Table S1A Blood cell type proportion in Tsimane Amerindians

Cell type	Gran	CD4+T	NK	Mono	Bcells	CD8+T
Mean	0.65	0.14	0.08	0.08	0.06	0.05
SD	0.10	0.06	0.05	0.02	0.03	0.04
Mean/SD	6.3	2.1	1.7	3.1	2.1	1.3

Older Tsimane cohort (n=310) from [Hovarth et al. Genome Biology (2016) 17:171]. GEO accession no. GSE72773.

Table S1B Blood cell type proportion in Caucasians

Cell type	Gran	CD4+T	NK	Mono	Bcells	CD8+T
Mean	0.68	0.13	0.07	0.08	0.05	0.04
SD	0.10	0.06	0.04	0.02	0.05	0.05
Mean/SD	6.6	2.2	1.7	3.3	1.1	1.0

Caucasians among the PEG cohort (n=289) from [Hovarth et al. Genome Biology (2016) 17:171]. GEO accession no. GSE72775.

Table S1C Blood cell type proportion in Hispanics

Cell type	Gran	CD4+T	NK	Mono	Bcells	CD8+T
Mean	0.67	0.10	0.09	0.08	0.06	0.05
SD	0.12	0.05	0.04	0.02	0.06	0.04
Mean/SD	5.8	1.9	2.1	3.6	1.0	1.2

Hispanics among the PEG cohort (n=46) from [Hovarth et al. Genome Biology (2016) 17:171]. GEO accession no. GSE72775.

Additional file 2: Supplementary note

Asymptotic distribution of ridge estimator

We here show that the ridge estimator $\widehat{\boldsymbol{\theta}}(\lambda)$ is asymptotically normally distributed with the mean and variance in equations (9) and (10). Since the ridge estimator minimizes formula (8), its partial derivatives equal zero:

$$\left(f(Y) - \boldsymbol{\mu}(\widehat{\boldsymbol{\theta}}(\lambda))\right) \cdot \left(\frac{\partial \boldsymbol{\mu}\left(\widehat{\boldsymbol{\theta}}(\lambda)\right)}{\partial \boldsymbol{\theta}}\right) - \lambda \begin{pmatrix} O & O & O \\ O & I & O \\ O & O & O \end{pmatrix} \widehat{\boldsymbol{\theta}}(\lambda) = \mathbf{0}, \quad \text{(A1)}$$

where the product of $f(Y) - \boldsymbol{\mu}(\boldsymbol{\theta})$ and the following Jacobian is taken by multiplying for each sample and then summing up over samples. The Taylor series of $\boldsymbol{\mu}$ and its Jacobian with regards to the variable $\widehat{\boldsymbol{\theta}}(\lambda)$ centered at the true parameter value $\boldsymbol{\theta}$ become

$$\boldsymbol{\mu}\left(\widehat{\boldsymbol{\theta}}(\lambda)\right) \approx \boldsymbol{\mu}(\boldsymbol{\theta}) + \left(\frac{\partial \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right)\left(\widehat{\boldsymbol{\theta}}(\lambda) - \boldsymbol{\theta}\right),$$

$$\left(\frac{\partial \boldsymbol{\mu}\left(\widehat{\boldsymbol{\theta}}(\lambda)\right)}{\partial \boldsymbol{\theta}}\right) \approx \left(\frac{\partial \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right) + \left(\frac{\partial^2 \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta} \partial \boldsymbol{\theta}^T}\right)\left(\widehat{\boldsymbol{\theta}}(\lambda) - \boldsymbol{\theta}\right),$$

where second or higher order terms of $\widehat{\boldsymbol{\theta}}(\lambda) - \boldsymbol{\theta}$ are neglected. By plugging into equation (A1), we obtain

$$\left(f(Y) - \boldsymbol{\mu}(\boldsymbol{\theta})\right) \cdot \left(\frac{\partial \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right) - \left\{\left(\frac{\partial \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right)^T \left(\frac{\partial \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right) - \left(f(Y) - \boldsymbol{\mu}(\boldsymbol{\theta})\right) \cdot \left(\frac{\partial^2 \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta} \partial \boldsymbol{\theta}^T}\right)\right\}\left(\widehat{\boldsymbol{\theta}}(\lambda) - \boldsymbol{\theta}\right)$$

$$-\lambda \begin{pmatrix} O & O & O \\ O & I & O \\ O & O & O \end{pmatrix} \widehat{\boldsymbol{\theta}}(\lambda) = \mathbf{0}.$$

Thus,

$$\widehat{\boldsymbol{\theta}}(\lambda) = Q(\lambda)^{-1}\, Q(0)\, \boldsymbol{\theta} + Q(\lambda)^{-1} \left\{\left(f(Y) - \boldsymbol{\mu}(\boldsymbol{\theta})\right) \cdot \left(\frac{\partial \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right)\right\}$$

$$= Q(\lambda)^{-1}\, Q(0)\, \boldsymbol{\theta} + Q(\lambda)^{-1} \left(\frac{\partial \boldsymbol{\mu}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right)^T \boldsymbol{\varepsilon},$$

where $\boldsymbol{\varepsilon} \sim N(\mathbf{0}, \sigma^2 I)$.