

基因、生活習慣與老化之關聯性

Associations of genes and lifestyle factors with aging

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實足年齡

Chronological age



年紀相仿，他/她為何看起來比較年輕？

若有詩書藏於心，歲月從不敗美人 《抱得美人歸》

生理年齡

Biological age

- 染色體頂端的「端粒」(telomere)長度 => 抽血進行 DNA 檢測
- Methylation age => 抽血驗特定基因位點的甲基化程度 (2021/08/21 talk)
- **Phenotypic age => 抽血驗腎功能指標 (creatinine)、肝功能指標 (albumin)、代謝功能指標 (fasting glucose) 等**

PhenoAge = Phenotypes + Age

- The third National Health and Nutrition Examination Survey (NHANES III)
- Levine *et al.* (*Aging*, 2018) used a Cox regularized regression model to regress the hazard of aging-related mortality on **42 clinical markers** and **chronological age**

Table 1. Phenotypic aging measures and Gompertz coefficients.

Variable		Units	Weight
Albumin	Liver	g/L	-0.0336
Creatinine	Kidney	umol/L	0.0095
Glucose, serum	Metabolic	mmol/L	0.1953
C-reactive protein (log)	Inflammation	mg/dL	0.0954
Lymphocyte percent 淋巴細胞百分比	Immune	%	-0.0120
Mean (red) cell volume 紅血球體積	Immune	fL	0.0268
Red cell distribution width 紅血球分布寬度	Immune	%	0.3306
Alkaline phosphatase	Liver	U/L	0.0019
White blood cell count 白血球數目	Immune	1000 cells/uL	0.0554
Age		Years	0.0804

免疫

Levine et al. (*Aging*, 2018)

Table 1. Phenotypic aging measures and Gompertz coefficients.

Variable			Units	Weight
Albumin	白蛋白 (肝功能)	Liver	g/L	-0.0336
Creatinine		Kidney	umol/L	0.0095
Glucose, serum		Metabolic	mmol/L	0.1953
C-reactive protein (log)		Inflammation	mg/dL	0.0954
Lymphocyte percent		Immune	%	-0.0120
Mean (red) cell volume		Immune	fL	0.0268
Red cell distribution width		Immune	%	0.3306
Alkaline phosphatase	鹼性磷酸酶	Liver	U/L	0.0019
White blood cell count		Immune	1000 cells/uL	0.0554
Age			Years	0.0804

Levine et al. (*Aging*, 2018)

Table 1. Phenotypic aging measures and Gompertz coefficients.

Variable		Units	Weight
Albumin	Liver	g/L	-0.0336
Creatinine	肌酸酐 (腎功能) Kidney	umol/L	0.0095
Glucose, serum	血糖值 (代謝) Metabolic	mmol/L	0.1953
C-reactive protein (log)	Inflammation	mg/dL	0.0954
Lymphocyte percent	C-反應蛋白 (發炎) Immune	%	-0.0120
Mean (red) cell volume	Immune	fL	0.0268
Red cell distribution width	Immune	%	0.3306
Alkaline phosphatase	Liver	U/L	0.0019
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Age	實足年齡	Years	0.0804

Levine et al. (*Aging*, 2018)

94,443 Taiwan Biobank Participants

PhenoAgeAccel			
TWB1			
	Regression		
	Coefficient	95% CI	<i>p</i> Value
Sex (female vs male)	-2.189	[-2.302, -2.076]	8.0×10^{-309}
BMI (kg/m ²)	0.177	[0.163, 0.191]	6.0×10^{-129}
Education (1-7)	-0.213	[-0.267, -0.159]	1.4×10^{-14}
Smoking (yes vs no)	1.134	[0.966, 1.303]	1.3×10^{-39}
Drinking (yes vs no)	0.640	[0.433, 0.847]	1.3×10^{-9}
Exercise (yes vs no)	-0.121	[-0.225, -0.017]	.023
<i>R</i> -square [†]		13.02%	

- 若有詩書藏於心，歲月從不敗美人 《抱得美人歸》

PhenoAgeAccel

TWB1

Regression

	Coefficient	95% CI	<i>p</i> Value
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- 平均而言，**男性**的老化速度較女性快約 **2.2** 年

PhenoAgeAccel			
TWB1			
Regression			
	Coefficient	95% CI	<i>p</i> Value
Sex (female vs male)	-2.189	[-2.302, -2.076]	8.0×10^{-309}
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Exercise (yes vs no)	-0.121	[-0.225, -0.017]	.023
<i>R</i> -square [†]		13.02%	

- 每上升一單位的 BMI, 平均老化快約 **0.18** 年

PhenoAgeAccel			
TWB1			
	Regression		
	Coefficient	95% CI	<i>p</i> Value
Sex (female vs male)	-2.189	[-2.302, -2.076]	8.0×10^{-309}
BMI (kg/m ²)	0.177	[0.163, 0.191]	6.0×10^{-129}
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- 抽菸催人老，平均約 **1.134** 年

PhenoAgeAccel			
TWB1			
	Regression		
	Coefficient	95% CI	<i>p</i> Value
Sex (female vs male)	-2.189	[-2.302, -2.076]	8.0×10^{-309}
BMI (kg/m ²)	0.177	[0.163, 0.191]	6.0×10^{-129}
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Drinking (yes vs no)	0.640	[0.433, 0.847]	1.3×10^{-9}
Exercise (yes vs no)	-0.121	[-0.225, -0.017]	.023
<i>R</i> -square [†]		13.02%	

- 喝酒催人老，平均約 **0.64** 年

PhenoAgeAccel			
TWB1			
Regression			
	Coefficient	95% CI	<i>p</i> Value
Sex (female vs male)	-2.189	[-2.302, -2.076]	8.0×10^{-309}
BMI (kg/m ²)	0.177	[0.163, 0.191]	6.0×10^{-129}
Education (1-7)	-0.213	[-0.267, -0.159]	1.4×10^{-14}
Smoking (yes vs no)	1.134	[0.966, 1.303]	1.3×10^{-39}
Drinking (yes vs no)	0.640	[0.433, 0.847]	1.3×10^{-9}
Exercise (yes vs no)	-0.121	[-0.225, -0.017]	.023
<i>R</i> -square [†]		13.02%	

- 有規律運動的人，平均年輕約 **0.12** 年

SNP	Chromosome	Base Pair	Gene	Effect Allele	Other Allele	Effect Allele Frequency (TWB1/TWB2)	Regression Coefficient (TWB1/TWB2)
PhenoAgeAccel							
rs1260326	2	27730940	<i>GCKR</i>	T	C	0.494/0.494	-0.201/-0.174
rs218265	4	55408999	—	C	T	0.326/0.336	0.231/0.151
rs11037480	11	5472472	<i>OR51B5</i>	C	T	0.013/0.016	-1.137/-0.969
rs1203979	16	261866	<i>LUC7L</i>	A	T	0.493/0.497	-0.323/-0.235
rs966965120	16	279723	<i>LUC7L</i>	A	G	0.113/0.111	-1.086/-1.026
rs56007737	16	287917	<i>FAM234A</i>	G	C	0.281/0.279	-0.381/-0.379
rs740000	16	319725	<i>FAM234A</i>	C	T	0.444/0.435	-0.285/-0.276
rs2685125	16	324403	<i>RGS11</i>	G	C	0.380/0.374	0.263/0.217
rs76038336	16	359611	<i>AXIN1</i>	C	G	0.065/0.060	-1.515/-1.847
rs1057209	16	381716	<i>AXIN1</i>	C	G	0.160/0.157	-0.591/-0.681
rs7206286	16	386179	<i>AXIN1</i>	G	A	0.349/0.340	-0.267/-0.285

Gene	Tissue
<i>FAM234A</i>	Visceral adipose (omentum)
<i>FAM234A</i>	Tibial artery
<i>FAM234A</i>	Lung
<i>FAM234A</i>	Spleen
<i>RGS11</i>	Adrenal gland
<i>RGS11</i>	Aorta artery
<i>RGS11</i>	Coronary artery
<i>RGS11</i>	Tibial artery
<i>RGS11</i>	Cells transformed fibroblasts
<i>RGS11</i>	Colon transverse
<i>RGS11</i>	Esophagus mucosa
<i>RGS11</i>	Left heart ventricle
<i>RGS11</i>	Lung
<i>RGS11</i>	Tibial nerve
<i>RGS11</i>	Skin—not sun exposed (suprapubic)
<i>RGS11</i>	Uterus

Conclusions

- **肥胖、抽菸**與飲酒皆顯著地與老化加速有關
- 教育、運動與老化減緩有關
- 平均而言，**男性**的老化速度較女性為快
- 許多健康相關表型，皆被發現男性的體染色體遺傳作用比女性來得強 (Lin *et al.*, 2020, *Human Molecular Genetics*)
- 低密度脂蛋白膽固醇、尿酸、空腹血糖值、糖化血色素等等

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Association Studies Article

ASSOCIATION STUDIES ARTICLE

Sex-specific autosomal genetic effects across 26 human complex traits

Wan-Yu Lin^{1,2,*†}, Chang-Chuan Chan^{2,3}, Yu-Li Liu⁴, Albert C. Yang^{5,6},
Shih-Jen Tsai^{6,7,8,‡} and Po-Hsiu Kuo^{1,2,*¶}

Research Article

Lifestyle Factors and Genetic Variants on 2 Biological Age Measures: Evidence From 94 443 Taiwan Biobank Participants

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Thank you for listening!