

## **Supplemental Material**

**Supplementary Method.**

**Supplementary Table 1.** Description of the cohort.

**Supplementary Table 2.** Smoking-associated (BS, 5mC and 5hmC) differentially methylated CpGs in Multiple Sclerosis (MS) patients and healthy controls (HC).

**Supplementary Table 3.** Overlapping smoking-associated BS-DMPs in Multiple Sclerosis (MS) between BAL cells and whole blood.

**Supplementary Table 4.** Gene ontology analyses.

**Supplementary Table 5.** Differentially expressed genes between Multiple Sclerosis (MS) patients and healthy controls (HC).

**Supplementary Figures. Supplementary Figure 1.** Analytical workflow. **Supplementary Figure 2.** Overlapping smoking-associated DMPs between Multiple Sclerosis (MS) patients and healthy controls (HC). **Supplementary Figure 3.** Smoking effect in blood and BAL BS-DMPs of MS individuals. **Supplementary Figure 4.** Distribution of smoking-associated changes in Multiple Sclerosis (MS) patients and healthy controls (HC) across gene features. **Supplementary Figure 5.** Gene ontology (GO) analysis of overlapping and non-overlapping smoking-associated BS, 5mC and 5hmC changes in MS patients.