; <sup>6</sup>Department of Medicine, Division of Cardiovascular Medicine, Vanderbilt University Medical Center, Nashville, TN, USA; <sup>7</sup>Division of Cardiovascular Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA; <sup>8</sup>Harvard Medical School, Boston, MA, USA; <sup>9</sup>Department of Anatomy, Physiology, and Genetics, F. Edward Hebert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA; <sup>10</sup>Boston University School of Medicine, Boston, MA, USA

Received June 27, 2024; Accepted October 6, 2024; Epub November 25, 2024; Published November 30, 2024

**Abstract:** Breast cancer is the second leading cause of cancer deaths among women. Multiple microRNAs (miRNAs) have been reported to be associated with breast cancer progression or metastasis. The purpose of the current study was to identify plasma extracellular miRNAs associated with incident breast cancer. Levels of 166 plasma miRNA were measured using qRT-PCR in 2140 Framingham Heart Study female participants with a median follow up of 15.7 years. Prospective analyses of the associations of miRNAs with the occurrence of 56 new-onset breast cancer events were conducted using proportional hazards regression. The expression levels miR-134-5p (P=0.002) and miR-505-3p (P=0.005) were found to be positively associated with incident breast cancer after adjusting for age, body mass index, and cigarette smoking. These results highlight plasma miRNAs as potential biomarkers of breast cancer risk. Validation of these findings in larger and more diverse cohorts is warranted.

**Keywords:** Breast cancer, microRNA, extracellular RNA, biomarker, risk factors

## Introduction

MicroRNAs (miRNAs) are small, non-coding RNAs comprised of 18-24 nucleotides that regulate gene expression by binding to complementary or near-complementary sequences in 3'-untranslated regions of messenger RNA (mRNA). In doing so, miRNAs can alter gene expression via mRNA transcript degradation or translational repression. It has been suggested that miRNAs regulate approximately two-thirds of human protein-coding genes [1, 2]. Accordingly, miRNAs have been implicated as powerful regulators of a range of physiological and pathophysiological processes [1].

While miRNAs can be found inside the cell, miRNAs are also found extracellularly in circulating blood and other body fluids [1, 3]. These miR-

NAs can be transported across cell membranes to mediate cell-to-cell communication [4]. Moreover, expression levels of extracellular miRNAs (ex-miRNAs) have been reported to be associated with a wide range of diseases, including cancer [5].

Ex-miRNAs play a role in numerous cancer-related processes, including cell proliferation, differentiation, and apoptosis [2]. Dysregulation of ex-miRNAs is often observed in various cancers due to altered miRNA biogenesis and perturbed transcription of miRNA-encoding genes. As a result, some ex-miRNAs become significantly overexpressed while the expression of others significantly decreases [6].

Given that ten percent of known human miRNAs can be detected in plasma, are stable, and

**Table 1.** Clinical characteristics of the study participants

Clinical characteristic	Mean (standard deviation)
Age, years	40 (9)
Systolic blood pressure, mmHg	113 (14)
Diastolic blood pressure, mmHg	73 (9)
Triglycerides, mg/dL	97 (62)
Total cholesterol, mg/dL	185 (34)
High-density lipoprotein, mg/dL	61 (16)
Fasting blood glucose, mg/dL	92 (18)
BMI, kg/m <sup>2</sup>	26 (6)
Dichotomous outcome	Number of participants (%)
Never smoker	1160 (54.8)
Former smoker	640 (30.3)
Current smoker	315 (14.9)
Type 2 diabetes mellitus	46 (2.2)
Incident breast cancer	56 (2.7)

can be measured by polymerase chain reaction (PCR), ex-miRNAs may be ideal candidates as cancer biomarkers [6]. Most studies of miRNAs and breast cancer have examined associations of miRNA expression in tumor tissue with prevalent breast cancer; there are few studies examining plasma miRNAs as predictors of new-onset breast cancer [7, 8]. Therefore, in the present study, we investigated associations of plasma ex-miRNAs with incident breast cancer in a large population.

### Sample collection

The Framingham Heart Study (FHS) is a population-based, observational cohort study established in 1948 to identify risk factors for the development of cardiovascular disease [9]. The study sample for the present investigation included female participants in the FHS Third Generation cohort (n=2,140 at Exam 1) in whom plasma miRNA levels were measured. A total of 24 participants with prevalent breast cancer were excluded, leaving 2,116 eligible participants. The FHS protocol was approved by the Boston Medical Center IRB; informed consent was provided by all participants.

Study participants attended the first examination in the years 2002-2005 and underwent a fasting blood draw. Plasma samples were immediately isolated (Applied Biosystems, catalog #A27828) and processed (ThermoFisher Flex Magnetic Particle Processor, 96DW) before being stored at -80°C until assay. The isolated miRNAs were converted to cDNA

(Applied Biosystems, catalog #A28-007) and synthesis and preamplification (Applied Biosystems, catalog #4484075) were performed. qRT-PCR (Applied Biosystems, catalog #A25576; BioMark HD, catalogue #BMKHD-BMKHD; Fluidigm, catalog #BMK-M-96.96) was used to quantify miRNAs and data are reported as cycle threshold (Ct) values. We required that an ex-miRNA be measurable in at least 50% of participants, yielding 166 ex-miRNAs that were carried forward in the analysis. The methods for plasma miRNA isolation and measurement have been previously reported and are described in greater detail elsewhere [10]. Self-reported smoking history was

obtained and cigarette smoking status (current/former/never) was defined according to previously published classifications [10].

Participants were prospectively followed through 2018 for the occurrence of incident breast cancer. Breast cancer events were identified by surveillance through routine examinations, health history updates, hospital admissions, or death records. Cancer cases were adjudicated and coded on the basis of tumor topology and morphology and graded by two independent physicians using International Classification of Diseases codes [11].

We used proportional hazards regression with plasma miRNA levels as the independent variable and incident breast cancer as the outcome. The covariates for the models were age, cigarette smoking status, and body mass index (BMI). All statistical analyses were conducted using SAS 9.4 (SAS Institute Inc. 2020. SAS/STAT® 15.2 User's Guide. Cary, NC: SAS Institute Inc.) procedure PHREG.

### Results and discussion

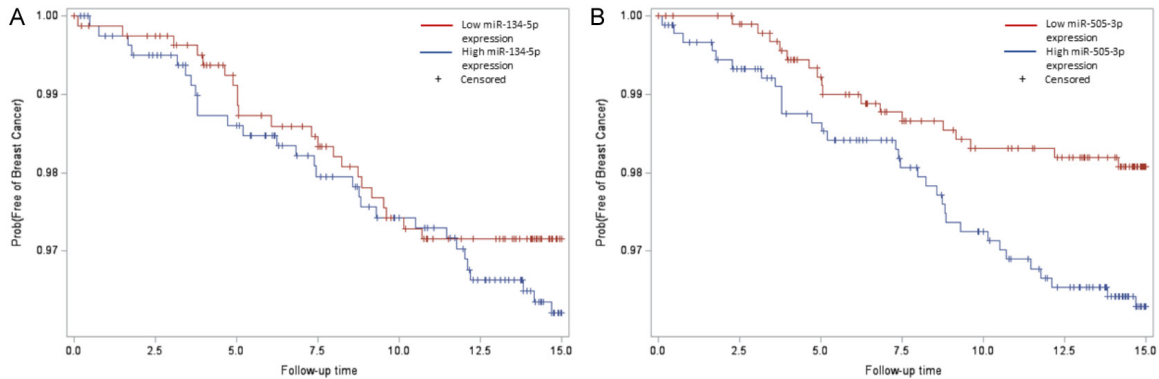
Among eligible participants (n=2116; mean age: 40±9 years), 1160 (55%) were never smokers, 640 (30%) were former smokers, and 315 (15%) were current smokers. During a median follow-up time of 15.7 years, 56 women developed new-onset breast cancer. The full table of clinical characteristics of the study participants can be found in **Table 1**.

## miRNA and breast cancer

**Table 2.** Ex-miRNAs associated with incident breast cancer in the FHS

Ex-miRNA	N analyzed	Event	Estimate*	Standard Error	Chi Squared	Probability Chi Squared	Hazard Ratio	HR Lower Confidence Level	HR Upper Confidence Level
134-5p	1594	51	-0.126	0.0413	9.296	2.30E-03	0.882	0.813	0.956
505-3p	1805	49	-0.163	0.0582	7.882	4.99E-03	0.849	0.758	0.952

\*Estimates are reported as Ct values such that a negative estimate indicates a higher Ct value (lower ex-miRNA expression).



**Figure 1.** Kaplan-Meier plots for ex-miRNAs. The x-axis “Follow-up time” indicates years to new breast cancer event, and the y-axis “Prob(Free of Breast Cancer)” indicates the proportion of participants with event-free survival. The variable ex-miRNA was defined as: if ex-miRNA  $\geq$  median Ct-value, then low ex-miRNA expression (red); if ex-miRNA  $<$  median Ct-value, then high ex-miRNA expression (blue). A. Among the 1622 female participants with analyzed miR-134-5p levels, there were 51 new breast cancer cases (among 811 participants with miR-134-5p levels above the median, there were 22 new breast cancer cases; among 811 participants with miR-134-5p levels below the median, there were 29 new breast cancer cases). B. Among the 1843 female participants with analyzed miR-505-3p levels, there were 49 new breast cancer cases (among 923 participants with miR-505-3p levels above median, there were 18 new breast cancer cases; among 920 participants with miR-505-3p levels below median, there were 32 new breast cancer cases).

Among the 166 plasma ex-miRNAs included in analysis, two ex-miRNAs (miR-134-5p and miR-505-3p) were associated with incident breast cancer at  $P < 0.005$  before adjusting for multiple testing (Table 2). The association results for all ex-miRNAs included in the prospective analyses are provided in Supplementary Table 1.

The Kaplan-Meier breast cancer-free survival plot for miR-134-5p (Figure 1A) indicates that there was a higher proportion of event-free survival for participants with low miR-134-5p expression (miR-134-5p  $\geq$  median Ct-values) compared to participants with high miR-134-5p expression (miR-134-5p  $<$  median Ct-values). The Kaplan-Meier survival plot for miR-505-3p depicts analogous behavior, i.e., lower miR-505-3p expression levels associated with higher event-free survival (Figure 1B).

The purpose of our study was to examine associations of plasma ex-miRNAs with new-onset breast cancer in middle-aged women. To this end, we identified two plasma ex-miRNAs (miR-

134-5p and miR-505-3p) whose expression levels were positively associated with incident breast cancer during a median follow-up of 15.7 years. Previous studies have enumerated a negative association between the expression levels of miR-134-5p and miR-505-3p and breast cancer progression in tumor samples or cell lines [12-16]. However, such studies examining miRNAs isolated from tumor tissue or cell lines demonstrate an association between cellular miRNAs and prevalent breast cancer. To our knowledge, this is the first study to demonstrate the association of extracellular miR-134-5p and miR-505-3p expression with incident breast cancer. These findings highlight the potential of ex-miRNAs to serve as biomarkers of breast cancer risk.

Discordance in the direction of effect of miRNAs on breast cancer has been observed between breast cancer tissue samples or cell lines and miRNAs derived from cell-free blood samples for other miRNAs, including miR-122, miR-145-5p, and miR-125b-5p [17-23]. For

example, expression levels of miR-122 isolated from human breast cancer cells have been reported to be negatively associated with prevalent breast cancer, whereas expression levels of serum miR-122 have been found to be positively associated with prevalent breast cancer [22, 23]. One proposed explanation for this apparent paradox may be that breast cancer cells secrete these miRNAs at higher rates than normal cells, decreasing cellular miRNA levels and increasing ex-miRNA levels [22]. The current study, however, is unable to provide a mechanism of differential expression or evidence of ex-miRNA communication with specific tissues or cell lines. Functional studies investigating the molecular targets and pathways of miR-134-5p and miR-505-3p are warranted.

The present study has several strengths, including a large sample size of middle-aged women with available plasma ex-miRNA and the availability of new-onset breast cancer outcomes during long-term follow-up. Yet, there are several limitations. Of the 166 plasma ex-miRNAs included in the analysis, only two ex-miRNAs were significantly associated with incident breast cancer after adjusting for covariates; these associations were not significant, however, after correcting for multiple testing. Statistical power was limited by the relatively small number of new-onset breast cancer cases in the study sample. Additionally, the study population consisted largely of participants of European ancestry. Future studies that include larger sample sizes and greater racial and ethnic diversity are warranted.

This population-based study reveals two plasma ex-miRNAs associated with incident breast cancer. Moreover, these findings motivate further investigation into the molecular targets and mechanistic pathways of the identified ex-miRNAs. This effort may help advance the utility of plasma ex-miRNAs as clinically useful biomarkers.

### Acknowledgements

The Framingham Heart Study is funded by National Institutes of Health contracts N01-HC-25195, HHSN268201500001, and 75N9-2019D00031. The laboratory work for this investigation was funded by the Division of Intramural Research, National Heart, Lung, and Blood Institute, National Institutes of Health,

Bethesda, MD and was conducted at the Uniformed Services University of Health Sciences, Bethesda, MD. This manuscript does not necessarily reflect the opinions or views of the NHLBI, NIH or DHHS.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Daniel Levy, Framingham Heart Study, 73 Mt. Wayte Avenue, Suite 2, Framingham, MA 01702, USA. E-mail: levyd@nih.gov

### References

- [1] Scott H. Extracellular microRNAs as messengers in the central and peripheral nervous system. *Neuronal Signal* 2017; 1: NS20170112.
- [2] Jansson MD and Lund AH. MicroRNA and cancer. *Mol Oncol* 2012; 6: 590-610.
- [3] Condrat CE, Thompson DC, Barbu MG, Bugnar OL, Boboc A, Cretoiu D, Suciuc N, Cretoiu SM and Voinea SC. miRNAs as biomarkers in disease: latest findings regarding their role in diagnosis and prognosis. *Cells* 2020; 9: 276.
- [4] Mori MA, Ludwig RG, Garcia-Martin R, Brandão BB and Kahn CR. Extracellular miRNAs: from biomarkers to mediators of physiology and disease. *Cell Metab* 2019; 30: 656-673.
- [5] Ortiz-Quintero B. Extracellular microRNAs as intercellular mediators and noninvasive biomarkers of cancer. *Cancers (Basel)* 2020; 12: 3455.
- [6] Wang H, Peng R, Wang J, Qin Z and Xue L. Circulating microRNAs as potential cancer biomarkers: the advantage and disadvantage. *Clin Epigenetics* 2018; 10: 59.
- [7] Li X, Zou W, Wang Y, Liao Z, Li L, Zhai Y, Zhang L, Gu S and Zhao X. Plasma-based microRNA signatures in early diagnosis of breast cancer. *Mol Genet Genomic Med* 2020; 8: e1092.
- [8] Zou R, Loke SY, Tang YC, Too HP, Zhou L, Lee ASG and Hartman M. Development and validation of a circulating microRNA panel for the early detection of breast cancer. *Br J Cancer* 2022; 126: 472-481.
- [9] Splansky GL, Corey D, Yang Q, Atwood LD, Cupples LA, Benjamin EJ, D'Agostino RB Sr, Fox CS, Larson MG, Murabito JM, O'Donnell CJ, Vasan RS, Wolf PA and Levy D. The third generation cohort of the National Heart, Lung, and Blood Institute's Framingham Heart Study: design, recruitment, and initial examination. *Am J Epidemiol* 2007; 165: 1328-1335.
- [10] Karlin H, Sooda M, Larson M, Rong J, Huan T, Mens MMJ, van Rooij FJA, Ikram MA,

- Courchesne P, Freedman JE, Joehanes R, Mueller GP, Kavousi M, Ghanbari M and Levy D. Plasma extracellular microRNAs associated with cardiovascular disease risk factors in middle-aged and older adults. *J Am Heart Assoc* 2024; 13: e033674.
- [11] Liu EE, Suthahar N, Paniagua SM, Wang D, Lau ES, Li SX, Jovani M, Takvorian KS, Kreger BE, Benjamin EJ, Meijers WC, Bakker SJL, Kieneker LM, Gruppen EG, van der Vegt B, de Bock GH, Gansevoort RT, Hussain SK, Hoffmann U, Splansky GL, Vasan RS, Larson MG, Levy D, Cheng S, de Boer RA and Ho JE. Association of cardiometabolic disease with cancer in the community. *JACC CardioOncol* 2022; 4: 69-81.
- [12] Yang C, Zhang G, Zhang Y, Zhang S, Li J and Liu Y. Exosome miR-134-5p restrains breast cancer progression via regulating PI3K/AKT pathway by targeting ARHGAP1. *J Obstet Gynaecol Res* 2021; 47: 4037-4048.
- [13] Su X, Zhang L, Li H, Cheng P, Zhu Y, Liu Z, Zhao Y, Xu H, Li D, Gao H and Zhang T. MicroRNA-134 targets KRAS to suppress breast cancer cell proliferation, migration and invasion. *Oncol Lett* 2017; 13: 1932-1938.
- [14] Wang J, Liu H and Li M. Downregulation of miR-505 promotes cell proliferation, migration and invasion, and predicts poor prognosis in breast cancer. *Oncol Lett* 2019; 18: 247-254.
- [15] Zhao P, Guan H, Dai Z, Ma Y, Zhao Y and Liu D. Long noncoding RNA DLX6-AS1 promotes breast cancer progression via miR-505-3p/RUNX2 axis. *Eur J Pharmacol* 2019; 865: 172778.
- [16] Pan JY, Zhang F, Sun CC, Li SJ, Li G, Gong FY, Bo T, He J, Hua RX, Hu WD, Yuan ZP, Wang X, He QQ and Li DJ. miR-134: a human cancer suppressor? *Mol Ther Nucleic Acids* 2017; 6: 140-149.
- [17] Ashirbekov Y, Abaildayev A, Omarbayeva N, Botbayev D, Belkozhayev A, Askandirova A, Neupokoyeva A, Utegenova G, Sharipov K and Aitkhozhina N. Combination of circulating miR-145-5p/miR-191-5p as biomarker for breast cancer detection. *PeerJ* 2020; 8: e10494.
- [18] Jusoh AR, Mohan SV, Lu Ping T, Tengku Din TADAAB, Haron J, Romli RC, Jaafar H, Nafi SN, Tuan Salwani TI and Yahya MM. Plasma circulating mirnas profiling for identification of potential breast cancer early detection biomarkers. *Asian Pac J Cancer Prev* 2021; 22: 1375-1381.
- [19] Tang W, Zhang X, Tan W, Gao J, Pan L, Ye X, Chen L and Zheng W. miR-145-5p suppresses breast cancer progression by inhibiting SOX2. *J Surg Res* 2019; 236: 278-287.
- [20] Matamala N, Vargas MT, Gonzalez-Campora R, Minambres R, Arias JI, Menendez P, Andres-Leon E, Gomez-Lopez G, Yanowsky K, Calvete-Candenas J, Inglada-Perez L, Martinez-Delgado B and Benitez J. Tumor microRNA expression profiling identifies circulating microRNAs for early breast cancer detection. *Clin Chem* 2015; 61: 1098-1106.
- [21] Li Y, Wang Y, Fan H, Zhang Z and Li N. miR-125b-5p inhibits breast cancer cell proliferation, migration and invasion by targeting KIAA1522. *Biochem Biophys Res Commun* 2018; 504: 277-282.
- [22] Saleh AA, Soliman SE, Habib MSE, Gohar SF and Abo-Zeid GS. Potential value of circulatory microRNA122 gene expression as a prognostic and metastatic prediction marker for breast cancer. *Mol Biol Rep* 2019; 46: 2809-2818.
- [23] Wang B, Wang H and Yang Z. MiR-122 inhibits cell proliferation and tumorigenesis of breast cancer by targeting IGF1R. *PLoS One* 2012; 7: e47053.



## miRNA and breast cancer

**Supplementary Table 1.** Associations between ex-miRNAs and incident breast cancer

exRNA	N_analyzed	Event	Censored	PctCens	DF	Estimate	StdErr	ChiSq	ProbChiSq	HazardRatio	HRLowerCL	HRUpperCL	covariate	panel
_100_5p	3538	44	3494	98.75635953	1	-0.086288195	0.082053705	1.105875871	0.292980203	0.917329823	0.781054381	1.077382093	age1 sex bmi1 currsmk1	1
_101_3p	3685	51	3634	98.61601085	1	-0.111043438	0.087794192	1.59975779	0.205937539	0.894899875	0.753431713	1.062930818	age1 sex bmi1 currsmk1	1
_103a_3p	2877	39	2838	98.64442127	1	0.02953847	0.079347514	0.1385828	0.709693985	1.029979058	0.881632656	1.203286712	age1 sex bmi1 currsmk1	1
_106b_3p	3555	50	3505	98.59353024	1	0.051515776	0.088619498	0.337926243	0.561028687	1.052865796	0.884993261	1.252581725	age1 sex bmi1 currsmk1	1
_106b_5p	1976	20	1956	98.98785425	1	-0.057791112	0.152718338	0.143198912	0.705121346	0.943847085	0.69969304	1.273197345	age1 sex bmi1 currsmk1	1
_107	3089	40	3049	98.70508255	1	-0.064760785	0.106904106	0.366974115	0.544658272	0.937291651	0.760112384	1.155770722	age1 sex bmi1 currsmk1	1
_10a_5p	3021	47	2974	98.44422377	1	-0.049816626	0.100270093	0.246834453	0.61931291	0.951403872	0.781654543	1.158017099	age1 sex bmi1 currsmk1	1
_125a_5p	3876	55	3821	98.58101135	1	-0.035562581	0.085010453	0.175001544	0.6757045	0.965062338	0.816947859	1.140030304	age1 sex bmi1 currsmk1	1
_125b_5p	3889	55	3834	98.58575469	1	-0.065197483	0.09003819	0.524334149	0.46899869	0.936882427	0.785316001	1.117701257	age1 sex bmi1 currsmk1	1
_126_3p	3789	54	3735	98.57482185	1	-0.044145923	0.106571417	0.17159306	0.678699868	0.956814326	0.776450752	1.17907498	age1 sex bmi1 currsmk1	1
_126_5p	3892	55	3837	98.58684481	1	-0.066379257	0.079597536	0.695449381	0.404317006	0.935775898	0.800605022	1.093768471	age1 sex bmi1 currsmk1	1
_130a_3p	3682	51	3631	98.61488322	1	-0.141502331	0.08645716	2.67870725	0.101698255	0.868053153	0.732746665	1.028344872	age1 sex bmi1 currsmk1	1
_140_3p	3679	52	3627	98.58657244	1	-0.051978119	0.095835796	0.294161355	0.587566094	0.949349639	0.78677511	1.145517602	age1 sex bmi1 currsmk1	1
_142_5p	3483	49	3434	98.59316681	1	-0.19474755	0.102431778	3.614719315	0.057270385	0.823042409	0.673336452	1.006033173	age1 sex bmi1 currsmk1	1
_143_3p	3755	54	3701	98.56191744	1	-0.010087723	0.095248465	0.011216834	0.915654112	0.989962988	0.821378474	1.193148771	age1 sex bmi1 currsmk1	1
_144_5p	2328	27	2301	98.84020619	1	0.132118532	0.13426645	0.968261066	0.325114247	1.141243586	0.877183674	1.484793846	age1 sex bmi1 currsmk1	1
_145_5p	3843	55	3788	98.56882644	1	-0.082765626	0.086737426	0.910514673	0.339977898	0.920566879	0.776648153	1.091154822	age1 sex bmi1 currsmk1	1
_146a_5p	3903	55	3848	98.59082757	1	-0.058748427	0.082736613	0.504193224	0.477663428	0.942943959	0.801789473	1.108948595	age1 sex bmi1 currsmk1	1
_148a_3p	3840	55	3785	98.56770833	1	-0.029238271	0.076581981	0.145763965	0.702616786	0.971185032	0.835824852	1.128466525	age1 sex bmi1 currsmk1	1
_150_5p	3892	55	3837	98.58684481	1	-0.110145601	0.097323448	1.280853155	0.257740466	0.89570371	0.740154705	1.083942494	age1 sex bmi1 currsmk1	1
_151a_3p	3796	55	3741	98.55110643	1	0.02962481	0.078106737	0.14385805	0.704475319	1.030067991	0.883855597	1.200467666	age1 sex bmi1 currsmk1	1
_151a_5p	2122	30	2092	98.5862394	1	0.084950245	0.124844791	0.463007921	0.496221562	1.088662899	0.852364481	1.390469611	age1 sex bmi1 currsmk1	1
_15a_5p	3867	55	3812	98.57770882	1	0.003937005	0.072969501	0.002911047	0.956971718	1.003944765	0.870157901	1.158301373	age1 sex bmi1 currsmk1	1
_15b_3p	3724	52	3672	98.60365199	1	0.00710279	0.084513376	0.00706329	0.933021938	1.007128075	0.8533885	1.188564128	age1 sex bmi1 currsmk1	1
_16_5p	3890	55	3835	98.58611825	1	-0.042105768	0.072252879	0.339604049	0.560057862	0.958768369	0.83216977	1.104626505	age1 sex bmi1 currsmk1	1
_181a_5p	3324	47	3277	98.58604091	1	-0.050984383	0.114019655	0.199946999	0.65476363	0.950293511	0.759983314	1.188259979	age1 sex bmi1 currsmk1	1
_182_5p	2218	25	2193	98.87285843	1	0.306320823	0.170515591	3.227192338	0.072424759	1.358418048	0.972501565	1.89747725	age1 sex bmi1 currsmk1	1
_185_5p	3840	55	3785	98.56770833	1	0.013947892	0.077185635	0.032654585	0.856598508	1.014045617	0.871679758	1.179663178	age1 sex bmi1 currsmk1	1
_18a_3p	2969	41	2928	98.61906366	1	0.095620411	0.090629916	1.113161193	0.291395806	1.100341307	0.921261861	1.314231104	age1 sex bmi1 currsmk1	1
_18a_5p	3190	46	3144	98.55799373	1	0.006786784	0.0936246	0.005254703	0.942212497	1.006809867	0.838019373	1.209597463	age1 sex bmi1 currsmk1	1
_191_5p	3787	54	3733	98.57406918	1	-0.018273784	0.080813054	0.051132137	0.821104853	0.981892169	0.83806094	1.150408264	age1 sex bmi1 currsmk1	1
_192_5p	3679	52	3627	98.58657244	1	-0.09193879	0.085158249	1.165585457	0.28031017	0.912160981	0.771941977	1.077849995	age1 sex bmi1 currsmk1	1
_194_5p	3606	51	3555	98.58569052	1	-0.086894183	0.082383801	1.112494206	0.291540405	0.916774101	0.780076361	1.077426255	age1 sex bmi1 currsmk1	1
_199a_3p	3908	55	3853	98.5926305	1	-0.080202515	0.081801255	0.961293558	0.326861182	0.922929421	0.786211036	1.083422487	age1 sex bmi1 currsmk1	1
_199a_5p	3649	52	3597	98.57495204	1	-0.036238547	0.079760919	0.206424507	0.64958439	0.964410209	0.824838989	1.127598311	age1 sex bmi1 currsmk1	1
_19a_3p	3811	55	3756	98.55680924	1	-0.014502376	0.06873163	0.044521013	0.832887247	0.985602277	0.861384849	1.127732685	age1 sex bmi1 currsmk1	1
_19b_3p	3537	50	3487	98.58637263	1	0.042173843	0.059370904	0.504590448	0.477490033	1.043075794	0.928494343	1.171797245	age1 sex bmi1 currsmk1	1
_20a_5p	3887	55	3832	98.58502701	1	-0.039074392	0.073081968	0.285866973	0.592881327	0.961679165	0.833340949	1.109782038	age1 sex bmi1 currsmk1	1
_20b_5p	3687	54	3633	98.53539463	1	0.089817555	0.08782974	1.045777438	0.306481589	1.093974675	0.920972068	1.299475448	age1 sex bmi1 currsmk1	1
_21_3p	3675	50	3625	98.63945578	1	-0.044529085	0.094586969	0.221628155	0.637802136	0.956447781	0.794600236	1.15126112	age1 sex bmi1 currsmk1	1

## miRNA and breast cancer

_22_3p	3895	55	3840	98.58793325	1	-0.066940743	0.077369195	0.74859153	0.386922527	0.93525062	0.803657916	1.0883906	age1 sex bmi1 currrsmk1	1
_22_5p	3657	52	3605	98.57806946	1	0.032208682	0.111065827	0.084097871	0.771819046	1.032732996	0.830708491	1.283888936	age1 sex bmi1 currrsmk1	1
_221_3p	3857	55	3802	98.57402126	1	-0.090225224	0.087850208	1.054800559	0.30440406	0.913725369	0.769196767	1.085410243	age1 sex bmi1 currrsmk1	1
_221_5p	2906	45	2861	98.4514797	1	0.088184395	0.093064008	0.897883473	0.343349864	1.092189498	0.910084608	1.310732969	age1 sex bmi1 currrsmk1	1
_222_3p	3850	55	3795	98.57142857	1	0.001874898	0.082178101	0.000520527	0.981797798	1.001876657	0.852833265	1.176967265	age1 sex bmi1 currrsmk1	1
_223_3p	3887	55	3832	98.58502701	1	-0.048660523	0.065146969	0.557911238	0.455103063	0.952504428	0.838327674	1.082231584	age1 sex bmi1 currrsmk1	1
_23a_3p	3723	52	3671	98.60327693	1	-0.078515734	0.09140364	0.737881134	0.390340473	0.924487514	0.772855195	1.105869727	age1 sex bmi1 currrsmk1	1
_23b_3p	2154	30	2124	98.60724234	1	-0.209638986	0.094207211	4.951944987	0.026061333	0.810876931	0.6741641	0.975313573	age1 sex bmi1 currrsmk1	1
_24_3p	3894	55	3839	98.58757062	1	-0.052779326	0.077089455	0.468746173	0.493564554	0.948589318	0.815566854	1.103308319	age1 sex bmi1 currrsmk1	1
_25_3p	3897	55	3842	98.58865794	1	-0.006828111	0.080122841	0.007262538	0.932086071	0.993195148	0.848855767	1.162077988	age1 sex bmi1 currrsmk1	1
_26a_5p	3781	54	3727	98.5718064	1	-0.060554709	0.096496231	0.393799493	0.530308958	0.941242273	0.779047043	1.137206057	age1 sex bmi1 currrsmk1	1
_26b_5p	3859	55	3804	98.5747603	1	-0.103909262	0.089785085	1.339368637	0.247145341	0.901307077	0.755870817	1.074726565	age1 sex bmi1 currrsmk1	1
_27a_3p	2843	36	2807	98.73373197	1	-0.192435985	0.096704629	3.959843731	0.046598029	0.824947125	0.682513088	0.997105801	age1 sex bmi1 currrsmk1	1
_27b_3p	3334	49	3285	98.53029394	1	-0.010716053	0.105628714	0.010292141	0.919193096	0.989341159	0.804330899	1.216907035	age1 sex bmi1 currrsmk1	1
_29a_3p	3793	52	3741	98.62905352	1	-0.07003078	0.094281379	0.551729338	0.457611947	0.932365121	0.775056858	1.121601222	age1 sex bmi1 currrsmk1	1
_29b_2_5p	3041	40	3001	98.68464321	1	0.003166519	0.076528824	0.001712041	0.966995494	1.003171538	0.863443151	1.165511746	age1 sex bmi1 currrsmk1	1
_29b_3p	3606	52	3554	98.55795896	1	0.055267478	0.103372428	0.285844512	0.592895855	1.056823254	0.863001579	1.294175371	age1 sex bmi1 currrsmk1	1
_29c_3p	3739	54	3685	98.55576357	1	0.037344304	0.095421233	0.153164697	0.695529221	1.038050364	0.860985275	1.251529602	age1 sex bmi1 currrsmk1	1
_30c_5p	3636	53	3583	98.54235424	1	-0.015235701	0.104278018	0.021347123	0.883837278	0.984879775	0.802826332	1.208216686	age1 sex bmi1 currrsmk1	1
_30d_5p	3679	52	3627	98.58657244	1	-0.086028228	0.089738957	0.919009326	0.337735225	0.91756833	0.769577704	1.094017714	age1 sex bmi1 currrsmk1	1
_30e_3p	2335	33	2302	98.58672377	1	0.022112287	0.101392011	0.047561972	0.827361268	1.022358576	0.838104569	1.247120104	age1 sex bmi1 currrsmk1	1
_320a_3p	3131	40	3091	98.72245289	1	-0.080411435	0.096131723	0.69968437	0.402889771	0.922736622	0.764276114	1.114051399	age1 sex bmi1 currrsmk1	1
_320e	3766	53	3713	98.59267127	1	-0.026822099	0.103300226	0.067419105	0.795132305	0.973534419	0.795100449	1.192011985	age1 sex bmi1 currrsmk1	1
_361_3p	2920	43	2877	98.52739726	1	0.015908061	0.116063698	0.018786318	0.890980849	1.016035267	0.809310517	1.275564376	age1 sex bmi1 currrsmk1	1
_361_5P	3732	54	3678	98.55305466	1	-0.044155695	0.088330692	0.249890752	0.617152013	0.956804976	0.804704082	1.137655175	age1 sex bmi1 currrsmk1	1
_363_3p	3754	53	3701	98.58817262	1	0.000205406	0.076436085	7.22155E-06	0.997855852	1.000205427	0.861046673	1.161854437	age1 sex bmi1 currrsmk1	1
_374a_5p	3629	51	3578	98.59465417	1	0.039826391	0.095673568	0.173283802	0.677209727	1.040630096	0.862698202	1.255260524	age1 sex bmi1 currrsmk1	1
_39_3p	3921	55	3866	98.59729661	1	-0.062574113	0.069436831	0.812100203	0.367500053	0.939343442	0.819822191	1.076289605	age1 sex bmi1 currrsmk1	1
_423_3p	3852	54	3798	98.59813084	1	-0.088045196	0.080494248	1.196414425	0.274039499	0.915719489	0.782070005	1.072208597	age1 sex bmi1 currrsmk1	1
_423_5p	3693	54	3639	98.53777417	1	-0.039263979	0.098794402	0.157951568	0.691049503	0.961496861	0.792234814	1.166921974	age1 sex bmi1 currrsmk1	1
_424_3p	3326	49	3277	98.52675887	1	0.096085329	0.099876119	0.925530744	0.336026958	1.100852995	0.905137633	1.338887338	age1 sex bmi1 currrsmk1	1
_424_5p	3791	54	3737	98.57557373	1	-0.050345058	0.087661295	0.329835903	0.56575573	0.950901252	0.800788799	1.129153145	age1 sex bmi1 currrsmk1	1
_425_3p	3630	53	3577	98.5399449	1	-0.098880987	0.092672154	1.138484378	0.285972814	0.90585051	0.75539456	1.08627357	age1 sex bmi1 currrsmk1	1
_425_5p	3784	54	3730	98.57293869	1	-0.041863074	0.081640762	0.262934842	0.608111011	0.959001083	0.817196231	1.125412775	age1 sex bmi1 currrsmk1	1
_451a	3908	55	3853	98.5926305	1	-0.004946905	0.063706122	0.006029826	0.938104912	0.995065311	0.878263506	1.127400792	age1 sex bmi1 currrsmk1	1
_484	3654	52	3602	98.57690203	1	0.011881008	0.092694158	0.016428648	0.898011047	1.011951867	0.843836771	1.213560036	age1 sex bmi1 currrsmk1	1
_486_5p	3893	55	3838	98.58720781	1	-0.02863866	0.079784427	0.128845456	0.719632126	0.97176754	0.83109326	1.13625293	age1 sex bmi1 currrsmk1	1
_532_5p	3799	54	3745	98.57857331	1	0.034652719	0.088804842	0.152265444	0.696379751	1.035260121	0.869878639	1.232083959	age1 sex bmi1 currrsmk1	1
_652_3p	3793	54	3739	98.57632481	1	-0.026834	0.087169149	0.094764399	0.758205401	0.973522833	0.82063045	1.15490073	age1 sex bmi1 currrsmk1	1
_660_5p	3834	54	3780	98.5915493	1	-0.052222674	0.091286658	0.32726804	0.567272211	0.949117499	0.793627369	1.135071777	age1 sex bmi1 currrsmk1	1
_7b_3p	3357	50	3307	98.51057492	1	-0.142698941	0.120178934	1.409888632	0.235074882	0.867015052	0.685062418	1.09729432	age1 sex bmi1 currrsmk1	1
_7b_5p	3013	41	2972	98.63923	1	-0.036060965	0.093614425	0.14838471	0.700083791	0.964581486	0.802886543	1.1588405	age1 sex bmi1 currrsmk1	1

## miRNA and breast cancer

_7g_5p	3879	55	3824	98.58210879	1	-0.081893834	0.082817347	0.977821944	0.322737125	0.921369771	0.783320884	1.083747762	age1 sex bmi1 currrsmk1	1
_7i_3p	3450	51	3399	98.52173913	1	-0.026390119	0.100226851	0.069328934	0.792316368	0.973955057	0.800249971	1.185365183	age1 sex bmi1 currrsmk1	1
_7i_5p	2976	41	2935	98.62231183	1	-0.015596622	0.096122786	0.026327426	0.871103252	0.984524375	0.81546741	1.188629041	age1 sex bmi1 currrsmk1	1
_92a_3p	3825	54	3771	98.58823529	1	-0.017525916	0.0861184	0.041416133	0.83873679	0.98262677	0.8300122	1.163302621	age1 sex bmi1 currrsmk1	1
_93_3p	3252	45	3207	98.61623616	1	-0.038657839	0.106334514	0.1321681	0.716194586	0.962079839	0.781086283	1.185013277	age1 sex bmi1 currrsmk1	1
_99b_5p	3061	48	3013	98.431885	1	-0.016292159	0.104620193	0.024250811	0.876248436	0.98383984	0.801440961	1.207750636	age1 sex bmi1 currrsmk1	1
_1_5p	3703	53	3650	98.56872806	1	-0.041103156	0.090001422	0.208569885	0.64789063	0.959730123	0.804525431	1.144876063	age1 sex bmi1 currrsmk1	2
_106a_5p	2629	40	2589	98.47850894	1	-0.058693512	0.100138333	0.34354171	0.557791979	0.942995742	0.774946691	1.147486634	age1 sex bmi1 currrsmk1	2
_122_5p	3893	54	3839	98.61289494	1	-0.065615821	0.066538991	0.972444225	0.324071352	0.936490576	0.8219877	1.0669437	age1 sex bmi1 currrsmk1	2
_127_3p	2344	32	2312	98.63481229	1	-0.085893907	0.107479181	0.638669269	0.424193085	0.917691587	0.74337903	1.132878135	age1 sex bmi1 currrsmk1	2
_128_3p	3794	54	3740	98.57670005	1	-0.001116191	0.081791769	0.000186233	0.989111816	0.998884432	0.850930253	1.172563914	age1 sex bmi1 currrsmk1	2
_133a_3p	3171	41	3130	98.70703248	1	0.040111946	0.094546391	0.179993801	0.671378568	1.040927295	0.864853133	1.252848134	age1 sex bmi1 currrsmk1	2
_134_5p	3063	51	3012	98.33496572	1	-0.125807484	0.04127113	9.292236244	0.002301271	0.881784588	0.813265698	0.956076301	age1 sex bmi1 currrsmk1	2
_139_5p	2088	28	2060	98.65900383	1	-0.069594855	0.090451695	0.591998833	0.441647222	0.932771651	0.781236842	1.113699337	age1 sex bmi1 currrsmk1	2
_142_3p	3779	54	3725	98.57105054	1	-0.037386006	0.091573719	0.16667729	0.683081847	0.963304223	0.805036874	1.152686362	age1 sex bmi1 currrsmk1	2
_148b_3p	3751	54	3697	98.5603839	1	-0.012177178	0.084806586	0.020617412	0.885826096	0.987896664	0.83661187	1.166538335	age1 sex bmi1 currrsmk1	2
_151b	3129	47	3082	98.49792266	1	0.020205948	0.109681511	0.03393842	0.853837865	1.02041147	0.823027337	1.265133638	age1 sex bmi1 currrsmk1	2
_152_3p	3347	50	3297	98.50612489	1	-0.040630488	0.110879867	0.13427609	0.714039	0.960183864	0.772633065	1.193261193	age1 sex bmi1 currrsmk1	2
_154_5p	3626	52	3574	98.56591285	1	0.03587452	0.066094626	0.294604852	0.587284632	1.036525775	0.91058451	1.179885744	age1 sex bmi1 currrsmk1	2
_155_5p	3265	49	3216	98.4992343	1	-0.073879222	0.097519305	0.573935942	0.448699103	0.928783864	0.767195556	1.124406235	age1 sex bmi1 currrsmk1	2
_16_2_3p	3853	54	3799	98.59849468	1	-0.08643265	0.081596347	1.122055216	0.289476343	0.91719732	0.781641916	1.076261273	age1 sex bmi1 currrsmk1	2
_17_5p	3869	55	3814	98.57844404	1	-0.005585136	0.062062046	0.008098701	0.92829295	0.994430432	0.88053596	1.123056784	age1 sex bmi1 currrsmk1	2
_181b_5p	3811	53	3758	98.6092889	1	-0.114375848	0.098837634	1.339133809	0.247186781	0.891922666	0.734846203	1.082574883	age1 sex bmi1 currrsmk1	2
_186_5p	3873	55	3818	98.57991221	1	0.003426881	0.066901794	0.002623751	0.959148175	1.00343276	0.880118937	1.144024132	age1 sex bmi1 currrsmk1	2
_193a_5p	3789	55	3734	98.54842966	1	-0.039485993	0.093374474	0.178825644	0.672384412	0.961283419	0.80051773	1.154335221	age1 sex bmi1 currrsmk1	2
_193b_3p	2425	29	2396	98.80412371	1	0.004222577	0.107712239	0.001536827	0.968729032	1.004231504	0.813109466	1.240276932	age1 sex bmi1 currrsmk1	2
_195_5p	3762	53	3709	98.59117491	1	0.037174039	0.092762071	0.160597444	0.68860706	1.037873636	0.865336977	1.244811805	age1 sex bmi1 currrsmk1	2
_200a_3p	3466	48	3418	98.61511829	1	-0.152823661	0.092764986	2.714019951	0.099470046	0.858281057	0.715595874	1.02941674	age1 sex bmi1 currrsmk1	2
_204_5p	3711	53	3658	98.57181353	1	-0.052390115	0.067994384	0.59368027	0.4409995	0.948958592	0.830558711	1.084236908	age1 sex bmi1 currrsmk1	2
_205_5p	3387	49	3338	98.553292	1	-0.124777447	0.064505851	3.741743184	0.053069053	0.882693327	0.777861655	1.001653062	age1 sex bmi1 currrsmk1	2
_210_3p	3697	53	3644	98.56640519	1	-0.064338248	0.078043103	0.67962509	0.409715853	0.937687775	0.804688592	1.092669105	age1 sex bmi1 currrsmk1	2
_28_3p	3736	53	3683	98.58137045	1	0.03346126	0.078577644	0.181337067	0.670226696	1.034027385	0.886434456	1.206194802	age1 sex bmi1 currrsmk1	2
_28_5p	2682	37	2645	98.62043251	1	0.022477636	0.118839534	0.03577498	0.849980936	1.022732162	0.810224775	1.290976415	age1 sex bmi1 currrsmk1	2
_301a_3p	3124	47	3077	98.49551857	1	0.003152241	0.090823901	0.001204588	0.972313244	1.003157214	0.839575112	1.198611514	age1 sex bmi1 currrsmk1	2
_301b_3p	2133	23	2110	98.92170652	1	-0.133956706	0.134278604	0.995211269	0.318472022	0.87462793	0.672241295	1.137945589	age1 sex bmi1 currrsmk1	2
_31_5p	2792	43	2749	98.45988539	1	-0.067213284	0.056320607	1.424215107	0.232710861	0.93499576	0.837277565	1.044118591	age1 sex bmi1 currrsmk1	2
_324_5p	3701	53	3648	98.56795461	1	-0.011892145	0.082897631	0.020579563	0.885930227	0.988178287	0.839987292	1.162513215	age1 sex bmi1 currrsmk1	2
_335_5p	3739	53	3686	98.58250869	1	-0.103099983	0.091292107	1.275412669	0.258753717	0.90203678	0.75425164	1.078778367	age1 sex bmi1 currrsmk1	2
_338_3p	3517	50	3467	98.57833381	1	-0.056729803	0.099841786	0.322847831	0.569901208	0.94484933	0.776921388	1.149074115	age1 sex bmi1 currrsmk1	2
_339_3p	2878	42	2836	98.54065323	1	-0.038100247	0.107430128	0.125777624	0.722850755	0.962616437	0.779845521	1.188223026	age1 sex bmi1 currrsmk1	2
_339_5p	3438	49	3389	98.57475276	1	-0.11795424	0.078311763	2.268679324	0.132012357	0.888736721	0.762279133	1.036172872	age1 sex bmi1 currrsmk1	2
_342_3p	3880	54	3826	98.60824742	1	-0.047135095	0.083861845	0.315907511	0.574077523	0.953958514	0.809368236	1.124379244	age1 sex bmi1 currrsmk1	2



## miRNA and breast cancer

_34a_5p	3236	50	3186	98.45488257	1	-0.03937685	0.097964804	0.161562954	0.687721601	0.961388342	0.79343446	1.164894633	age1 sex bmi1 currrsmk1	2
_365a_3p	2963	41	2922	98.6162673	1	-0.096440783	0.125688726	0.588747135	0.442904003	0.908063669	0.709789977	1.161723402	age1 sex bmi1 currrsmk1	2
_374b_5p	3650	53	3597	98.54794521	1	-0.059634972	0.097421606	0.374706717	0.540449816	0.942108366	0.778350913	1.140318793	age1 sex bmi1 currrsmk1	2
_375_3p	3734	54	3680	98.55382967	1	-0.119194442	0.078942239	2.279781017	0.131070379	0.88763519	0.760394131	1.036168217	age1 sex bmi1 currrsmk1	2
_376a_3p	3825	54	3771	98.58823529	1	0.000557932	0.067494595	6.83321E-05	0.993404502	1.000558088	0.876578478	1.142072858	age1 sex bmi1 currrsmk1	2
_378a_3p	3540	51	3489	98.55932203	1	-0.061857241	0.103545223	0.356878963	0.55024471	0.940017073	0.767357758	1.151525595	age1 sex bmi1 currrsmk1	2
_382_5p	3734	51	3683	98.63417247	1	-0.057837633	0.071936723	0.646427336	0.421392903	0.943803178	0.819688393	1.086711055	age1 sex bmi1 currrsmk1	2
_421	3323	50	3273	98.49533554	1	-0.041514508	0.102765784	0.163193447	0.686233245	0.959335417	0.784325047	1.173396726	age1 sex bmi1 currrsmk1	2
_431_5p	2644	36	2608	98.63842663	1	-0.136763887	0.059596248	5.266293208	0.021742263	0.872176134	0.776025122	0.980240443	age1 sex bmi1 currrsmk1	2
_483_3p	3007	43	2964	98.57000333	1	0.001929638	0.109773787	0.000308997	0.985975258	1.001931501	0.807975913	1.24244636	age1 sex bmi1 currrsmk1	2
_485_3p	3509	49	3460	98.60359077	1	-0.079404989	0.054600553	2.114956829	0.145866167	0.923665774	0.829924865	1.027994819	age1 sex bmi1 currrsmk1	2
_494_3p	3315	48	3267	98.5520362	1	0.06063275	0.084513344	0.514711608	0.473106319	1.062508636	0.900315195	1.253921525	age1 sex bmi1 currrsmk1	2
_495_3p	3671	51	3620	98.61073277	1	-0.060078109	0.071938314	0.69744826	0.403642446	0.941690976	0.817851406	1.084282411	age1 sex bmi1 currrsmk1	2
_499a_5p	3394	51	3343	98.49734826	1	0.015078748	0.094283888	0.025577353	0.872936836	1.015193006	0.843905906	1.22124615	age1 sex bmi1 currrsmk1	2
_500a_5p	2903	39	2864	98.65656218	1	0.035332157	0.099136009	0.127021556	0.721540403	1.035963754	0.853021223	1.258140912	age1 sex bmi1 currrsmk1	2
_502_3p	2367	32	2335	98.64807774	1	-0.025857528	0.144413566	0.032059594	0.857896926	0.974473915	0.734252051	1.293288061	age1 sex bmi1 currrsmk1	2
_505_3p	3466	49	3417	98.58626659	1	-0.163432276	0.058211864	7.882294348	0.004992111	0.84922401	0.757656295	0.951858281	age1 sex bmi1 currrsmk1	2
_532_3p	2436	34	2402	98.60426929	1	0.015974601	0.104121045	0.023538727	0.878064425	1.016102877	0.828532763	1.246136667	age1 sex bmi1 currrsmk1	2
_543	3747	54	3693	98.55884708	1	-0.109248065	0.055479559	3.877586649	0.048934851	0.896507998	0.804136698	0.999490002	age1 sex bmi1 currrsmk1	2
_584_5p	3773	53	3720	98.59528227	1	-0.120150701	0.083013629	2.094854251	0.147795805	0.886786787	0.75362949	1.043471383	age1 sex bmi1 currrsmk1	2
_590_3p	3402	52	3350	98.47148736	1	-0.00284303	0.085512403	0.001105363	0.973477624	0.997161007	0.843290093	1.179107975	age1 sex bmi1 currrsmk1	2
_590_5p	3431	52	3379	98.48440688	1	-0.015636957	0.091962747	0.028912164	0.864982005	0.984484666	0.822110365	1.178929373	age1 sex bmi1 currrsmk1	2
_625_3p	3617	53	3564	98.53469726	1	-0.060674565	0.075376949	0.647942148	0.420849378	0.941129466	0.811873555	1.090963816	age1 sex bmi1 currrsmk1	2
_629_5p	3553	50	3503	98.59273853	1	0.033577847	0.100187865	0.112324744	0.737512813	1.034147945	0.849772375	1.258527583	age1 sex bmi1 currrsmk1	2
_656_3p	2774	39	2735	98.59408796	1	0.060564981	0.094290805	0.412576495	0.520664667	1.062436633	0.883166441	1.278096118	age1 sex bmi1 currrsmk1	2
_7_5p	2757	36	2721	98.69423286	1	0.006578511	0.119225966	0.003044483	0.955997588	1.006600197	0.796841024	1.271576043	age1 sex bmi1 currrsmk1	2
_7a_5p	2614	33	2581	98.73756695	1	-0.138237408	0.061509586	5.050862605	0.024613682	0.870891911	0.77198205	0.982474554	age1 sex bmi1 currrsmk1	2
_885_5p	2955	39	2916	98.68020305	1	-0.116249365	0.063306618	3.371964173	0.066314649	0.890253197	0.786369845	1.007860056	age1 sex bmi1 currrsmk1	2
_92b_3p	3910	54	3856	98.61892583	1	-0.061409903	0.08246052	0.554606148	0.456441708	0.940437673	0.800091204	1.105402749	age1 sex bmi1 currrsmk1	2
_95_3p	2997	48	2949	98.3983984	1	0.099113075	0.095691327	1.07279501	0.300314972	1.104191149	0.915359422	1.331977432	age1 sex bmi1 currrsmk1	2
_1260a	3744	53	3691	98.58440171	1	-0.117488354	0.135141768	0.755806187	0.384644161	0.889150867	0.682248476	1.158799604	age1 sex bmi1 currrsmk1	3
_1290	3290	48	3242	98.54103343	1	0.035041286	0.10536784	0.110597144	0.739465318	1.035662466	0.842420582	1.273231882	age1 sex bmi1 currrsmk1	3
_136_3p	2461	38	2423	98.45591223	1	0.077561258	0.122289973	0.402261061	0.525923855	1.080648429	0.850336875	1.373339275	age1 sex bmi1 currrsmk1	3
_30a_3p	2640	39	2601	98.52272727	1	0.033994231	0.122869265	0.076546252	0.78203356	1.034578639	0.813161857	1.316285251	age1 sex bmi1 currrsmk1	3
_30b_5p	2752	40	2712	98.54651163	1	-0.018702199	0.124502639	0.022564632	0.880594767	0.981471601	0.768954955	1.252721631	age1 sex bmi1 currrsmk1	3
_3135b	3570	53	3517	98.51540616	1	-0.057388978	0.113822631	0.254214164	0.614123263	0.944226715	0.755423142	1.180218131	age1 sex bmi1 currrsmk1	3
_340_5p	3745	54	3691	98.55807744	1	0.025067011	0.089662729	0.0781594	0.779807406	1.025383831	0.860132607	1.222383609	age1 sex bmi1 currrsmk1	3
_369_3p	3672	53	3619	98.55664488	1	-0.016169646	0.073709078	0.04812371	0.826360927	0.98396038	0.85160133	1.136891167	age1 sex bmi1 currrsmk1	3
_376_3p	3791	54	3737	98.57557373	1	-0.046876726	0.070009409	0.448334054	0.503127149	0.954205019	0.831858731	1.094545484	age1 sex bmi1 currrsmk1	3
_4306	2990	43	2947	98.56187291	1	0.043243053	0.112440941	0.147905303	0.700545216	1.044191658	0.837664898	1.301637708	age1 sex bmi1 currrsmk1	3
_582_5p	2168	37	2131	98.29335793	1	0.036210178	0.140981797	0.065968291	0.797300027	1.036873752	0.786542071	1.366878157	age1 sex bmi1 currrsmk1	3
_744_5p	3055	45	3010	98.52700491	1	-0.053980934	0.105426366	0.262169588	0.608633521	0.947450171	0.770579219	1.164918289	age1 sex bmi1 currrsmk1	3