
가속노화 분석 가이드라인

[Guideline for accelerated aging analysis]

유전체연구기술개발과
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1

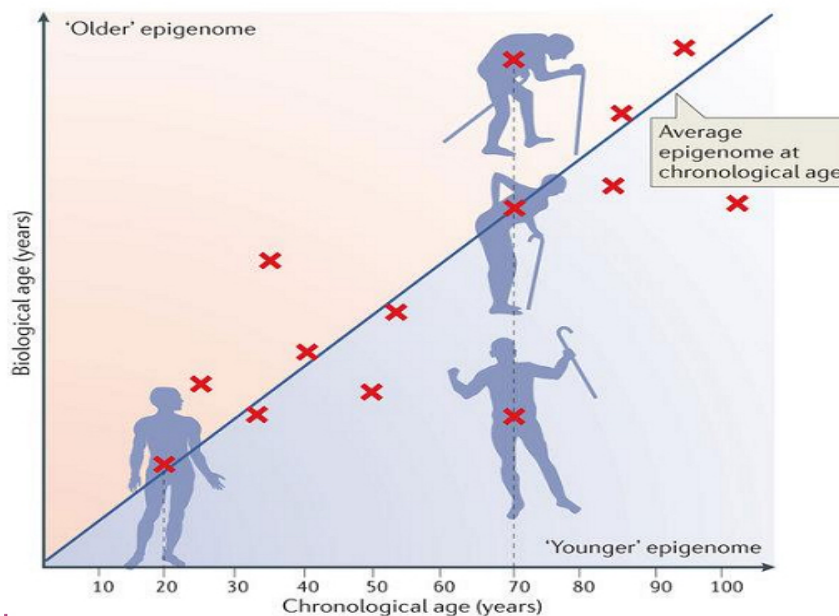
가속노화 개요

□ 가속노화란?

- 생물학적 나이(biological age)*가 연대기 나이(chronological age)**에 비해 더 빠르게 증가하는 상태를 의미하며, 특히 비정상적으로 가속된 노화는 건강수명을 감소시킴

* 연대기 나이: 출생 후 경과된 시간

** 생물학적 나이: 유전, 환경 영향에 따라 인간 노화속도의 변화를 추적할 수 있는 생체나이



<그림 1. 연대기 나이와 생물학적 나이 차이에 따른 노화 (Benayoun et al. Nat Rev Mol Cell Biol. 2016)>

□ 주요 노화 바이오마커

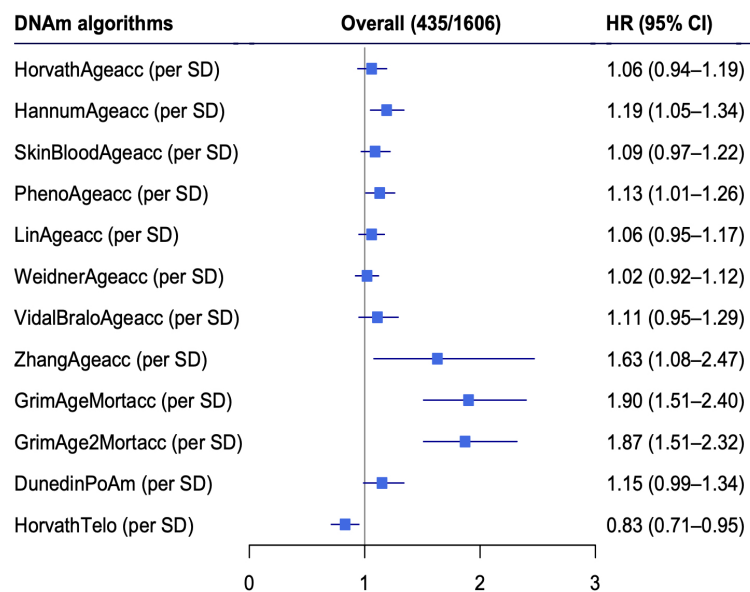
- DNA 메틸화 패턴을 기반으로 측정한 후성유전학적 나이(epigenetic age)와 실제 나이의 차이를 통해 가속노화를 평가할 수 있음
- 현재까지 개발된 주요 노화 바이오마커는 다음과 같음

<표 1. 주요 노화 바이오마커 종류 및 계산 방법>

Biomarkers	Criterion	Component elements	
Telomere length	Replicative cellular aging	Leukocyte telomere length	Berglund et al., 2016
Horvath clock	Chronological age	353 age-associated CpGs	Horvath et al., 2013
Hannum clock	Chronological age	71 age-associated CpGs	Hannum et al., 2013
PhenoAge clock	Blood-chemistry PhenoAge	513 PhenoAge-associated CpGs	Levine et al., 2018
GrimAge clock	Mortality Risk	Smoking pack-years and seven plasma proteins-associated CpGs (1,030 unique sites)	Lu et al., 2019
DunedinPACE	indicators of organ-system integrity	Pace of aging	Belsky et al., 2022

□ 가속노화 연구 동향

- 최근 오믹스 기반 노화 연구가 활발해지면서 생물학적 나이를 평가하고 질환과의 연관성을 규명하는 다양한 연구가 진행되고 있음
- 미국의 50세 이상 성인을 대상으로 DNA methylation 기반 생체나이 시계와 심혈관 질환 사망률 위험의 연관성을 확인한 연구에서 GrimAge clock의 가속도가 클수록 심혈관 질환 위험이 유의미하게 증가하는 결과를 보고함



<그림 2. DNAmAge와 심혈관 질환 사망률 위험간의 연관성
(Cui X et al. J Am Heart Assoc. 2025)>

- CpG site를 기반으로 계산된 DNA methylation estimator of telomere length(DNAmtl)와 심혈관계 질환(Cardiovascular disease, CVD)의 연관성을 분석한 결과, 텔로미어 길이가 1 kilobases 증가할 때 심혈관 질환의 발생이 53% 낮았고, 텔로미어 길이가 가장 짧은 그룹보다 가장 긴 그룹은 심혈관 질환의 발생이 50%로 낮음

<표 2. DNAmtl과 CVD의 연관성 (Wang Q et al. Clin Epigenetics. 2024)>

	Model 1	Model 2	Model 3
Continuous			
Per 1 kilobases increment	0.43(0.26-0.72) <0.001	0.52(0.27-0.98) 0.044	0.47 (0.23-0.95) 0.036
Categorical			
T1	Reference	Reference	Reference
T2	0.70(0.49-0.99) 0.042	0.74 (0.49-1.11) 0.145	0.74(0.48-1.15) 0.186
T3	0.43(0.29-0.65) <0.01	0.47(0.28-0.77) 0.003	0.50(0.29-0.85) 0.011
P for trend	<0.001	0.003	0.011

* Model 1: adjusted for age

* Model 2: Model1, adjusted for gender, race/ethnicity, BMI, PIR, education levels, alcohol consumption, smoking status

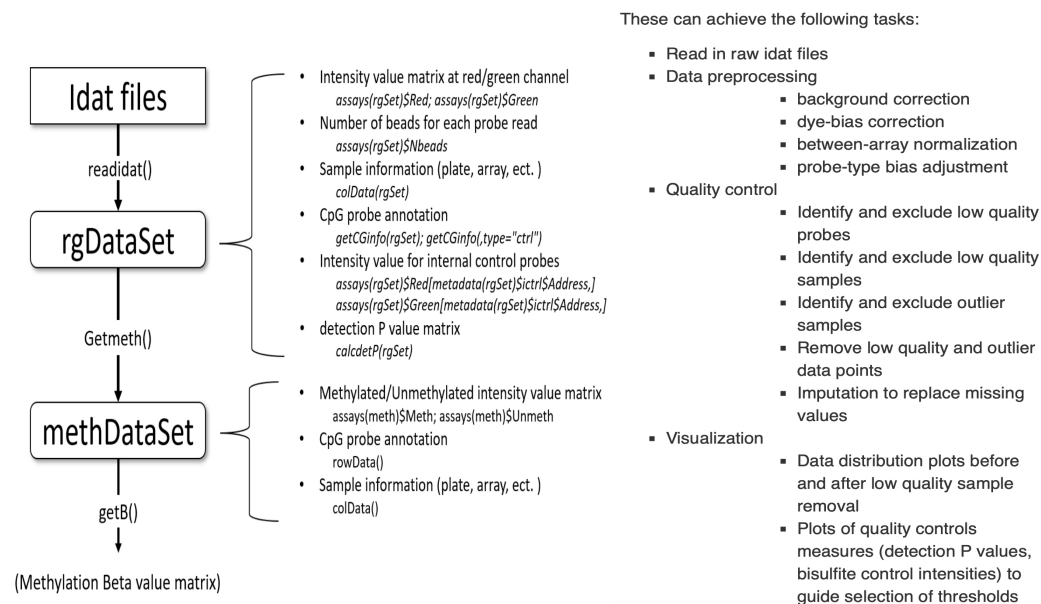
* Model 3: Model2, adjusted for hypertension, DM, TC, TG, HDL-C, SBP, DBP, eGFR, medication use(anti-hypertensive agents, hypoglycemic agents, statins)

* T1: shortest DNAmtl, T3: longest DNAmtl

□ DNA methylation 데이터 품질관리

- DNA methylation age 계산에 앞서 신뢰도 높은 데이터를 확보하기 위해 R의 ENmix 패키지를 사용하여 품질관리를 진행함

* 참고: <https://bioconductor.org/packages/release/bioc/vignettes/ENmix/inst/doc/ENmix.html>



<그림 3. Methylation data 정제 파이프라인 (ENmix User's Guide)>

□ DNA Methylation Age Calculator 입력 파일 준비

- DNA Methylation Age Calculator 웹사이트에 업로드 할 sample annotation 및 methylation data 파일을 준비함

* 참고: <https://dnamage.clockfoundation.org>

- Sample annotation 파일

- .csv 형식 파일
- 입력 정보: Sample ID, Age, Sex, Tissue 등

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	OriginalOrder	id	title	geo_accession	TissueDetailed	Tissue	diseaseStatus	Age	PostMortemInterval	CauseofDeath	individual	Female	Caucasian	FemaleOriginal
2	3	GSM946048	Autism_occ_AN09714	GSM946048	Fresh frozen brain tissue	Brain Occipital Cortex	1	60	26.5	cancer	18	0	NA	NA
3	4	GSM946049	Control_occ_AN05475	GSM946049	Fresh frozen brain tissue	Brain Occipital Cortex	0	39		cardiac	2	0	NA	NA
4	7	GSM946052	Autism_occ_AN08166	GSM946052	Fresh frozen brain tissue	Brain Occipital Cortex	1	28	43	cancer	3	0	NA	NA
5	9	GSM946054	Autism_occ_AN06420	GSM946054	Fresh frozen brain tissue	Brain Occipital Cortex	1	39	14	cardiac	6	0	NA	NA
6	10	GSM946055	Autism_occ_AN19511	GSM946055	Fresh frozen brain tissue	Brain Occipital Cortex	1	8	22.2	cancer	4	0	NA	NA
7	11	GSM946056	Autism_occ_AN09730	GSM946056	Fresh frozen brain tissue	Brain Occipital Cortex	1	22	25	hypoxia	8	0	NA	NA
8	14	GSM946059	Control_occ_UMB4670	GSM946059	Fresh frozen brain tissue	Brain Occipital Cortex	0	4	17	cardiac	28	0	NA	NA
9	17	GSM946062	Control_occ_UMB4543	GSM946062	Fresh frozen brain tissue	Brain Occipital Cortex	0	28	13	other	35	0	NA	NA
10	19	GSM946064	Autism_occ_AN08873	GSM946064	Fresh frozen brain tissue	Brain Occipital Cortex	1	5	25.5	hypoxia	21	0	NA	NA

<그림 4. Sample annotation 파일 예시 (DNA Methylation Age Calculator)>

- Methylation data 파일

- IDAT 파일 또는 CpG site beta 값 중 선택
- Beta 값 사용 시 .csv 형식으로 작성 후 .zip 형식으로 압축
- 첫 번째 열: CpG 식별 ID
- 헤더(첫 번째 행): Sample ID
- 데이터: Beta 값 (0~1 사이의 값)

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	ProbeID	GSM946048	GSM946049	GSM946052	GSM946054	GSM946055	GSM946056	GSM946059	GSM946062	GSM946064	GSM946065	GSM946066	GSM946067	GSM946073	GSM9460
2	cg00000292	0.705961431	0.728790365	0.704587006	0.750851623	0.715302226	0.63440712	0.681816613	0.635320371	0.727532164	0.777193913	0.601302367	0.751631378	0.671318843	0.7678656
3	cg00002426	0.272443435	0.27398577	0.310648656	0.278648844	0.178116582	0.26856398	0.329730878	0.501223179	0.196823442	0.281686752	0.202653657	0.221132393	0.237562732	0.1881566
4	cg00003994	0.037032466	0.014692376	0.017115722	0.028960542	0.016254482	0.024279664	0.012705737	0.020628148	0.015136485	0.010465486	0.028988007	0.014494483	0.032983973	0.0250966
5	cg00005847	0.133246824	0.12048361	0.120860048	0.106933997	0.109781934	0.12935425	0.102437983	0.123934306	0.104037878	0.108495207	0.12248214	0.125264064	0.131823124	0.0909844
6	cg00006414	0.030939062	0.019238754	0.021715651	0.013162699	0.018125106	0.024314687	0.019883573	0.014283214	0.018448821	0.017268119	0.017920511	0.018347118	0.018080366	0.0135911
7	cg00007981	0.069973968	0.071518078	0.06547106	0.071903687	0.091368001	0.050759477	0.029428944	0.056418546	0.045815471	0.037745957	0.041334305	0.0578533	0.035448784	0.0414555
8	cg00008493	0.992719199	0.993204428	0.992958316	0.993988096	0.990718175	0.993595553	0.99327851	0.996285623	0.992087621	0.99389629	0.994363283	0.99302085	0.995184558	0.9926722
9	cg00008713	0.02145768	0.020226023	0.018673253	0.016909791	0.016207283	0.01426383	0.01721178	0.018941862	0.019436096	0.018815147	0.015322217	0.019880511	0.017104402	0.0180181
10	cg00009407	0.010457567	0.005184467	0.00410315	0.006713128	0.007575285	0.005175612	0.005425126	0.006243924	0.006421381	0.006799044	0.00712126	0.007694335	0.006623017	0.0047533
11	cg00010193	0.634211887	0.635333579	0.620599352	0.639022421	0.599294514	0.590539149	0.594123614	0.583218964	0.610391875	0.630675269	0.618029489	0.616924493	0.61650951	0.5932585
12	cg00011459	0.96170754	0.967188015	0.955909118	0.937418814	0.960908386	0.930832805	0.940097614	0.962788358	0.951000443	0.949500837	0.942328237	0.9673508	0.930843457	0.9378551
13	cg00012199	0.007031004	0.005195848	0.00639629	0.007688353	0.003970845	0.00849436	0.006272251	0.004907457	0.00607382	0.005943509	0.005520571	0.008050619	0.007728826	0.0067846
14	cg00012386	0.027587839	0.03125253	0.020575688	0.020955178	0.023009528	0.015181802	0.018835012	0.023493109	0.027591573	0.016406037	0.030911096	0.023080923	0.024706833	0.0291678
15	cg00012792	0.025206845	0.025953047	0.031571295	0.025945964	0.027536842	0.023158617	0.025262766	0.025490522	0.02561854	0.023987126	0.029929646	0.032568497	0.026207177	0.0352271
16	cg00013618	0.945071544	0.934224335	0.935316359	0.940588786	0.938782958	0.933117967	0.927241412	0.92864055	0.932432338	0.926540548	0.937869607	0.928042666	0.929495965	0.9318707
17	cg00014085	0.009495937	0.009643207	0.011847067	0.015400896	0.01897439	0.009786809	0.014925778	0.009760714	0.010054093	0.015926945	0.014331222	0.019046581	0.013755507	0.0156381
18	cg00014837	0.965734173	0.950079573	0.943700392	0.953072542	0.945679056	0.947595491	0.947171104	0.957860813	0.943703295	0.942573182	0.933036452	0.937963811	0.93679047	0.9624001
19	cg00015770	0.085470689	0.07591741	0.093154564	0.096944626	0.073247299	0.072933254	0.072192273	0.079983018	0.072809565	0.063572793	0.06591072	0.118508921	0.101682977	0.0702284
20	cg00016968	0.778303626	0.798075556	0.707738283	0.658241403	0.706335634	0.692345324	0.672601042	0.667959776	0.725834887	0.664054437	0.752733409	0.667085618	0.741490368	0.6783292
21	cg00019495	0.135158094	0.197419621	0.424711078	0.327092736	0.146503801	0.382927703	0.380794573	0.52528796	0.294071968	0.28521308	0.225366886	0.331304412	0.213714575	0.2246721

<그림 5. Methylation data 파일 예시 (DNA Methylation Age Calculator)>

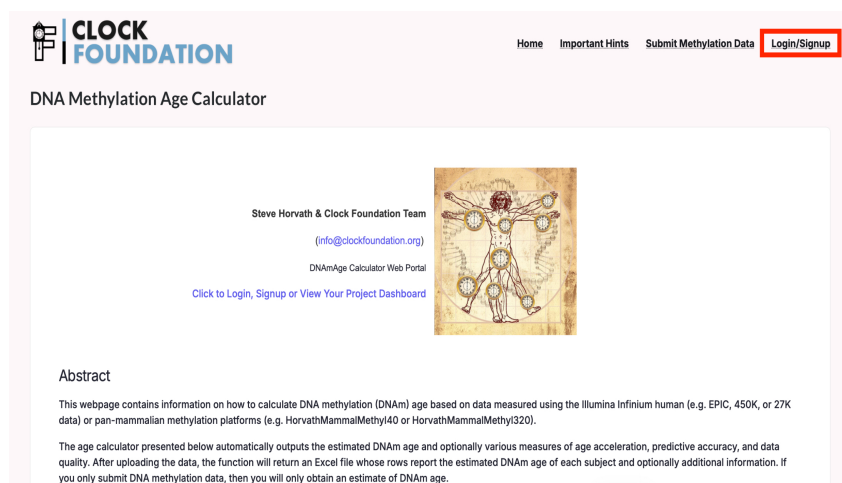
3

DNA methylation age 계산 방법

□ DNA Methylation Age Calculator 사용법

○ DNA Methylation Age Calculator 웹사이트를 통해 다양한 epigenetic age를 계산할 수 있음

- 브라우저에서 <https://dnamage.clockfoundation.org> 접속
- 초기 화면에서 “Login/Signup” 버튼을 클릭하여 회원가입 후 로그인



<그림 6. DNA Methylation Age Calculator 사이트 초기 화면>

- 메뉴의 “New Submissions” 버튼 클릭 후, 사용하는 메틸레이션 데이터 플랫폼 종류 선택 및 프로젝트 이름 입력

<그림 7. Submit Methylation Data: Enter Project Details>

- Sample Annotation 파일 업로드

- Sample Annotation 파일은 메틸화 데이터가 생성될 때 샘플 레이아웃 오류가 없는지 확인하는 등 QC 지표를 수행하는 데 사용됨
- 3GB 미만의 .csv 형식 파일만 업로드 가능

The screenshot shows the 'Submit Methylation Data' web interface. At the top, there's a navigation bar with 'Home', 'Important Hints', 'Submit Methylation Data', 'Dashboard', and 'Logout'. Below this, a progress bar indicates five steps: 1. Enter Project Details, 2. Provide Sample Data (current step), 3. Provide Methylation Data, 4. Analysis Upgrade Options (\$), and 5. Complete. The main content area is titled 'Submit Methylation Data' and features a section for 'Sample Annotation File *'. It includes a file selection button labeled '파일 선택' and a text input field. Below the input field, there's a note: 'Sample annotation files are used to perform QC metrics, including to ensure there were no sample layout errors when the methylation data was generated. One file only. 3 GB limit. Allowed types: csv.' At the bottom, there are two buttons: '< Previous' and 'Next >'.

<그림 8. Submit Methylation Data: Provide Sample Data>

- Methylation Data 파일 업로드

- 3GB 미만의 .zip 형식의 파일만 업로드 가능

The screenshot shows the 'Submit Methylation Data' web interface, Step 3: Provide Methylation Data. The progress bar at the top shows five steps: 1. Enter Project Details, 2. Provide Sample Data, 3. Provide Methylation Data (current step), 4. Analysis Upgrade Options (\$), and 5. Complete. The main content area is titled 'Submit Methylation Data' and features a section for 'Methylation Data (ZIP of IDAT files) *'. It includes a file selection button labeled '파일 선택' and a text input field. Below the input field, there's a note: 'Larger files (>1GB) can take [] to upload, depending on your internet connection. You can alternatively provide a web link below to pick-up your methylation data in the field below, if you're having trouble with uploading or simply prefer this method. One file only. 3 GB limit. Allowed types: zip.' Below this, there's a section for 'Link to Methylation Data (OPTIONAL)' with a text input field. Below that, there's a section for 'GEO Accession ID' with a text input field. At the bottom, there are two buttons: '< Previous' and 'Next >'.

<그림 9. Submit Methylation Data: Provide Methylation Data>

- 분석 업그레이드 옵션 선택 (유료 선택사항)
- 추가 품질관리, EWAS 분석 등 유료 옵션을 통해 추가 분석이 가능함

<그림 10. Submit Methylation Data: Analysis Upgrade Options(\$)>

- “Submit” 버튼을 클릭하여 파일을 제출함
- 파일 제출 후 며칠 이내에 결과 파일이 로그인한 이메일 주소로 전송됨
- 결과 파일에는 각 샘플별 다양한 epigenetic age 계산값이 포함됨

	CurrentName	FieldType	DNAmPrediction	AlternativeNames	Description
1	CurrentName				
2	SiD	SampleAnnotation	FALSE	SampleID	Sample ID used by Clock Foundation
3	OriginalOrderInBatch	SampleAnnotation	FALSE		Column-wise numeric order on plate during methylation processing or for original plate submission
4	Plate_Number	SampleAnnotation	FALSE		Microplate number upon methylation processing
5	Well_Address	SampleAnnotation	FALSE		Row and column on a microplate
6	Sentrix_ID	SampleAnnotation	FALSE		ID that represents the Illumina microarray or beadchip ID
7	Sentrix_Position	SampleAnnotation	FALSE		Position of sample on the beadchip including a row and column value
8	Age	SampleAnnotation	FALSE		Chronological age at time of sample collection
9	Tissue	SampleAnnotation	FALSE		Tissue or sample type provided, such as whole blood, PBMC, saliva, brain, liver, skin, etc.
10	Female	SampleAnnotation	FALSE		Female = 1, Male=0
11	Sex	SampleAnnotation	FALSE		Male or Female
12	Basename	SampleAnnotation	FALSE		Links to the Sample ID to the methylation array data. Basename combines the Sentrix_ID and Sentrix_Position.
13	Collection.Date	SampleAnnotation	FALSE		
14	Row	SampleAnnotation	FALSE		
15	Col	SampleAnnotation	FALSE		
16	Comment	QualityControl	FALSE		
17	noMissingPerSample	QualityControl	FALSE		The number of missing probes out of ~850K EPIC array probes. High numbers indicate low quality samples or different species.
18	meanMethBySample	QualityControl	FALSE		The mean beta value before normalization.
19	minMethBySample	QualityControl	FALSE		The minimum beta value before normalization.
20	maxMethBySample	QualityControl	FALSE		The max beta value before normalization.
21	corSampleVsGoldstandard	QualityControl	FALSE		High values indicate high sample quality. The measure is a Pearson correlation between each sample and average methylation pattern in a
22	meanAbsDifferenceSampleVsGoldstandard	QualityControl	FALSE		The mean absolute difference between the sample and a gold standard reference. A large value spells trouble and a comment will be added
23	meanXChromosome	QualityControl	FALSE		Mean beta value across the X chromosomal markers. This variable is used for predicting gender. Female samples should have a higher value
24	Alcohol	DNAm_Trait	TRUE		
25	Body Mass Index	DNAm_Trait	TRUE		
26	Body Fat %	DNAm_Trait	TRUE		
27	HDL Cholesterol	DNAm_Trait	TRUE		
28	Smoking	DNAm_Trait	TRUE		
29	Waist:Hip Ratio	DNAm_Trait	TRUE		
30	DNAmGait_noAge	DNAm_Trait	TRUE		
31	DNAmGrip_noAge	DNAm_Trait	TRUE		
32	DNAmVO2max	DNAm_Trait	TRUE		
33	DNAmGait_wAge	DNAm_Trait	TRUE		

<그림 11. 결과 파일 예시 (DNA Methylation Age Calculator)>

□ Epigenetic age acceleration이란?

- Epigenetic age acceleration(EAA)은 실제 나이를 고려하여 생물학적 노화의 가속 정도를 나타냄

□ EAA 계산 방법

- 상기 계산된 epigenetic age를 종속변수로, 실제 나이를 독립변수로 하는 선형 회귀분석의 잔차(residual)로 계산됨
 - 같은 나이를 가진 사람들의 평균 epigenetic age를 기준으로, 개인이 평균에서 얼마나 벗어나 있는지를 볼 수 있음
 - Horvath, Hannum, PhenoAge, GrimAge의 EAA 계산 (R 프로그래밍)

예시: GrimAge Acceleration

```
data$GrimAgeEAA <- lm(DNAMGrimAge ~ chronological age, data=data)$residual
```

- DunedinPACE 계산 (ENmix 패키지 사용)
 - DunedinPACE는 이미 노화 속도를 나타내는 지표이므로 별도의 잔차 계산 불필요

```
library(ENmix)
```

```
# beta: CpG site의 beta value matrix
```

```
mAGE <- methylAge(beta)
```

□ DNAmTL이란?

- DNAmTL은 텔로미어 길이(Telomere length)와 연관된 140개 CpG site의 메틸화 수준을 활용하여 계산된 텔로미어 길이 추정 가능한 후성유전학 바이오마커임

- 참고 논문: Lu AT et al. DNA methylation-based estimator of telomere length. Aging (Albany NY). 2019.

□ DNAmTL 계산 방법

- 140개 CpG의 메틸화 수준에 각각의 가중치를 곱하여 합산하는 선형 모델 형태로 실제 텔로미어 측정 단위와 동일한 kilobase(kb)를 사용함

$$DNAmTL = 7.92478005 + \sum_{i=1}^{140} \beta_i \times CpG_i, \beta_i : CpG \text{ 사이트의 가중치}$$

DNAmTL 계산 예시(R 코드)

DNAmTL_variable.xlsx: 논문에서 제공하고 있는 값이며, [별첨]에 있음

var_list: Elastic Net Regression을 통해 선택된 140개의 CpG 사이트와 가중치

epic1: 전처리가 완료된 Methylation data

```
var_list <- read_xlsx("DNAmTL_variable.xlsx")
```

intercept행 제거

```
var_list <- var_list[-1, ]
```

```
epic1 <- read.table("EPICv2_1_DNAmTL_CpG.txt")
```

```
epic1_t <- data.frame(t(epic1))
```

140개의 CpG 사이트 선택

```
epic1_t <- epic1_t[, var_list$Variable, drop=FALSE]
```

DNAmTL 계산

```
DNAmTL <- as.matrix(epic1_t) %*% var_list$Coefficient + 7.92478005
```


- Illumina Infinium 450K 또는 EPIC(850K) 메틸화 어레이 데이터 중, Elastic Net Regression 모델을 사용하여 선택된 140개의 CpG site 추출
- 추출된 CpG site의 전처리 및 정규화 진행 후 DNAmTL 계산

□ DNAmTLadjAge

- DNAmTL은 나이와 강한 음의 상관관계를 가지기 때문에 생물학적 노화 지표로 활용하기 위해 나이 보정을 수행함
- DNAmTLadjAge: DNAmTL을 종속변수로, 실제 연령을 독립 변수로 하여 선형 회귀 분석을 수행한 후 잔차를 구함
 - 양의 잔차: 나이 대비 텔로미어가 길어 생물학적으로 더 젊음을 의미
 - 음의 잔차: 나이 대비 텔로미어가 짧아 생물학적으로 노화가 진행됨을 의미

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- Levine ME. An epigenetic biomarker of aging for lifespan and healthspan. *Aging (Albany NY).* 2018 Apr 18;10:573-591.
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CpG site

출처: Lu AT et al. DNA methylation-based estimator of telomere length. Aging (Albany NY). 2019.

Variable	Coefficient	Variable	Coefficient
Intercept	7.92478005	cg01614102	-0.0009244
cg05528516	-0.0349019	cg20742385	0.00035546
cg00060374	0.19265502	cg05019423	0.06208786
cg12711627	0.17826976	cg19825410	0.0404215
cg06853416	0.05488373	cg02963381	-0.0823562
cg01901101	-0.2881372	cg00843787	-0.1013827
cg21393163	0.23130666	cg08107689	-0.0776044
cg22866430	-0.132384	cg04875128	-0.1023381
cg16047567	0.27831143	cg26709300	-0.2501914
cg18768612	0.03168893	cg27093918	0.08507297
cg24049493	-0.1480327	cg02282640	0.0883252
cg08893087	0.16454508	cg02380595	0.00225187
cg03984502	-1.5903597	cg04658841	-0.1441279
cg19233405	-0.2361275	cg07955474	0.04546008
cg05694771	-0.1190738	cg07708487	0.11330694
cg24739596	-0.0648983	cg00974523	0.01460735
cg06370057	-0.0479755	cg15825321	-0.0151549
cg24457743	0.04501349	cg14244013	-0.0670537
cg18148156	-0.3370151	cg25583580	0.25088276
cg19935065	-0.0719261	cg18826274	0.02758728
cg10549018	-0.1077919	cg18836174	0.30033869
cg24903144	-0.0287228	cg06994022	0.02997208
cg17782974	-0.2482773	cg19283806	0.11523472
cg13357922	0.11593384	cg23686403	0.4335783
cg23908305	0.19950832	cg02194396	0.05184491
cg15742496	0.06547325	cg07069844	-0.2229028
cg27639942	-0.0314091	cg00593900	-0.0890809
cg27312916	-0.3067828	cg13523818	0.01968372
cg02121547	0.05326649	cg26950531	-0.0719754
cg26827653	0.06589462	cg06673536	-0.0386957
cg16593899	0.35220048	cg19327213	-0.2615188
cg02319782	0.64659446	cg26636010	-0.0102656
cg26276120	0.23015357	cg10550416	-0.0011971
cg12745325	0.01925007	cg01603921	-0.0191199
cg07677157	0.02363594	cg23631636	1.06494378
cg07910460	-0.006545	cg07374224	-0.104763

Variable	Coefficient	Variable	Coefficient
cg06139893	0.36626756	cg07739478	0.04425225
cg09374293	0.27114748	cg08453194	0.67143634
cg21461082	0.0861276	cg21288889	-0.3193508
cg01239389	-0.0460397	cg17885226	-0.0297804
cg06845706	-0.0736532	cg06638568	-0.1418962
cg15223899	-0.0794693	cg20978460	0.62619401
cg00733150	-0.143119	cg03366574	-0.0009939
cg18405719	0.13249564	cg10536999	0.74322414
cg04508804	-0.0163919	cg08972170	-0.3827843
cg00840990	0.00929486	cg06132400	0.04816449
cg09217898	0.00222377	cg07076816	0.00224032
cg05023043	-0.2418849	cg00739278	0.06189469
cg19651128	-0.0441973	cg10691866	0.02216875
cg02810967	0.11554199	cg00277397	0.09497454
cg09435170	0.06657483	cg14989226	0.25274557
cg00580497	0.29459951	cg09596818	-0.0383243
cg00461022	-0.0035336	cg22633390	-0.0811874
cg22657457	0.01814921	cg03473532	0.01608011
cg10616795	0.01405961	cg00029246	0.08689729
cg06677021	-0.0278232	cg22530232	-0.0582999
cg02403883	-0.0261236	cg12133423	-0.0608059
cg21777188	-0.1309127	cg16479633	-0.3490548
cg03335262	-0.0439933	cg18898125	-0.1288619
cg27582059	-0.0133799	cg16886403	0.24983076
cg08985570	-0.0174455	cg07211259	0.2854159
cg27577149	-0.1097953	cg14577706	0.05640253
cg13650304	-0.0044991	cg00232500	0.0909359
cg19247475	-0.0195104	cg05072215	0.00554399
cg10679597	-0.0010193	cg13753488	0.01714544
cg18104870	-0.011462	cg13764516	-0.3415648
cg16867657	-0.9413173	cg07096038	-0.0985537
cg22328256	-0.0588772	cg16203368	-0.1030243
cg17636541	0.29341411	cg00780578	-0.0544718
cg01517384	0.01340956	cg16708895	-0.127514
cg27014438	0.06418881		