

Evidence for Correlations Between BMI-Associated SNPs and circRNAs

Luisa Sophie Rajcsanyi^{1,2*}, Inga Diebels¹, Lydia Pastoors¹, Deniz Kanber³, Triinu Peters^{1,2}, Anna-Lena Volckmar⁴, Yiran Zheng^{1,2}, Martin Grosse³, Christoph Dieterich^{5,6}, Johannes Hebebrand^{1,2}, Frank J. Kaiser³, Bernhard Horsthemke³ and Anke Hinney^{1,2*}

¹ Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Essen, University of Duisburg-Essen, Essen, Germany.

² Center for Translational Neuro- and Behavioural Sciences, University Hospital Essen, Essen, Germany.

³ Institute of Human Genetics, University Hospital Essen, Essen, Germany

⁴ Institute of Pathology, University Hospital Heidelberg, Heidelberg, Germany

⁵ Department of Internal Medicine III, University Hospital Heidelberg, Heidelberg, Germany

⁶ German Center for Cardiovascular Research (DZHK), Partner site Heidelberg/Mannheim, Heidelberg, Germany

*corresponding authors

Supplementary Materials

[Supplementary Table S1:](#) Overview of circRNA Datasets

[Supplementary Table S2:](#) Overview of Analysed GWAS Data

[Supplementary Table S3:](#) Assignment of SNPs of the GWAS Studies Analysing Additional Phenotypes

[Supplementary Table S4:](#) List of Used Primers

[Supplementary Table S5:](#) Results of the Analysis of BMI-SNPs Pertaining to their Localisation on circRNA Genomic Loci.

[Supplementary Table S6:](#) Results of the Sensitivity Analysis

[Supplementary Table S7:](#) Results When Considering the Linkage Disequilibrium of SNPs

[Supplementary Table S8:](#) CircRNA Location of SNPs Extracted from GWAS Pertaining Various Phenotypes

[Supplementary Table S9:](#) Gender-Separated Analysis of BMI-SNPs on the Genomic Loci of circRNAs

[Supplementary Table S10:](#) Enrichment Analysis of Significant BMI-SNPs between Females and Males on circRNAs

[Supplementary Table S11:](#) Descriptive Statistics of the Normalised Primer Extension Assay Data

[Supplementary Figure S1:](#) Significant Enrichment of BMI-SNPs Significant in Females

[Supplementary Figure S2:](#) 20 circRNAs with the Highest Numbers of miRNA Target Sites

[Supplementary Figure S3:](#) 20 miRNAs with the Highest Numbers of Linked circRNAs

[Supplementary Figure S4:](#) Exemplary SNaPshot Output for One Homozygous G/G Carrier of rs4752856

[Supplementary Figure S5:](#) Exemplary SNaPshot Output for the Homozygous A/A Carrier of rs4752856

[Supplementary Figure S6:](#) Exemplary SNaPshot Output for One Heterozygous (G/A) Carrier of the SNP rs4752856

Supplementary Table S1: Overview of circRNA Datasets.

CircRNA database	Genome version	n circRNAs
circAtlas v2.0 ¹	GRCh38	564,515
	GRCh37*	564,456*
circBase ²	GRCh37	89,374
CIRCpediaV2 ³	GRCh38	179,076
circVAR ⁴	GRCh38	286,445

The number of circRNAs reported refers to the total number of circRNAs that remained in the study following the data processing (e.g. removal of inconclusive data). *The circAtlas v2.0 dataset based on the GRCh37 genome version was exclusively used to verify the deviations between BMI-SNPs significant for females and males.

Supplementary Table S2: Overview of Analysed GWAS Data.

GWAS study	Authors	Source	n SNPs	Link to source
Body mass index	Yengo et al. 2018	GIANT consortium	2,324,569	https://portals.broadinstitute.org/collaboration/giant/index.php/Main_Page
Amyotrophic lateral sclerosis (ALS)	Iacoangeli et al. 2020	NHGRI-EBI GWAS catalog	10,815,403	https://www.ebi.ac.uk/gwas/studies/GCST90013429
Anorexia nervosa	Watson et al. 2018	PGC website	8,219,102	https://www.med.unc.edu/pgc/
Autism spectrum disorder	Grove et al. 2019	PGC website	9,112,386	https://www.med.unc.edu/pgc/
Body mass index (female)	Pulit et al. 2019	GIANT consortium	27,380,251	https://portals.broadinstitute.org/collaboration/giant/index.php/Main_Page
Body mass index (male)	Pulit et al. 2019	GIANT consortium	27,380,253	https://portals.broadinstitute.org/collaboration/giant/index.php/Main_Page
Body height	Yengo et al. 2018	GIANT consortium website	2,334,001	https://portals.broadinstitute.org/collaboration/giant/index.php/Main_Page
Chronic Kidney Disease	Wuttke et al. 2019	NHGRI-EBI GWAS catalog	9,585,588	https://www.ebi.ac.uk/gwas/studies/GCST008064
Epilepsy	ILAE consortium et al. 2018	NHGRI-EBI GWAS catalog	4,880,491	https://www.ebi.ac.uk/gwas/studies/GCST007343
Heart failure	Shah & Henry et al. 2020	Cardiovascular Disease Knowledge Portal	8,281,262	http://www.broadcvdi.org/
Pernicious anemia	Glanville et al. 2021	NHGRI-EBI GWAS catalog	9,419,702	https://www.ebi.ac.uk/gwas/studies/GCST90014450
Ulcerative colitis	De Lange et al. 2017	NHGRI-EBI GWAS catalog	9,588,015	https://www.ebi.ac.uk/gwas/studies/GCST004133

The number of SNPs refers to the total number of SNPs included, regardless of the significance level and can deviate from the total set of SNPs included in the respective studies. All data was downloaded in the genome version GRCh37. EBI: European Bioinformatics Institute; GIANT: Genetic Investigation of Anthropometric Traits; GWAS: genome-wide association study; ILAE: International League Against Epilepsy; NHGRI: National Human Genome Research Institute; PGC: Psychiatric Genomics Consortium; SNP: single nucleotide polymorphism.

Supplementary Table S3: Assignment of SNPs of the GWAS Studies Analysing Additional Phenotypes.

Phenotype classification	GWAS	Group classification	Number of SNPs
Anthropometric	Body height ⁵	Significant ($P < 5 \times 10^{-8}$)	130,933
		Non-significant ($P \geq 5 \times 10^{-8}$)	2,203,068
Neurological	Amyotrophic lateral sclerosis ⁶	Significant ($P < 5 \times 10^{-8}$)	185
		Non-significant ($P \geq 5 \times 10^{-8}$)	10,815,218
	Epilepsy ⁷	Significant ($P < 5 \times 10^{-8}$)	118
		Non-significant ($P \geq 5 \times 10^{-8}$)	4,880,373
Peripheral	Chronic kidney disease ⁸	Significant ($P < 5 \times 10^{-8}$)	1,443
		Non-significant ($P \geq 5 \times 10^{-8}$)	9,584,145
	Heart failure ⁹	Significant ($P < 5 \times 10^{-8}$)	295
		Non-significant ($P \geq 5 \times 10^{-8}$)	8,280,967
	Pernicious anemia ¹⁰	Significant ($P < 5 \times 10^{-8}$)	150
		Non-significant ($P \geq 5 \times 10^{-8}$)	9,419,552
	Ulcerative colitis ¹¹	Significant ($P < 5 \times 10^{-8}$)	7,697
		Non-significant ($P \geq 5 \times 10^{-8}$)	9,580,318
Psychiatric	Anorexia Nervosa ¹²	Significant ($P < 5 \times 10^{-8}$)	326
		Non-significant ($P \geq 5 \times 10^{-8}$)	8,218,776
	Autism spectrum disorder ¹³	Significant ($P < 5 \times 10^{-8}$)	93
		Non-significant ($P \geq 5 \times 10^{-8}$)	9,112,293

The classification of the SNP data into significant and non-significant variants was based on the genome-wide P-value threshold of 5×10^{-8} . The sources of the SNP data can be found in Supplementary Table S2.

Supplementary Table S4: List of Used Primers.

Amplicon	Forward primer (5'-3')	Reverse primer (5'-3')
rs4752856 on gDNA	AATGGGGTCTTGCTCAGTTG	TCCTGCATGGTTTGGTACTG
rs4752856 on circRNA (divergent primers)	AATGGGGTCTTGCTCAGTTG	TCCCTTTGTGCTTGTCTCCA
rs4752856 SNaPshot- specific primer	TGTCTGGCCTGAACAATATTATTC	-
Digestion control - SHBG	CTTCCCTGTCTCTCCTCTGGC	CCCAGTGATTGTGCAGTTGG

The primer pair amplifying the SNP rs4752856 on the circRNA was ordered as high performance liquid chromatography (HPLC) purified primers.

Supplementary Table S5: Results of the Analysis of BMI-SNPs Pertaining to their Localisation on circRNA Genomic Loci.

Database	SNP classification	n SNPs on circRNAs (percentage)	n SNPs not on circRNAs (percentage)	Statistics			
				Chi-Square	P-value	OR	95% CI
circAtlas v2.0	Significant ($P < 5 \times 10^{-8}$)	25,669 (62.86%)	15,166 (37.14%)	1012	< 0.0001	1.39	[1.36, 1.42]
	Non-significant ($P \geq 5 \times 10^{-8}$)	1,255,157 (54.96%)	1,028,577 (45.04%)				
circBase	Significant ($P < 5 \times 10^{-8}$)	9,949 (24.36%)	30,886 (75.64%)	1057	< 0.0001	1.46	[1.43, 1.49]
	Non-significant ($P \geq 5 \times 10^{-8}$)	413,361 (18.10%)	1,870,373 (81.90%)				
CIRCpediaV2	Significant ($P < 5 \times 10^{-8}$)	12,913 (31.62%)	27,922 (68.38%)	1721	< 0.0001	1.56	[1.53, 1.59]
	Non-significant ($P \geq 5 \times 10^{-8}$)	522,965 (22.90%)	1,760,769 (77.10%)				
circVAR	Significant ($P < 5 \times 10^{-8}$)	15,561 (38.11%)	25,274 (61.89%)	1112	< 0.0001	1.41	[1.38, 1.44]
	Non-significant ($P \geq 5 \times 10^{-8}$)	695,130 (30.44%)	1,588,604 (69.56%)				

The total number and ratio of significant and non-significant SNPs which are either located on circRNAs or outside the genomic loci are shown. The SNPs were extracted from a BMI GWAS meta-analysis performed by Yengo et al. (2018). Results were obtained by applying a custom R script to the SNP and circRNA data of the respective database. The statistical output was generated with GraphPad Prism (version: 9.2.0) using the Chi-square test and the Woolf logit intervals to calculate the 95% confidence interval of the odds ratio. CircAtlas v2.0 results are based on the GRCh38 dataset. OR: odds ratio. P: P-value.

Supplementary Table S6: Results of the Sensitivity Analysis.

Database	SNP classification	n SNPs on circRNAs (ratio)	n SNPs not on circRNAs (ratio)	Statistics			
				Chi-Square	P-value	OR	95% CI
circAtlas v2.0	Significant ($P < 5 \times 10^{-8}$)	25,669 (62.86%)	15,166 (37.14%)	---	---	---	---
	Non-Significant ($P \geq 5 \times 10^{-7}$)	1,246,892 (54.93%)	1,022,903 (45.07%)	1019	< 0.0001	1.39	[1.36, 1.42]
	Non-Significant ($P \geq 5 \times 10^{-6}$)	1,233,915 (54.89%)	1,104,264 (45.11%)	1031	< 0.0001	1.39	[1.36, 1.42]
	Non-Significant ($P \geq 5 \times 10^{-5}$)	1,214,293 (54.82%)	1,000,755 (45.18%)	1047	< 0.0001	1.40	[1.37, 1.42]
circBase	Significant ($P < 5 \times 10^{-8}$)	9,949 (24.36%)	30,886 (75.64%)	---	---	---	---
	Non-Significant ($P \geq 5 \times 10^{-7}$)	410,164 (18.07%)	1,859,631 (81.93%)	1068	< 0.0001	1.46	[1.43, 1.49]
	Non-Significant ($P \geq 5 \times 10^{-6}$)	405,043 (18.02%)	1,843,136 (81.98%)	1089	< 0.0001	1.47	[1.43, 1.50]
	Non-Significant ($P \geq 5 \times 10^{-5}$)	397,889 (17.96%)	1,817,159 (82.04%)	1109	< 0.0001	1.47	[1.44, 1.51]
CIRCpediaV2	Significant ($P < 5 \times 10^{-8}$)	12,913 (31.62%)	27,922 (68.38%)	---	---	---	---
	Non-Significant ($P \geq 5 \times 10^{-7}$)	519,175 (22.87%)	1,750,620 (77.13%)	1732	< 0.0001	1.56	[1.53, 1.59]
	Non-Significant ($P \geq 5 \times 10^{-6}$)	512,978 (22.82%)	1,735,201 (77.18%)	1757	< 0.0001	1.56	[1.53, 1.60]
	Non-Significant ($P \geq 5 \times 10^{-5}$)	504,181 (22.76%)	1,710,867 (77.24%)	1782	< 0.0001	1.57	[1.54, 1.60]
circVAR	Significant ($P < 5 \times 10^{-8}$)	15,561 (38.11%)	25,274 (61.89%)	---	---	---	---
	Non-Significant ($P \geq 5 \times 10^{-7}$)	690,154 (30.41%)	1,579,641 (69.59%)	1121	< 0.0001	1.41	[1.38, 1.44]
	Non-Significant ($P \geq 5 \times 10^{-6}$)	682,152 (30.34%)	1,566,027 (69.66%)	1141	< 0.0001	1.41	[1.39, 1.44]
	Non-Significant ($P \geq 5 \times 10^{-5}$)	670,786 (30.28%)	1,544,262 (69.72%)	1159	< 0.0001	1.42	[1.39, 1.45]

Our sensitivity analysis led to a more distinct delimitation of significant and non-significant SNPs by defining three novel P-value cut-offs and removing all non-significant SNPs with a P-value within the range of these novel thresholds and the initial one (5×10^{-8}). The SNPs were extracted from the BMI GWAS meta-analysis performed by Yengo et al. (2018). Results were obtained by applying a custom R script to the re-defined SNP data and the circRNA data of the respective databases. The statistical output was generated with GraphPad Prism (version 9.2.0) using a two-sided Chi-square test and the Woolf logit intervals to calculate the 95% confidence intervals of the odds ratio. Results of the circAtlas v2.0 dataset are based on the GRCh38-derived data. CI: confidence interval. OR: odds ratio.

Supplementary Table S7: Results When Considering the Linkage Disequilibrium of SNPs.

Database	SNP classification	n SNPs on circRNAs (ratio)	n SNPs not on circRNAs (ratio)	Statistics			
				Chi-square	P-value	OR	95% CI
circAtlas v2.0	Significant (within 1 Mb region)	457,487 (56.77%)	348,421 (43.23%)	1386	< 0.0001	1.11	[1.10, 1.12]
	Non-significant (not within 1 Mb region)	823,339 (54.21%)	695,322 (45.79%)				
	Significant (in regions of high LD)	45,166 (58.58%)	31,938 (41.42%)	390	< 0.0001	1.16	[1.14, 1.18]
	Non-significant (not within regions of high LD)	1,235,660 (54.50%)	1,011,805 (45.50%)				
circBase	Significant (within 1 Mb region)	161,311 (20.02%)	644,597 (79.98%)	2701	< 0.0001	1.20	[1.19, 1.21]
	Non-significant (not within 1 Mb region)	261,999 (17.25%)	1,256,662 (82.75%)				
	Significant (in regions of high LD)	16,588 (21.51%)	60,516 (78.49%)	584.3	< 0.0001	1.24	[1.22, 1.26]
	Non-significant (not within regions of high LD)	406,722 (18.10%)	1,840,743 (81.90%)				
CIRCpediaV2	Significant (within 1 Mb region)	205,663 (25.52%)	600,245 (74.48%)	4231	< 0.0001	1.23	[1.23, 1.24]
	Non-significant (not within 1 Mb region)	330,215 (21.74%)	1,188,446 (78.26%)				
	Significant (in regions of high LD)	21,030 (27.27%)	56,074 (72.73%)	801.4	< 0.0001	1.26	[1.24, 1.28]
	Non-significant (not within regions of high LD)	514,848 (22.91%)	1,732,617 (77.09%)				
circVAR	Significant (within 1 Mb region)	262,084 (32.52%)	543,824 (67.48%)	2204	< 0.0001	1.15	[1.14, 1.16]
	Non-significant (not within 1 Mb region)	448,607 (29.54%)	1,070,054 (70.46%)				
	Significant (in regions of high LD)	26,314 (34.13%)	50,790 (65.87%)	474.8	< 0.0001	1.18	[1.17, 1.20]
	Non-significant (not within regions of high LD)	684,377 (30.45%)	1,563,088 (69.55%)				

To correct for the linkage disequilibrium of the SNPs, we re-defined all non-significant SNPs within a 1 Mb region surrounding a significant SNP ($P < 5 \times 10^{-8}$) and non-significant SNPs within regions of high LD (as stated in plinkQC¹⁴) as significant as well. The data displayed is based on the SNP data extracted from the BMI GWAS meta-analysis conducted by Yengo et al. (2018). The two-sided Chi-square test and odds ratio using the Woolf logit intervals were calculated with GraphPad Prism (version 9.2.0). The significant level was set to 95%. Results of the circAtlas v2.0 dataset are based on the GRCh38 data. CI: confidence interval. LD: linkage disequilibrium. OR: odds ratio.

Supplementary Table S8: CircRNA Location of SNPs Extracted from GWAS Pertaining Various Phenotypes.

Phenotype classification	GWAS	SNP classification	n SNPs on circRNAs (ratio)	n SNPs not on circRNAs (ratio)	Statistics			
					Chi-Square	P-value*	OR	95% CI
Anthropometric	Body height ⁵	Significant	41,529 (31.72%)	89,404 (68.28%)	16,787	< 0.0001	2.19	[2.17, 2.22]
		Non-significant	384,987 (17.48%)	1,818,081 (82.52%)				
Neurological	Amyotrophic lateral sclerosis ⁶	Significant	18 (9.73%)	167 (90.27%)	9.08	0.003	0.48	[0.30, 0.78]
		Non-significant	1,978,337 (18.29%)	8,836,881 (81.71%)				
	Epilepsy ⁷	Significant	10 (8.47%)	108 (91.53%)	7.05	0.008	0.43	[0.22, 0.82]
		Non-significant	870,094 (17.83%)	4,010,279 (82.17%)				
Peripheral	Chronic kidney disease ⁸	Significant	450 (31.19%)	993 (68.81%)	162.7	<0.0001	2.03	[1.82, 2.27]
		Non-significant	1,746,337 (18.22%)	7,837,808 (81.78%)				
	Heart failure ⁹	Significant	59 (20%)	236 (80%)	0.78	0.38	1.14	[0.85, 1.51]
		Non-significant	1,492,677 (18.03%)	6,788,290 (81.97%)				
	Pernicious anemia ¹⁰	Significant	13 (8.67%)	137 (91.33%)	8.99	0.003	0.43	[0.24, 0.76]
		Non-significant	1,704,296 (18.09%)	7,715,256 (81.91%)				
	Ulcerative colitis ¹¹	Significant	1,096 (14.24%)	6,601 (85.76%)	88.75	< 0.0001	0.74	[0.69, 0.78]
		Non-significant	1,762,928 (18.40%)	7,817,390 (81.60%)				
Psychiatric	Anorexia nervosa ¹²	Significant	168 (51.53%)	158 (48.47%)	244.7	< 0.0001	4.83	[3.88, 6.00]
		Non-significant	1,483,926 (18.06%)	6,734,850 (81.94%)				
	Autism spectrum disorder ¹³	Significant	40 (43.01%)	53 (56.99%)	36.80	< 0.0001	3.40	[2.26, 5.12]
		Non-significant	1,655,688 (18.17%)	7,456,605 (81.83%)				

To explore whether the detected enrichment of BMI-associated SNPs on circRNA genomic loci can be detected in further phenotypes and traits, we analysed additional GWAS studies pertaining anthropometric traits, neurological, peripheral and psychiatric disorders. The SNPs were classified based on their P-value into sets of significant ($P < 5 \times 10^{-8}$) and non-significant ($P \geq 5 \times 10^{-8}$) variants. The custom R script was applied for those SNPs and the circRNA data extracted exclusively from circBase. The two-sided Chi-square test and the odds ratio applying the Woolf logit intervals were computed with GraphPad Prism (version 9.2.0). The significance level was set to 95%. The Bonferroni correction was performed based on the total number of GWAS studies investigated ($n = 10$; as stated in Table 1). Thus, the corrected P-value threshold is 0.005 (*). CI: confidence interval. OR: odds ratio.

Supplementary Table S9: Gender-Separated Analysis of BMI-SNPs on the Genomic Loci of circRNAs.

GWAS	Gender	SNP classification	Number of SNPs on circRNAs (ratio)	Number of SNPs not on circRNAs (ratio)	Statistics			
					Chi-Square	P-value	OR	95% CI
BMI (Pulit et al. 2019)	Female	Significant ($P < 5 \times 10^{-8}$)	7,109 (25.71%)	20,544 (74.29%)	715.5	< 0.0001	1.44	[1.40,1.48]
		Non-significant ($P \geq 5 \times 10^{-8}$)	5,292,550 (19.35%)	22,060,048 (80.65%)				
	Male	Significant ($P < 5 \times 10^{-8}$)	5,372 (23.52%)	17,461 (76.48%)	254.8	< 0.0001	1.28	[1.24, 1.32]
		Non-significant ($P \geq 5 \times 10^{-8}$)	5,294,287 (19,35%)	22,063,133 (80.65%)				

An additional BMI GWAS¹⁵ was analysed to investigate whether deviations of circRNA genomic loci localisation of genome-wide significant BMI-SNPs between males and females are present. Therefore, the respective SNP data was grouped based on the P-value of 5×10^{-8} . The two-sided Chi-square test and the odds ratio based on the Woolf logit intervals (confidence level: 95%) were computed with GraphPad Prism (version 9.2.0). CI: confidence interval. OR: odds ratio.

Supplementary Table S10: Enrichment Analysis of Significant BMI-SNPs between Females and Males on circRNAs.

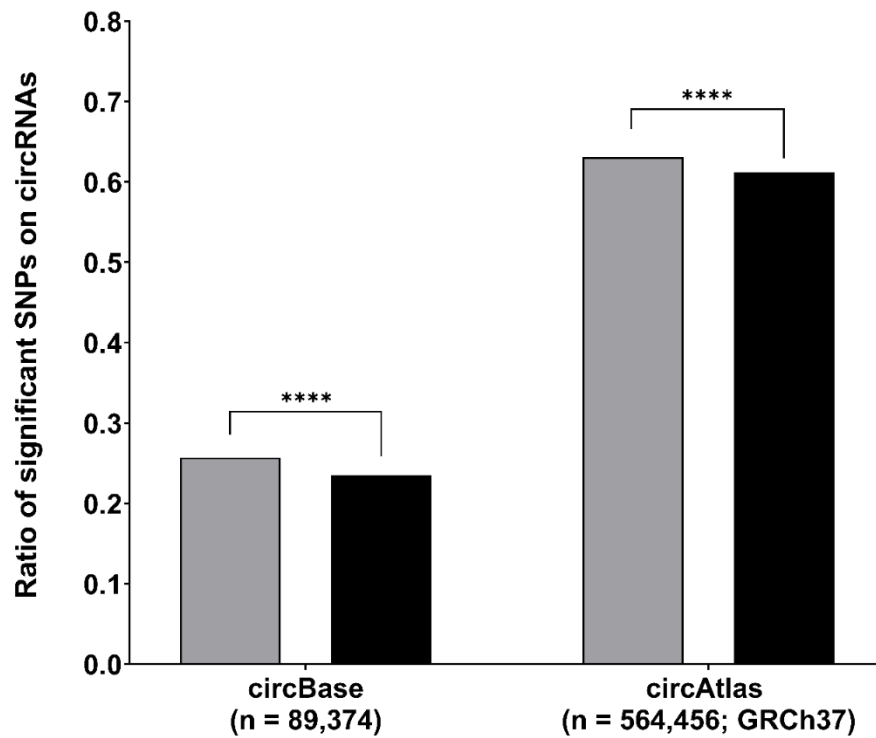
GWAS	Database	Gender	SNP classification	Number of SNPs on circRNAs (ratio)	Number of SNPs not on circRNAs (ratio)	Statistics			
						Chi-Square	P-value	OR	95% CI
BMI (Pulit et al. 2019)	circBase (hg19)	Female	Significant ($P < 5 \times 10^{-8}$)	7,109 (25.71%)	20,544 (74.29%)	31.95	< 0.0001	1.13	[1.08, 1.17]
		Male	Significant ($P < 5 \times 10^{-8}$)	5,372 (23.52%)	17,461 (76.48%)				
	circAtlas v2.0 (hg19)	Female	Significant ($P < 5 \times 10^{-8}$)	17,439 (63.06%)	10,214 (36.94%)	18.98	< 0.0001	1.08	[1.05, 1.12]
		Male	Significant ($P < 5 \times 10^{-8}$)	13,968 (61.17%)	8,865 (38.83%)				

It was analysed whether deviations of circRNA-located and significant BMI-SNPs between females and males are present. Therefore, significant SNPs ($P < 5 \times 10^{-8}$) in females and males extracted from a gender-specific GWAS for BMI¹⁵ were investigated. For the analysis of the circAtlas v2.0 data, an additional dataset based on the older genome version, GRCh37, was downloaded from the circAtlas v2.0 website. This contained marginally less (564,456 circRNAs in total) than the GRCh38 dataset (see Supplementary Table S1). The two-sided Chi-square test and the odds ratio based on the Woolf logit intervals (confidence level 95%) were calculated with GraphPad Prism (version 9.2.0). CI: confidence interval. OR: odds ratio.

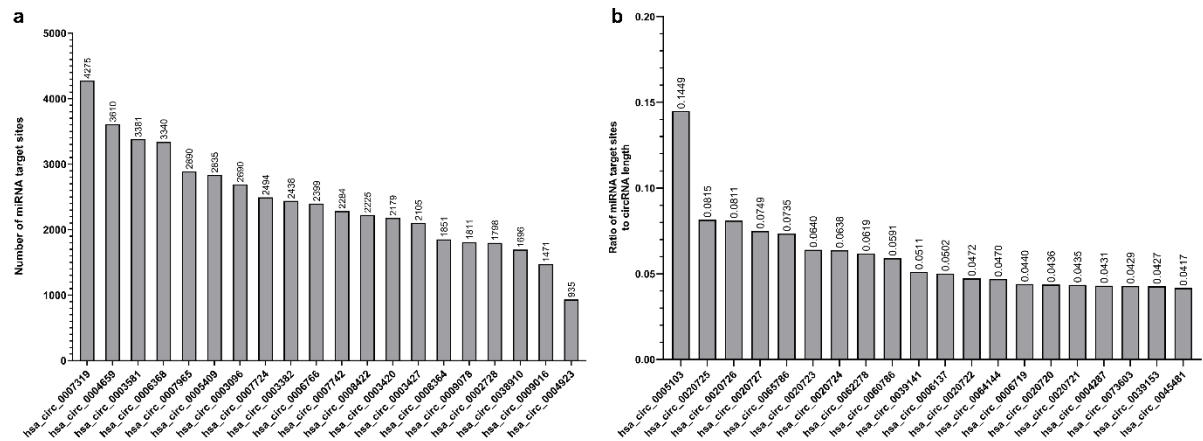
Supplementary Table S11: Descriptive Statistics of the Normalised Primer Extension Assay Data.

Subject	Mean	Standard error	95% CI	Median	Variance	Standard deviation
Subject 1	1.17	0.08	[0.82, 1.52]	1.18	0.02	0.14
Subject 2	1.21	0.11	[0.74, 1.68]	1.17	0.04	0.19
Subject 3	1.34	0.08	[1.01, 1.67]	1.41	0.02	0.13
Subject 6	1.30	0.11	[0.81, 1.79]	1.33	0.04	0.20
Subject 7	1.29	0.03	[1.17, 1.40]	1.29	0.002	0.05
Subject 8	1.22	0.07	[0.92, 1.51]	1.28	0.01	0.12
Subject 9	1.22	0.07	[0.94, 1.51]	1.19	0.01	0.11
Subject 10	2.16	0.17	[1.41, 2.91]	2.19	0.09	0.30
All	1.36	0.12	[1.09, 1.64]	1.255	0.11	0.33

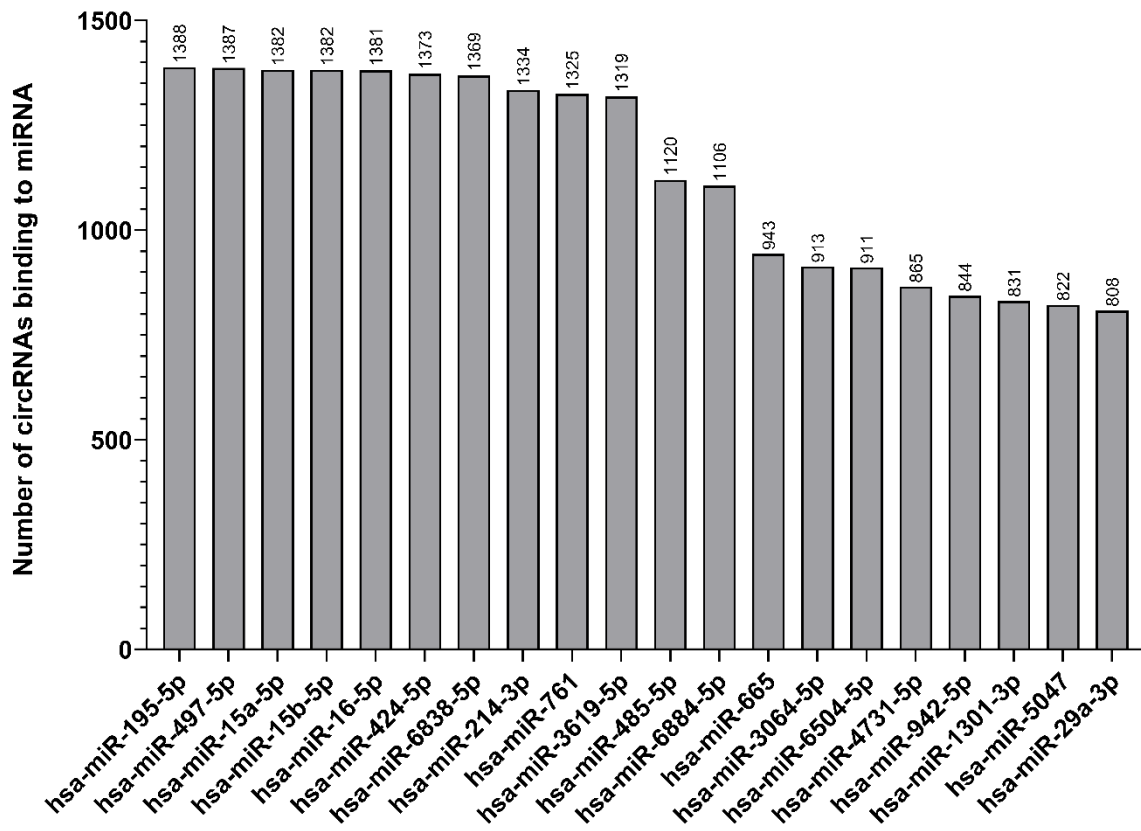
The data is based on the A/G circRNA/DNA normalised data produced in the primer extension assay (see Equation (1) and see Table 2). The descriptive statistics were calculated with SPSS. The confidence intervals were computed based on the t-test.



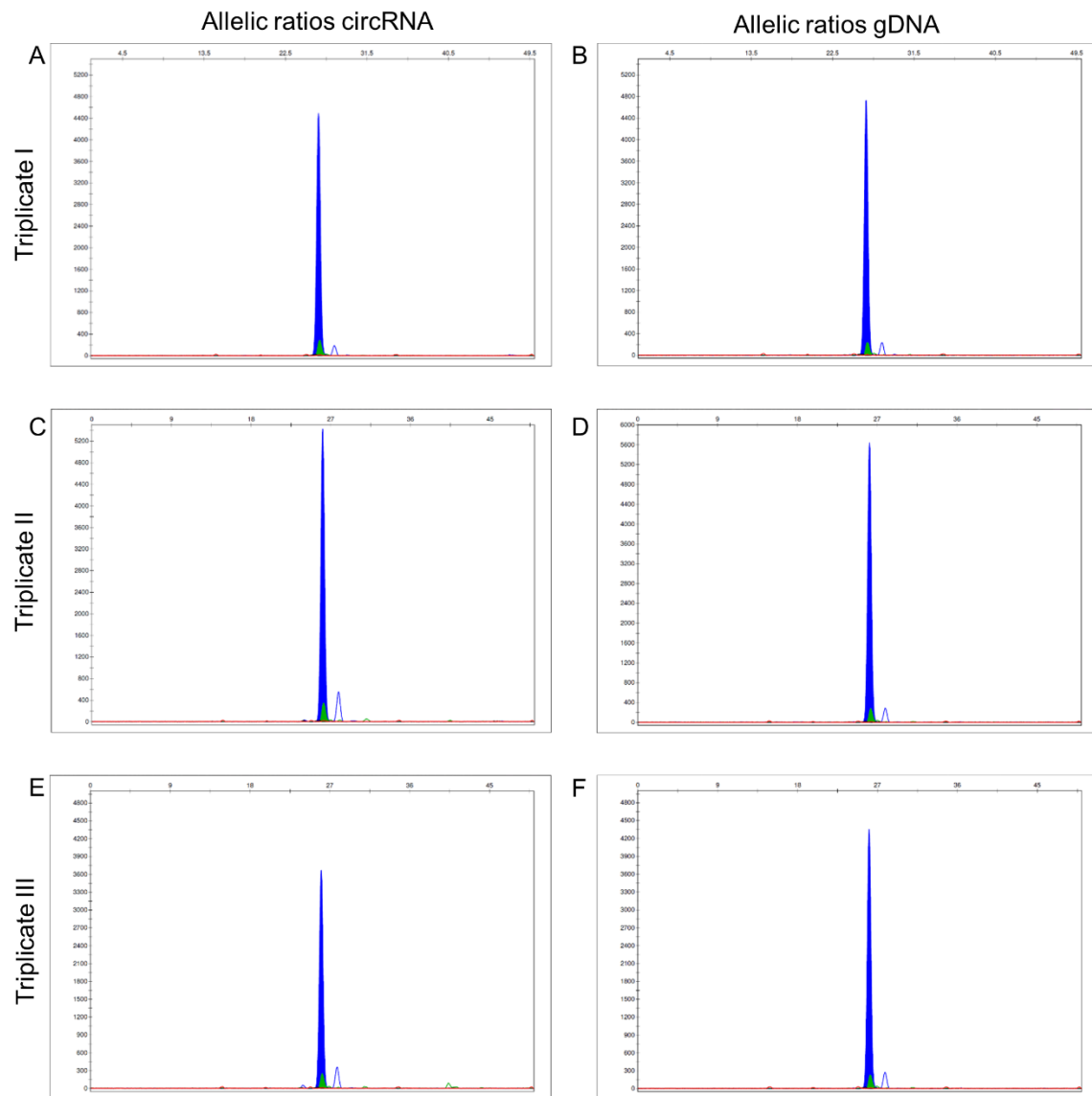
Supplementary Figure S1: Significant Enrichment of BMI-SNPs Significant in Females. Here, SNPs classified as significant ($P < 5 \times 10^{-8}$) in females (grey) and males (black) were analysed regarding their circRNA localisation using a custom R script. The numbers shown in the parentheses represent the number of circRNAs included in the corresponding dataset. For this analysis, an alternative circAtlas v2.0 dataset based on the older genome version GRCh37 was used. This contained marginally less circRNAs than the GRCh38 dataset (see Supplementary Table S1). The results of the statistical test can be found in Supplementary Table S10. **** $P < 0.0001$.



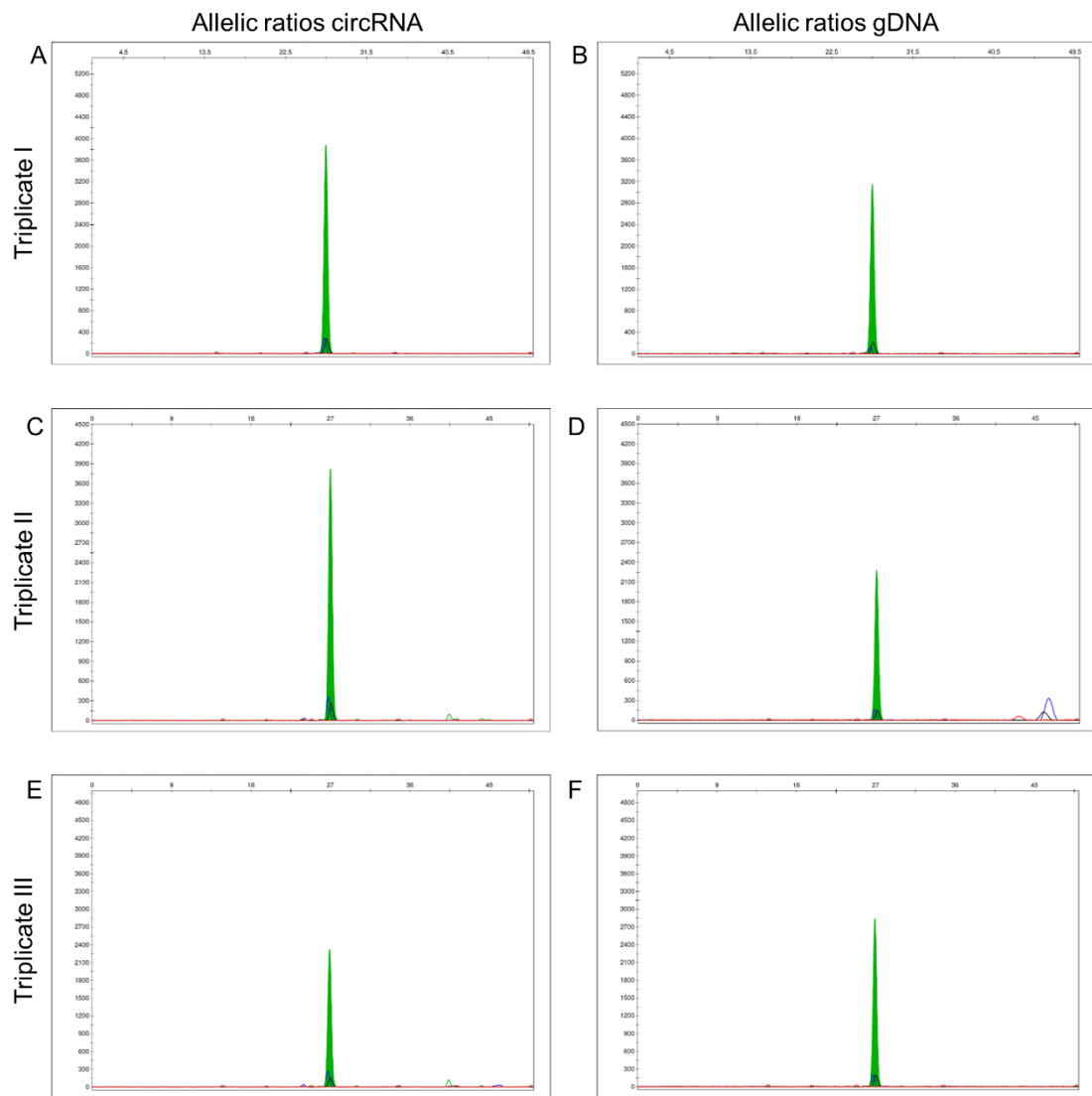
Supplementary Figure S2: 20 circRNAs with the Highest Numbers of miRNA Target Sites. Correlations of miRNAs and circRNAs were investigated for circBase-derived circRNAs containing at least one significant SNP for BMI ($P < 5 \times 10^{-8}$; 9,949 SNPs; see Supplementary Table S5). An additional dataset from the Encyclopedia of RNA Interactions (ENCORI¹⁶) database was downloaded. This included data regarding already known miRNA-circRNA interactions of circBase circRNAs supported by Ago CLIP-sequencing data. Here, the 20 circRNAs with the highest raw numbers of miRNAs linked (a) and the highest ratio of miRNAs normalised on the total length of the circRNA (b) are represented. The length of the circRNAs was calculated with the start and stop position stated in the circBase dataset.



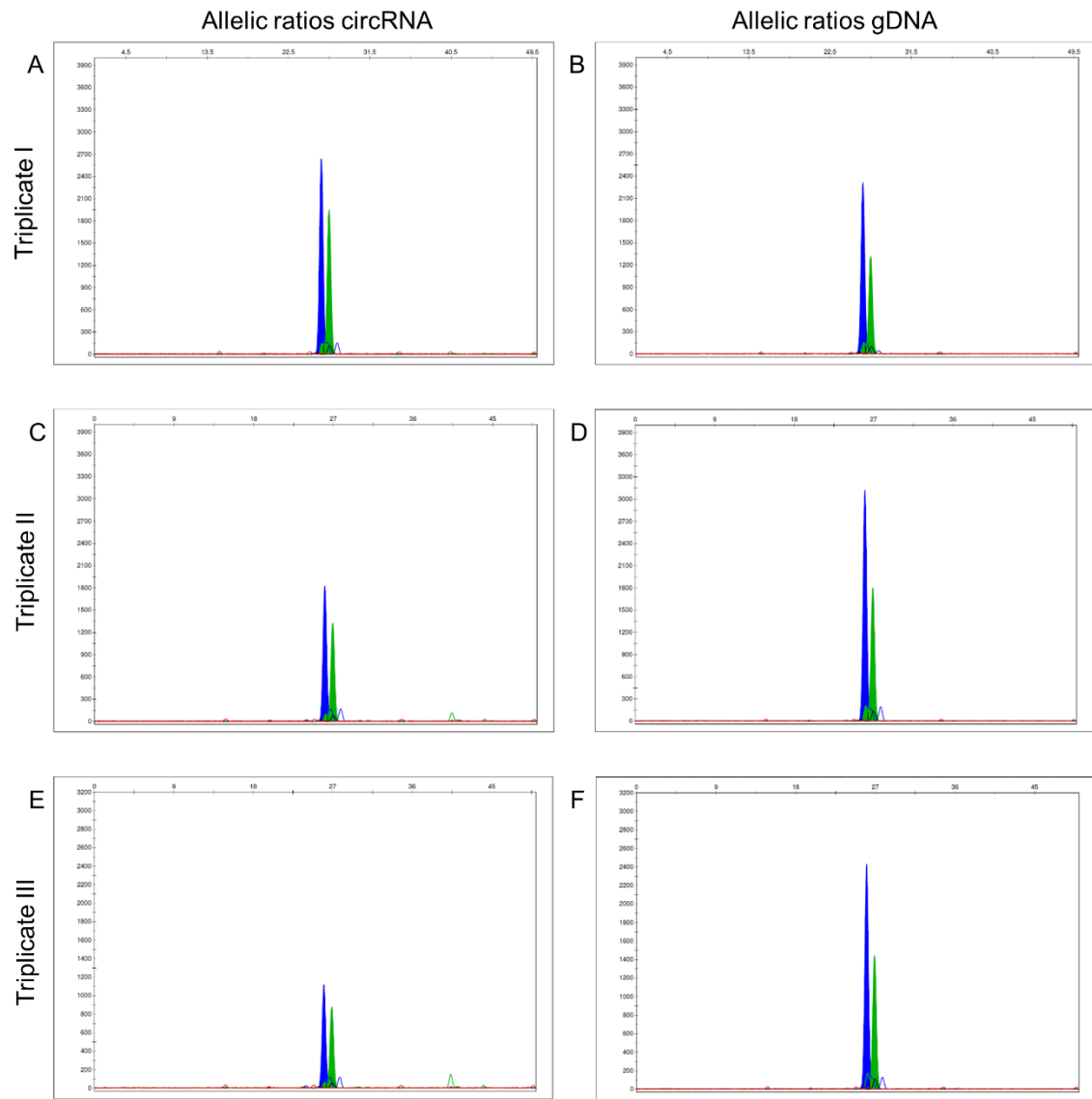
Supplementary Figure S3: 20 miRNAs with the Highest Numbers of Linked circRNAs. To explore putative miRNA-circRNA interactions, a dataset containing known interactions supported by Ago CLIP-sequencing data was downloaded from the ENCORI¹⁶. Here, the 20 miRNAs with the highest raw numbers of circRNAs linked to are represented.



Supplementary Figure S4: Exemplary SNaPshot Output for One Homozygous G/G Carrier of rs4752856. Here, the primer extension products containing the G-allele of the circRNA (A, C and E) and of the genomic DNA (B, D and F) are shown for all three triplicates. As homozygous individuals solely acted as an experimental controls, the yielded data was not further analysed. These plots were generated with the GeneMapper 4.0 software (Applied Biosystems, Foster City, CA, USA). Blue: G-allele



Supplementary Figure S5: Exemplary SNaPshot Output for the Homozygous A/A Carrier of rs4752856. Here, the primer extension products containing the A-allele of the circRNA (A, C and E) and genomic DNA (B, D and F) are shown. The experiment was performed in triplicates. As this homozygous individual acted as an experimental internal control, no further analyses were conducted. Green: A-allele (risk allele).



Supplementary Figure S6: Exemplary SNaPshot Output for One Heterozygous (G/A) Carrier of the SNP rs4752856. The primer extension products of a heterozygous carrier (here: subject 7) as presented in the GeneMapper 4.0 software (Applied Biosystems, Foster City, CA, USA) on the circRNA (A, C and E) and on the gDNA (B, D and F) are shown. This assay was performed in triplicates. The corresponding analysis of the allelic ratios (A/G) as well as the normalisation of the ratios of circRNA with genomic DNA are represented in Figure 6, Table 2 and Supplementary Table S11. Blue: G-allele. Green: A-allele (risk allele).

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