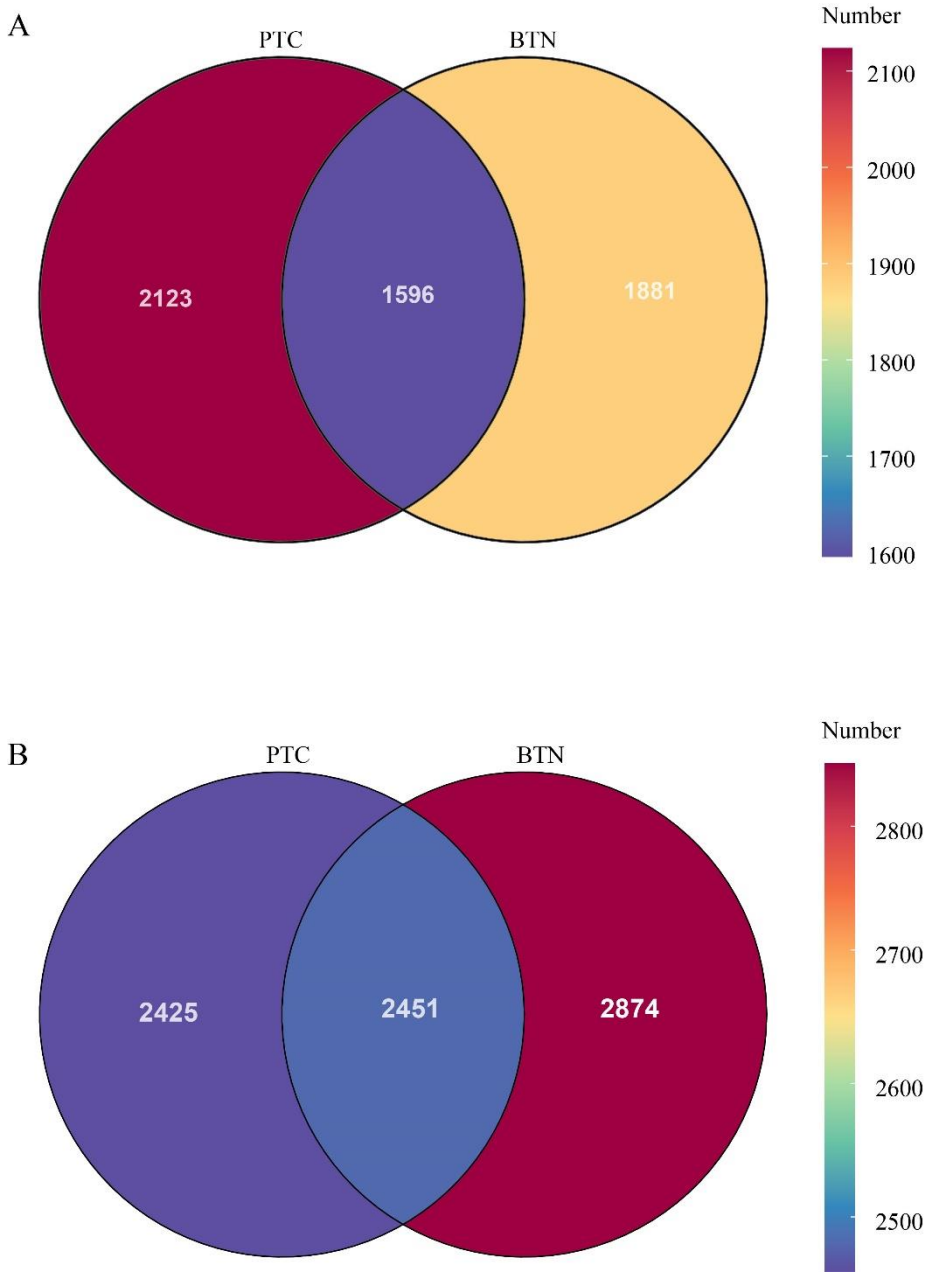
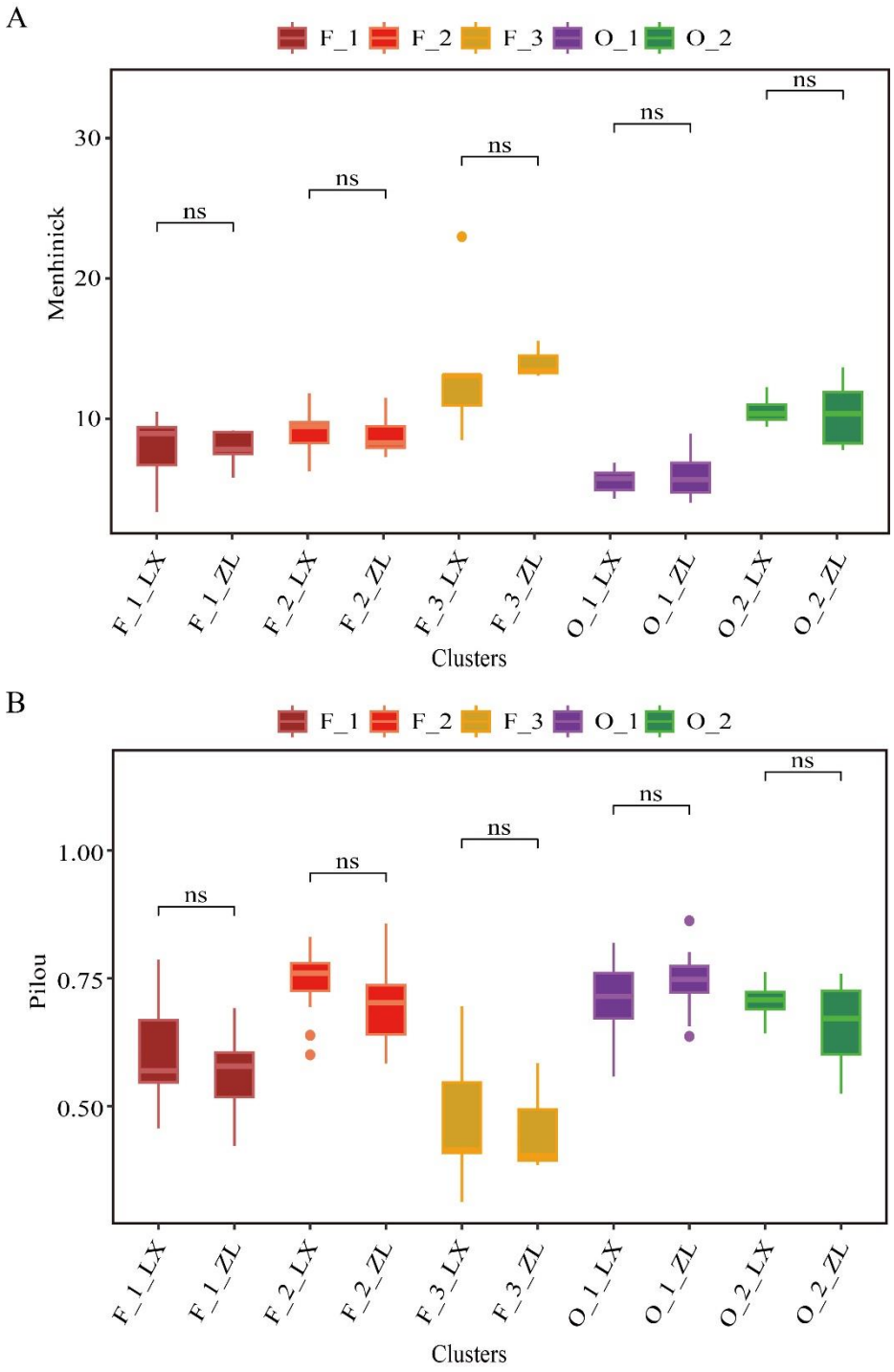
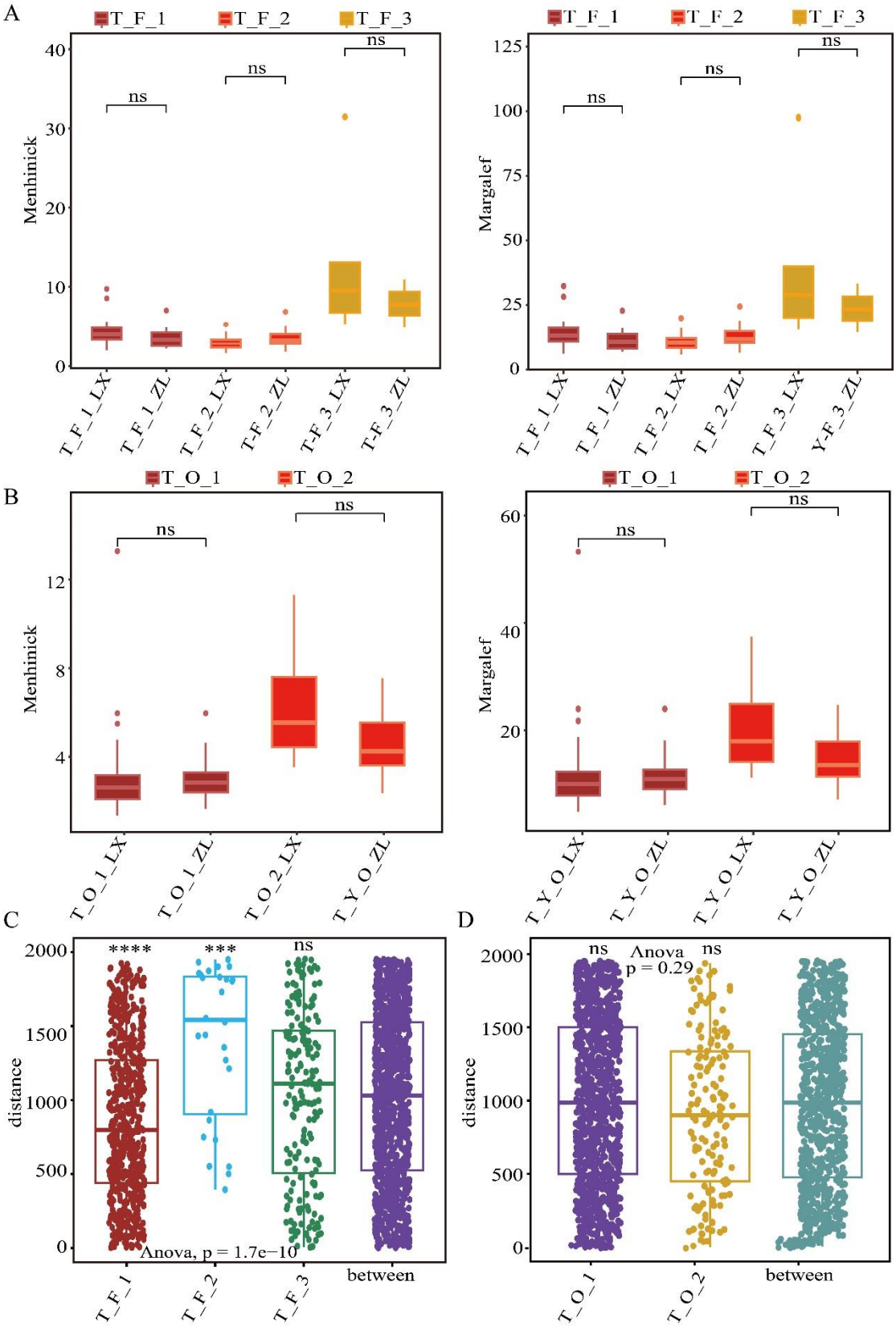


Supplementary Figure 1 Venn diagram showing ASV of the groups. (**A**) The ASV of oral samples. (**B**) The ASV of fecal samples. PTC, Papillary thyroid carcinoma; BTN, Benign thyroid nodules.



Supplementary Figure 2 Comparison of microbial richness and evenness within fecal and oral microbiota subclusters in BTN and PTC patients. (**A**) Richness across different samples within subcluster. (**B**) Evenness across different samples within subcluster. ns: no significance. ns, not significant.



Supplementary Figure 3 Comparison of α-diversity and β-diversity within tissue microbiota subclusters in BTN and PTC patients. (**A**) Richness across different samples

within tissue subcluster corresponding to fecal cluster. (**B**) Richness across different samples within tissue subcluster corresponding to fence cluster. (**C**) β-diversity of tissue cluster corresponding to fecal cluster. (**D**) β-diversity of tissue cluster corresponding to oral cluster. ***$p < 0.001$, ****$p < 0.0001$; ns, not significant.

Supplementary Table 1 Primers sequences used for sequencing

Primers for 16S rRNA	
Regions	
V3-V4	341F: 5'-CCTACGGGNGGCWGCAG-3'
	805R: 5'-GACTACHVGGGTATCTAATCC-3'
Primers for 5R 16S rRNA	
Regions	First round
V2	F1: 5'-TGGCGAACGGGTGAGTAA-3'
	R1: 5'-AGACGTGTGCTCTTCCGATCTCCGTGTCTCAGTCCCARTG-3'
V3	F2: 5'-ACTCCTACGGGAGGCAGC-3'
	R2: 5'-AGACGTGTGCTCTTCCGATCTGTATTACCGCGGCTGCTG-3'
V5	F3: 5'-GTGTAGCGGTGRAATGCG-3'
	R3: 5'-AGACGTGTGCTCTTCCGATCTCCCGTCAATTCMTTTGAGTT-3
V6	F4: 5'-GGAGCATGTGGWTTAATTCGA-3
	R4: 5'-AGACGTGTGCTCTTCCGATCTCGTTGCGGGACTTAACCC-3'
V8	F5: 5'-GGAGGAAGGTGGGGATGAC-3'
	R5: 5'-AGACGTGTGCTCTTCCGATCTAAGGCCCGGGAACGTATT-3'
Regions	Second round
V2	FF1:5'AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGA CGCTCTTCCGATCTTGGCGAACGGGTGAGTAA-3'
V3	FF2:5'AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGA CGCTCTTCCGATCTACTCCTACGGGAGGCAGC-3'
V5	FF3:5'AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGA CGCTCTTCCGATCTGTGTAGCGGTGRAATGCG-3'
V6	FF4:5'AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGA CGCTCTTCCGATCTGGAGCATGTGGWTTAATTCGA-3'
V8	FF5:5'AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGA CGCTCTTCCGATCTGGAGGAAGGTGGGGATGAC-3'
Common reverse primer	RR5:5'CAAGCAGAAGACGGCATACGAGATNNNNNNNNGTGACTGGAG TTCAGACGTGTGCTCTTCCGATCT-3'

Supplementary Table 2 Sequencing data statistics of oral and fecal samples

Oral	Sample ID	Reads	Q30 (%)	GC (%)	Fecal	Sample ID	Reads	Q30 (%)	GC (%)
PTC	O_ZL_32	75872	93.25	52.27	PTC	F_ZL_32	59936	93.53	53.75
	O_ZL_31	75053	93.15	51.61		F_ZL_31	55189	93.43	53.91
	O_ZL_30	75684	90.92	51.86		F_ZL_30	68704	92.94	53.97
	O_ZL_29	79784	93.37	52.95		F_ZL_29	72716	91.56	52.40
	O_ZL_28	78775	93.98	51.51		F_ZL_28	75884	93.26	54.15
	O_ZL_27	68014	93.14	53.20		F_ZL_27	69282	93.11	53.79
	O_ZL_26	75507	93.32	51.95		F_ZL_26	70681	93.53	53.32
	O_ZL_25	75149	93.56	51.91		F_ZL_25	63830	92.85	51.57
	O_ZL_24	72850	93.61	50.16		F_ZL_24	72264	93.18	53.07
	O_ZL_23	75723	93.51	52.19		F_ZL_23	73977	93.82	55.30
	O_ZL_22	79721	93.56	52.37		F_ZL_22	65574	92.65	52.33
	O_ZL_21	76045	93.98	51.66		F_ZL_21	66018	91.36	52.08
	O_ZL_20	75842	94.17	51.98		F_ZL_20	55998	93.97	56.78
	O_ZL_19	76550	93.29	51.67		F_ZL_19	57998	93.71	54.21
	O_ZL_18	79183	93.32	52.48		F_ZL_18	71460	93.38	54.58
	O_ZL_17	76252	93.38	52.10		F_ZL_17	73297	93.73	56.93
	O_ZL_16	79213	93.53	52.79		F_ZL_16	62957	93.68	52.11
	O_ZL_15	72643	92.99	52.09		F_ZL_15	68489	93.55	53.35
	O_ZL_14	72895	92.12	52.07		F_ZL_14	72963	93.61	53.59
	O_ZL_13	80785	94.10	51.58		F_ZL_13	64268	93.80	54.28
	O_ZL_12	67909	94.22	51.73		F_ZL_12	69949	92.38	52.78
	O_ZL_11	68197	93.76	51.72		F_ZL_11	65137	93.45	53.31
	O_ZL_10	76150	93.70	52.57		F_ZL_10	73400	93.48	53.10
	O_ZL_9	77844	93.38	51.48		F_ZL_9	66868	93.39	54.99
	O_ZL_8	78256	93.72	52.48		F_ZL_8	53514	94.01	52.25
	O_ZL_7	69747	93.55	52.80		F_ZL_7	66870	94.13	54.67
	O_ZL_6	78347	90.90	51.93		F_ZL_6	66001	93.36	52.03
	O_ZL_5	76922	94.40	52.66		F_ZL_5	58215	90.30	54.28
	O_ZL_4	75119	92.14	51.98		F_ZL_4	75650	92.09	52.03
	O_ZL_3	73725	94.12	52.19		F_ZL_3	68488	92.97	52.29
	O_ZL_2	79120	92.31	53.69		F_ZL_2	59367	93.06	53.70
	O_ZL_1	73935	90.67	53.58		F_ZL_1	73158	91.69	52.96
BTN	O_LX_32	74430	89.41	50.87	BTN	F_LX_32	66128	93.42	56.32
	O_LX_31	71404	91.55	52.49		F_LX_31	72138	93.33	53.39
	O_LX_30	68389	92.26	51.59		F_LX_30	69497	92.99	54.98
	O_LX_29	68989	91.71	52.50		F_LX_29	67592	92.22	53.29
	O_LX_28	78535	91.72	52.48		F_LX_28	67358	91.20	53.71
	O_LX_27	73041	93.45	52.47		F_LX_27	63584	91.84	52.97
	O_LX_26	71399	91.63	52.78		F_LX_26	46456	92.99	53.68

	O_LX_25	65834	92.59	52.69		F_LX_25	62004	93.01	54.60
	O_LX_24	73425	90.44	53.25		F_LX_24	70518	92.77	52.63
	O_LX_23	65715	91.91	52.69		F_LX_23	64267	92.68	52.59
	O_LX_22	79521	92.25	50.84		F_LX_22	54967	91.91	57.00
	O_LX_21	73250	91.70	53.20		F_LX_21	72673	92.10	54.17
	O_LX_20	70792	93.58	52.18		F_LX_20	71705	91.37	54.87
	O_LX_19	76579	91.57	51.52		F_LX_19	72608	92.68	56.66
	O_LX_18	66007	91.77	52.18		F_LX_18	64244	92.32	54.65
	O_LX_17	63632	93.13	53.62		F_LX_17	61215	93.98	54.58
	O_LX_16	72016	90.17	52.18		F_LX_16	77212	93.41	52.12
	O_LX_15	69948	91.27	51.72		F_LX_15	67387	90.80	53.43
	O_LX_14	79991	92.45	51.93		F_LX_14	59048	92.49	54.44
	O_LX_13	66055	91.78	52.20		F_LX_13	74781	93.87	53.64
	O_LX_12	78747	93.10	53.38		F_LX_12	69982	90.74	53.54
	O_LX_11	77773	92.73	52.34		F_LX_11	76177	91.71	55.86
	O_LX_10	75588	91.76	52.26		F_LX_10	66394	91.09	52.95
	O_LX_9	71060	91.82	52.26		F_LX_9	65269	91.53	54.45
	O_LX_8	67595	89.61	52.15		F_LX_8	66728	91.74	54.54
	O_LX_7	71619	91.17	52.91		F_LX_7	60051	90.52	52.62
	O_LX_6	79486	92.10	52.56		F_LX_6	55578	92.08	52.76
	O_LX_5	71679	91.75	52.72		F_LX_5	57849	90.47	52.74
	O_LX_4	68798	91.41	52.27		F_LX_4	65670	90.32	53.45
	O_LX_3	79339	93.15	53.81		F_LX_3	67574	91.35	53.24
	O_LX_2	76386	92.15	53.87		F_LX_2	62407	91.76	51.99
	O_LX_1	74763	93.32	51.74		F_LX_1	57124	91.64	55.17

PTC, Papillary thyroid carcinoma; BTN, Benign thyroid nodules

Supplementary Table 3 The alpha diversity index of gut microbial community clusters and oral microbial community clusters.

Alpha diversity	Menhinick index				Pilou evenness			
	Mean	Standard Error	Max	Min	Mean	Standard Error	Max	Min
F_1	7.949	1.845	10.51	3.354	0.59	0.093	0.786	0.422
F_2	8.92	1.281	11.832	6.254	0.723	0.073	0.857	0.583
F_3	13.833	4.232	22.981	8.485	0.469	0.127	0.695	0.313
O_1	5.761	1.015	8.944	4.025	0.723	0.065	0.863	0.558
O_2	10.41	1.835	13.671	7.778	0.67	0.075	0.762	0.524

Supplementary Table 4 The beta diversity index of gut microbial community clusters and oral microbial community clusters

Clusters	Mean	Standard Error	Max	Min	p	p.adjust
F_1	2291.077	860.528	4350	7	5.28E-175	5.30E-175
F_2	652.357	575.468	1740	9	3.26E-18	3.30E-18
F_3	2585.389	1236.423	5809	5	1.23E-47	1.20E-47
O_1	998.078	765.697	3657	1	0	0
O_2	531.706	352.058	1488	12	1.36E-93	1.40E-93
between	4742.291	1968.695	7875	61	-	-

P values were obtained by comparing each cluster with between.

Supplementary Table 5 Sequencing data statistics of tissue samples

Tissue	Sample ID	Reads	Q30 (%)	GC (%)	Tissue	Sample ID	Reads	Q30 (%)	GC (%)
PTC	T_ZL_32	192305	94.96	54.91	BTN	T_LX_32	175303	97.25	55.03
	T_ZL_31	161996	93.97	55.62		T_LX_31	153509	91.94	58.39
	T_ZL_30	189532	93.69	55.33		T_LX_30	183546	92.16	57.86
	T_ZL_29	187370	95.46	55.22		T_LX_29	181206	94.50	55.95
	T_ZL_28	189655	95.78	56.92		T_LX_28	186612	93.88	56.45
	T_ZL_27	197417	95.20	54.98		T_LX_27	182978	94.97	54.84
	T_ZL_26	187972	94.47	55.53		T_LX_26	190145	94.93	54.92
	T_ZL_25	192553	93.80	56.40		T_LX_25	189315	94.31	55.67
	T_ZL_24	195426	94.16	56.47		T_LX_24	186551	94.76	54.75
	T_ZL_23	176412	93.17	56.30		T_LX_23	185301	93.16	56.88
	T_ZL_22	193672	93.71	55.93		T_LX_22	197959	93.56	55.99
	T_ZL_21	183847	95.30	55.28		T_LX_21	177517	94.45	57.63
	T_ZL_20	181758	93.48	56.82		T_LX_20	188183	93.53	56.55
	T_ZL_19	188937	95.78	55.02		T_LX_19	187878	96.28	53.36
	T_ZL_18	196135	94.72	54.95		T_LX_18	191688	94.80	55.31
	T_ZL_17	193239	94.81	57.30		T_LX_17	188162	96.53	54.85
	T_ZL_16	193699	94.15	56.02		T_LX_16	173092	95.97	55.23
	T_ZL_15	175628	93.58	56.34		T_LX_15	191866	96.11	54.03
	T_ZL_14	193896	94.42	56.67		T_LX_14	196460	94.86	55.60
	T_ZL_13	193832	95.05	55.61		T_LX_13	194631	95.69	54.59
	T_ZL_12	197851	94.95	55.84		T_LX_12	189867	94.06	56.17
	T_ZL_11	186029	95.47	55.47		T_LX_11	193968	95.67	54.67
	T_ZL_10	181791	94.59	58.34		T_LX_10	197186	94.71	54.80
	T_ZL_9	194144	94.06	57.47		T_LX_9	182243	94.83	55.12
	T_ZL_8	165338	94.11	58.58		T_LX_8	194005	94.93	55.13
	T_ZL_7	191861	90.77	62.62		T_LX_7	196103	94.40	55.36
	T_ZL_6	181418	91.98	60.76		T_LX_6	180707	94.55	56.16
	T_ZL_5	188009	94.03	59.15		T_LX_5	180278	94.94	55.78
	T_ZL_4	187347	93.98	58.22		T_LX_4	188127	93.16	56.89
	T_ZL_3	174218	94.48	57.43		T_LX_3	182942	96.31	53.98
	T_ZL_2	186066	94.66	55.47		T_LX_2	184323	95.12	55.12
	T_ZL_1	191029	93.98	56.70		T_LX_1	177324	96.03	54.48

PTC, Papillary thyroid carcinoma; BTN, Benign thyroid nodules

Supplementary Table 6 Logistic regression analysis of gut Menhinick index and oral Menhinick index versus tumor

	Estimate	**Standard error**	**z-value**	**p-value**
Intercept	0.61	0.25	2.51	0.01
Gut Menhinick	0.08	0.02	4.61	3.98e-06
Oral Menhinick	56	0.02	1.08	0.28