RESEARCH

DNA methylation associations with markers of inflammation in elderly men

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Abstract

Background: Epigenetic alterations are one of the hallmarks of aging, as age-related changes have been observed with various epigenetic markers, such as DNA methylation and post-translational modification of histones. Epigenome-wide association studies (EWAS) take an unbiased approach and test each DNA methylation marker for trait association. EWAS have found that specific DNA methylation sites in blood are associated with markers of inflammation, namely, C-reactive protein (CRP). CRP is also associated with multiple age-related conditions and diseases; thus, identifying molecular associations with CRP could help elucidate mechanisms important for aging. In this study, we report an EWAS of multiple markers of inflammation in elderly men and we examine whether biological aging defined by DNA methylation is associated with inflammation markers.

Methods: DNA methylation was assayed using the Illumina Infinium MethylationEpic array using DNA isolated from whole blood.

Results: Text

Conclusions:

Keywords: EWAS; CRP

Content

Text and results for this section, as per the individual journal's instructions for authors.

Section title

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In this section we examine the growth rate of the mean of Z_0, Z_1 and Z_2. In addition, we examine a common modeling assumption and note the importance of considering the tails of the extinction time T_x in studies of escape dynamics. We

will first consider the expected resistant population at vT_x for some $v > 0$, (and temporarily assume $\alpha = 0$)

$$E\big[Z_1(vT_x)\big] = \int_0^{v\wedge 1} Z_0(uT_x)\exp(\lambda_1)\,du.$$

If we assume that sensitive cells follow a deterministic decay $Z_0(t) = xe^{\lambda_0 t}$ and approximate their extinction time as $T_x \approx -\frac{1}{\lambda_0}\log x$, then we can heuristically estimate the expected value as

$$\begin{aligned} &E\big[Z_1(vT_x)\big] \\ &\quad = \frac{\mu}{r}\log x \int_0^{v\wedge 1} x^{1-u}x^{(\lambda_1/r)(v-u)}\,du. \end{aligned} \tag{1}$$

Thus we observe that this expected value is finite for all $v > 0$ (also see [1, 2, 3, 4, 5, 6]).

```
eset_Mvals <- read_rds("../data/formatted/eset_Mvals_clean.rds")
f_dat <- fData(eset_Mvals)
sum(f_dat$CVprobe >= 100)
## [1] 5532
sum(f_dat$CVprobe < 100)
## [1] 684481
eset_Mvals <- eset_Mvals[f_dat$CVprobe < 100,]
core_vars <- c("ID", "SITE", "V3AGE1")
outcome_var <- c("CYCRPJH", "CYTNFR2JH", "CYIFNGJH", "CYIL1BJH", "CYIL6JH", "CYTNFJH")

p_dat1 <- pData(eset_Mvals)
pheno <- read_csv("../data/pheno/INFLAME.CSV") %>%
        select(ID, SITE, CYCRPJH, LALYMP)
##
## -- Column specification --------------------------------------------------------
## cols(
##   .default = col_double(),
##   SITE = col_character(),
##   ID = col_character()
## )
## i Use `spec()` for the full column specifications.
phenoV3 <- read_csv("../data/pheno/v3feb21.csv", guess_max = 4682)
##
## -- Column specification --------------------------------------------------------
## cols(
##   .default = col_double(),
##   ID = col_character(),
##   V3DATE = col_character(),
##   V3HVDATE = col_character(),
##   SITE = col_character(),
```

```
##   GISEDOD = col_character(),
##   CISTAFF = col_character(),
##   LSSTAFF = col_character(),
##   TMSTAFF = col_character(),
##   TBSTAFF = col_character(),
##   HWSTAFF = col_character(),
##   GSSTAFF = col_character(),
##   NFCSTAFF = col_character(),
##   NFWSTAFF = col_character(),
##   BPAASTAF = col_character(),
##   NPSTAFF = col_character(),
##   BPSTAFF = col_character(),
##   SCSTAFF = col_character(),
##   SCUSTAFF = col_character(),
##   V3AMSTF = col_character(),
##   TMTIMEM = col_time(format = "")
##   # ... with 1 more columns
## )
## i Use `spec()` for the full column specifications.
phenoV3 <- phenoV3 %>%
        select(ID, HWBMI, TURSMOKE, V3AGE1)
pheno2 <- inner_join(pheno, phenoV3, by = "ID") %>%
        mutate(SITE = as.factor(SITE),
               TURSMOKE = factor(as.character(TURSMOKE), levels = c("0", "1", "2"),
                                 labels = c("never", "former", "current"))
               )

#Work on CRP right now. Make loop for other inflammatory markers later.
p_dat <- p_dat1 %>%
  left_join(pheno2, c("Sample_Name" = "ID")) %>%
  arrange(sampOrder)
map_int(p_dat, function(x) sum(is.na(x)))
```

```
#Must remove missings from eset and pData
mykeep <- !is.na(p_dat$SITE) & !is.na(p_dat$V3AGE1) & !is.na(p_dat$HWBMI) & !is.na(p_dat$TURSMO
eset_Mvals_mod <- eset_Mvals[, mykeep]
p_dat <- p_dat[mykeep, ]
dim(eset_Mvals_mod)


dim(p_dat)
```

```r
#Make table 1
p_dat %>%
        summarize(mean_CRP = mean(CYCRPJH), sd_CRP = sd(CYCRPJH)) %>%
        kable()
```

mean_CRP	sd_CRP
3.010294	4.000611

Appendix

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Acknowledgements
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Abbreviations
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Availability of data and materials
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Authors' contributions
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Figures

Figure 1 Sample figure title

Figure 2 Sample figure title

Table 1 Sample table title. This is where the description of the table should go

	B1	B2	B3
A1	0.1	0.2	0.3
A2	...	..	.
A3	..	.	.

Tables

Additional Files

Additional file 1 — Sample additional file title
Additional file descriptions text (including details of how to view the file, if it is in a non-standard format or the file extension). This might refer to a multi-page table or a figure.

Additional file 2 — Sample additional file title
Additional file descriptions text.