

Supplementary Table S1. The basic information of AIT patients and health control in 850K

Group	Sample	Sex	Age (years)	BMI (kg/m ²)	TSH (mIU/L)	FT ₃ (pmol/L)	FT ₄ (pmol/L)	TPOAb (IU/mL)	TgAb (IU/mL)	Thyroid ultrasound
Control	Con-1	Female	30	25.71	3.59	5.95	17.18	11.74	8	Normal
	Con-2	Female	32	23.92	0.51	4.71	19.73	9.21	7	Normal
	Con-3	Female	34	25.39	1.58	4.46	12.97	9.73	7	Normal
	Con-4	Female	39	21.51	2.51	4.87	16.53	7.48	6	Normal
	Con-5	Female	42	25.39	1.75	3.97	20.54	< 5.00	6	Normal
	Con-6	Female	46	22.83	3.78	4.72	17.57	11.20	6	Normal
	Con-7	Female	46	19.81	2.90	4.98	18.75	20.19	5	Normal
	Con-8	Female	46	24.09	2.32	4.74	16.09	7.50	6	Normal
	Con-9	Female	48	22.03	0.76	4.10	16.61	11.28	8	Normal
	Con-10	Female	54	19.83	3.03	3.87	15.16	8.55	4	Normal
AIT	AIT-1	Female	30	20.70	> 100.00	2.55 ↓	3.54 ↓	> 1300.00	41	Bilateral diffuse thyroid lesions
	AIT-2	Female	31	25.71	> 100.00	5.04	7.60 ↓	> 1300.00	36	Bilateral diffuse thyroid lesions, Abnormal hypoechoic area of left thyroid, Cystic nodule of right thyroid
	AIT-3	Female	34	23.15	5.84	4.67	15.11	> 1300.00	39	Bilateral diffuse thyroid lesions, left thyroid nodule
	AIT-4	Female	40	23.14	6.57	4.75	17.85	> 1300.00	31	Bilateral goiter with diffuse lesions, Cystic and solid nodules of the right thyroid
	AIT-5	Female	40	20.03	93.49	2.95 ↓	3.85 ↓	215.10	18	Bilateral goiter with diffuse lesions
	AIT-6	Female	42	23.88	14.98	5.79	10.30 ↓	> 1300.00	32	Goiter with diffuse lesions, Calcification in the right thyroid parenchyma, Bilateral thyroid nodules and partial nodules with calcification
	AIT-7	Female	44	20.96	4.86	4.64	17.62	> 1300.00	34	Bilateral diffuse thyroid lesions
	AIT-8	Female	48	24.89	> 100.00	< 0.40 ↓	0.72 ↓	> 1300.00	29	Bilateral diffuse thyroid lesions
	AIT-9	Female	51	21.26	4.66	3.95	13.84	> 600.00	36	Goiter with diffuse lesions
	AIT-10	Female	54	19.81	8.27	4.37	17.73	459.10	53	Bilateral diffuse thyroid lesions

Note. AIT, autoimmune thyroiditis; Con, control; BMI, body mass index; TSH, thyroid stimulating hormone; TPOAb, thyroid peroxidase antibodies; TgAb, thyroglobulin antibodies; FT₃, free triiodothyronine; FT₄, free thyroxine; ↓, indicates lower than the reference ranges.

Supplementary Table S2. GO and KEGG enrichment results of NK cells in 850K

ID	Description	P	Gene ID
GO:0002717	positive regulation of natural killer cell mediated immunity	0.0364*	KLRC3/SH2D1B
GO:0002715	regulation of natural killer cell mediated immunity	0.0683	KLRC3/SH2D1B
GO:0002420	natural killer cell mediated cytotoxicity directed against tumor cell target	0.0932	KLRC3
GO:0002423	natural killer cell mediated immune response to tumor cell	0.0932	KLRC3
GO:0002855	regulation of natural killer cell mediated immune response to tumor cell	0.0932	KLRC3
GO:0002858	regulation of natural killer cell mediated cytotoxicity directed against tumor cell target	0.0932	KLRC3
GO:0035747	natural killer cell chemotaxis	0.1020	KLRC3
GO:0002228	natural killer cell mediated immunity	0.1222	KLRC3/SH2D1B
GO:0045954	positive regulation of natural killer cell mediated cytotoxicity	0.2471	KLRC3
GO:0042269	regulation of natural killer cell mediated cytotoxicity	0.3372	KLRC3
GO:0042267	natural killer cell mediated cytotoxicity	0.4334	KLRC3
GO:0030101	natural killer cell activation	0.5654	KLRC3
hsa04650	natural killer cell mediated cytotoxicity	0.1490	KLRC3/KLRC1/SH2D1B

Note. *P < 0.05, t test.

Supplementary Table S3. Primer sequences in MethylTarget™

Gene	Primer F	Primer R
<i>KLRC1</i>	GTGTAATTAAAGGGTGAGGTGGAG	CTCCTAACCTCRTAATCRACATACCTC
<i>KLRC3</i>	GGAGATGAGTTAGTAGAGAAATAGGAGATTAG	ACCTCAACCTCCCAAACAAC
<i>SH2D1B</i>	TTGGAAATTATGGTAGTTGAAGATAGA	ACCCCTATAATAACCAAAACCTAAACA

Supplementary Table S4. Primer sequences in QRT-PCR

Gene	Primer F	Primer R
<i>KLRC1</i>	5'-GGGTGACAATGAATGGTTGG-3'	5'-GATCCACACTGGGCTGATTTA-3'
<i>KLRC3</i>	5'-GTTTACTGCCACCTCCAGAA-3'	5'-TCTGCTCCAGGAAAGGAATAAG-3'
<i>β-actin</i>	5'-CCTTCTCTGGGCATGGAGTCCTG-3'	5'-GGAGCAATGATCTTGATCTTC-3'

Supplementary Table S5. Correlation between DNA methylation levels of the candidate genes and age, iodine nutrition levels, and thyroid function in AIT patients

Characteristics		KLRC1	KLRC3	SH2D1B
UIC (μg/L)	<i>r</i>	−0.016	0.070	0.069
	<i>P</i>	0.833	0.359	0.366
SIC (μg/L)	<i>r</i>	−0.223	0.066	−0.105
	<i>P</i>	0.004*	0.393	0.175
Age (years)	<i>R</i>	−0.134	−0.235	−0.089
	<i>P</i>	0.080	0.002*	0.241
FT ₃ (pmol/L)	<i>r</i>	−0.105	−0.018	0.011
	<i>P</i>	0.171	0.810	0.887
FT ₄ (pmol/L)	<i>r</i>	−0.111	0.084	−0.020
	<i>P</i>	0.150	0.267	0.789
TSH (μIU/mL)	<i>r</i>	−0.083	0.040	0.015
	<i>P</i>	0.278	0.597	0.843

Note. UIC, urinary iodine concentration; SIC, serum iodine concentration; FT₃, free triiodothyronine; FT₄, free thyroxine; TSH, thyroid stimulating hormone; *r*, Pearson correlation coefficient; *R*, Spearman correlation coefficient; * *P* < 0.05.

Supplementary Table S6. DNA methylation levels of candidate genes and CpG sites between AIT and control groups stratifying by sex

Gene	Site	Male		Female	
		Group.diff	P	Group.diff	P
<i>KLRC1</i>	–	–0.019	0.010 [*]	–0.015	$3.12 \times 10^{-8**}$
	28	–0.006	0.516	–0.012	$3.69 \times 10^{-5**}$
	97	–0.017	0.239	–0.009	0.158
	138	–0.025	0.170	–0.005	0.184
	142	–0.033	0.017 [*]	–0.029	$1.78 \times 10^{-9**}$
	144	–0.032	0.012 [*]	–0.030	$7.81 \times 10^{-11**}$
	154	–0.012	0.054	–0.009	$1.14 \times 10^{-5**}$
	182	–0.007	0.203	–0.009	$3.48 \times 10^{-6**}$
<i>KLRC3</i>	–	0.050	0.351	0.047	0.052
	65	0.054	0.360	0.048	0.076
	99	0.070	0.350	0.067	0.043 [*]
	122	0.072	0.282	0.066	0.030 [*]
	133	0.075	0.316	0.066	0.043 [*]
	162	0.040	0.429	0.049	0.038 [*]
	174	0.026	0.413	0.022	0.115
	178	0.015	0.570	0.010	0.339
<i>SH2D1B</i>	–	0.010	0.830	–0.034	0.096
	81	0.010	0.830	–0.034	0.096

Note. Group.diff, the methylation level of case-the methylation level of control; ^{*}*P* < 0.05, ^{**}*P* < 0.001.

Supplementary Table S7. DNA methylation levels of candidate genes and CpG sites between AIT and control groups stratifying by age

Gene	Site	≤ 29 years		30–39 years		40–49 years		> 50 years	
		Group.diff	P	Group.diff	P	Group.diff	P	Group.diff	P
KLRC1	–	–0.015	0.599	–0.016	0.006*	–0.013	0.001*	–0.018	0.173
	28	–0.002	0.434	–0.010	0.019*	–0.010	0.058	–0.013	0.141
	97	0.004	0.070	–0.011	0.928	–0.001	0.012*	–0.015	0.086
	138	–0.009	0.685	0.004	0.393	–0.016	0.043*	–0.005	0.176
	142	–0.038	0.908	–0.038	<0.001**	–0.019	0.404	–0.030	0.001*
	144	–0.044	0.680	–0.038	<0.001**	–0.019	0.528	–0.033	0.001*
	154	–0.010	0.848	–0.006	0.023*	–0.006	0.046*	–0.012	0.031*
	182	–0.008	0.008*	–0.010	0.010*	–0.007	0.132	–0.008	0.506
KLRC3	–	0.192	0.311	0.061	0.316	0.056	0.406	–0.003	0.596
	65	0.203	0.496	0.065	0.260	0.048	0.177	0.001	0.745
	99	0.267	0.363	0.094	0.173	0.061	0.386	0.001	0.990
	122	0.250	0.299	0.087	0.159	0.065	0.321	0.006	0.799
	133	0.243	0.295	0.094	0.209	0.072	0.231	–0.002	0.703
	162	0.197	0.200	0.067	0.252	0.037	0.448	0.005	0.413
	174	0.099	0.197	0.018	0.972	0.029	0.478	–0.002	0.899
	178	0.078	0.823	0.010	0.313	0.022	0.787	–0.015	0.320
SH2D1B	–	0.010	0.079	–0.003	0.531	–0.030	0.019*	–0.046	0.017*
	81	0.010	0.079	–0.003	0.531	–0.030	0.019*	–0.046	0.017*

Note. Group.diff, the methylation level of case-the methylation level of control; **P* < 0.05, ***P* < 0.001.

Supplementary Table S8. DNA methylation levels of candidate genes and CpG sites between AIT and control groups stratifying by SIC

Gene	Site	< 50 µg/L		50–109.9 µg/L		≥ 110 µg/L	
		Group.diff	P	Group.diff	P	Group.diff	P
<i>KLRC1</i>	–	0.003	0.812	–0.016	< 0.001**	–0.029	0.265
	28	0.006	0.122	–0.012	0.001*	–0.035	0.757
	97	0.001	0.856	–0.008	0.157	–0.069	0.189
	138	–0.006	0.796	–0.007	0.252	–0.019	0.513
	142	0.018	0.281	–0.031	< 0.001**	–0.028	0.319
	144	0.009	0.345	–0.032	< 0.001**	–0.028	0.539
	154	0.003	0.471	–0.009	0.001*	–0.012	0.477
	182	–0.011	0.290	–0.009	0.012*	–0.009	0.575
<i>KLRC3</i>	–	–0.067	0.385	0.050	0.490	0.020	0.357
	65	–0.133	0.302	0.052	0.357	0.039	0.309
	99	–0.122	0.452	0.070	0.273	0.036	0.475
	122	–0.090	0.401	0.068	0.443	0.064	0.630
	133	–0.115	0.365	0.070	0.382	0.025	0.467
	162	–0.058	0.364	0.051	0.659	0.007	0.481
	174	–0.042	0.948	0.023	0.710	–0.011	0.286
	178	–0.059	0.902	0.013	0.316	–0.019	0.128
<i>SH2D1B</i>	–	–0.021	0.599	–0.023	0.001*	0.024	0.684
	81	–0.021	0.599	–0.023	0.001*	0.024	0.684

Note. Group.diff, the methylation level of case-the methylation level of control; * $P < 0.05$, ** $P < 0.001$, t test.

Supplementary Table S9. DNA methylation levels of candidate genes and CpG sites between AIT and control groups stratifying by UIC

Gene	Site	< 100 µg/L		100–199 µg/L		200–299 µg/L		> 300 µg/L	
		Group.diff	P	Group.diff	P	Group.diff	P	Group.diff	P
KLRC1	–	–0.009	0.189	–0.015	0.127	–0.015	0.149	–0.016	< 0.001**
	28	–0.003	0.331	–0.016	0.136	–0.007	0.038*	–0.009	0.015*
	97	–0.009	0.049*	–0.011	0.504	–0.004	0.923	–0.008	0.489
	138	–0.007	0.068	–0.007	0.939	–0.005	0.598	–0.009	0.001*
	142	–0.016	0.012*	–0.023	0.005*	–0.035	0.011*	–0.033	0.002*
	144	–0.025	0.022*	–0.025	0.020*	–0.036	0.009*	–0.034	0.001*
	154	–0.004	0.638	–0.009	0.471	–0.009	0.082	–0.010	0.001*
	182	–0.003	0.486	–0.011	0.740	–0.007	0.043*	–0.008	0.059
KLRC3	–	–0.060	0.737	0.058	0.304	0.057	0.354	0.061	0.570
	65	–0.079	0.615	0.069	0.199	0.057	0.099	0.064	0.996
	99	–0.093	0.824	0.083	0.210	0.068	0.104	0.088	0.991
	122	–0.083	0.586	0.081	0.267	0.073	0.033*	0.085	0.714
	133	–0.080	0.538	0.088	0.200	0.074	0.054	0.082	0.745
	162	–0.040	0.728	0.049	0.310	0.066	0.013*	0.058	0.103
	174	–0.025	0.821	0.027	0.967	0.044	0.001*	0.028	0.420
	178	–0.019	0.439	0.011	0.370	0.018	0.248	0.018	0.093
SH2D1B	–	0.036	0.767	0.009	0.501	–0.037	0.008*	–0.040	0.021*
	81	0.036	0.767	0.009	0.501	–0.037	0.008*	–0.040	0.021*

Note. Group.diff, the methylation level of case-the methylation level of control; * $P < 0.05$, ** $P < 0.001$, t test.

Supplementary Table S10. DNA methylation levels of candidate genes and related CpG sites among cases in three areas

Gene	Site	IFA	IAA	IEA	P
<i>KLRC1</i>	–	0.896 ± 0.025	0.886 ± 0.022	0.889 ± 0.029	0.081
	28	0.895 ± 0.028	0.888 ± 0.029	0.892 ± 0.032	0.951
	97	0.740 ± 0.050	0.732 ± 0.054	0.745 ± 0.054	0.522
	138	0.934 ± 0.046	0.938 ± 0.018	0.933 ± 0.025	0.814
	142	0.900 ± 0.048 ^a	0.879 ± 0.044	0.879 ± 0.049	0.022 [*]
	144	0.901 ± 0.045 ^a	0.879 ± 0.040	0.884 ± 0.047	0.017 [*]
	154	0.954 ± 0.018 ^a	0.945 ± 0.016	0.943 ± 0.022	0.002 [*]
	182	0.950 ± 0.018	0.944 ± 0.015	0.944 ± 0.018	0.125
<i>KLRC3</i>	–	0.653 ± 0.207	0.639 ± 0.232	0.684 ± 0.190	0.573
	65	0.616 ± 0.230	0.596 ± 0.263	0.693 ± 0.211	0.510
	99	0.539 ± 0.282	0.520 ± 0.313	0.578 ± 0.258	0.602
	122	0.573 ± 0.263	0.555 ± 0.291	0.619 ± 0.232	0.480
	133	0.550 ± 0.278	0.536 ± 0.314	0.593 ± 0.254	0.590
	162	0.670 ± 0.204	0.657 ± 0.224	0.700 ± 0.187	0.577
	174	0.801 ± 0.113	0.792 ± 0.132	0.812 ± 0.114	0.739
	178	0.821 ± 0.096	0.817 ± 0.109	0.832 ± 0.097	0.752
<i>SH2D1B</i>	–	0.155 ± 0.191	0.197 ± 0.171	0.194 ± 0.206	0.278
	81	0.155 ± 0.191	0.197 ± 0.171	0.194 ± 0.206	0.278

Note. Group.diff, the methylation level of case-the methylation level of control; ^aSignificant differences compared to IFA; ^{*}Significant differences among three groups; *P*<0.05.