

## Supplementary Information 1

### Linear models used for the EWAS of smoking in different brain regions

#### **anterior cingulate cortex (ACC) + putamen (PUT):**

$$\begin{aligned} DNAm \sim & \text{smoking status} + \text{age} + \text{sex} + \text{PMI} + \text{neuronal cell fraction} + \text{AUD status} \\ & + PC1_{cp} + PC2_{cp} + PC3_{cp} + PC4_{cp} + PC5_{cp} + PC6_{cp} + PC7_{cp} + PC8_{cp} \\ & + PC9_{cp} + PC10_{cp} \end{aligned}$$

#### **Brodmann Area 9 (BA9):**

PC1<sub>cp</sub> and PC7<sub>cp</sub> removed due to multicollinearity

$$\begin{aligned} DNAm \sim & \text{smoking status} + \text{age} + \text{sex} + \text{PMI} + \text{neuronal cell fraction} + \text{AUD status} \\ & + \text{batch} + PC2_{cp} + PC3_{cp} + PC4_{cp} + PC5_{cp} + PC6_{cp} + PC8_{cp} + PC9_{cp} \\ & + PC10_{cp} + PC1_{geno} + PC2_{geno} + PC3_{geno} + PC4_{geno} \end{aligned}$$

#### **caudate nucleus (CN) + ventral striatum (VS):**

PC5<sub>cp</sub> removed due to multicollinearity

$$\begin{aligned} DNAm \sim & \text{smoking status} + \text{age} + \text{sex} + \text{PMI} + \text{neuronal cell fraction} + \text{AUD status} \\ & + \text{batch} + PC1_{cp} + PC2_{cp} + PC3_{cp} + PC4_{cp} + PC6_{cp} + PC7_{cp} + PC8_{cp} \\ & + PC9_{cp} + PC10_{cp} \end{aligned}$$