

PM_{2.5} Interferes With Peripheral Amyloid- β Clearance Via An Albumin-centered Exposure Interface

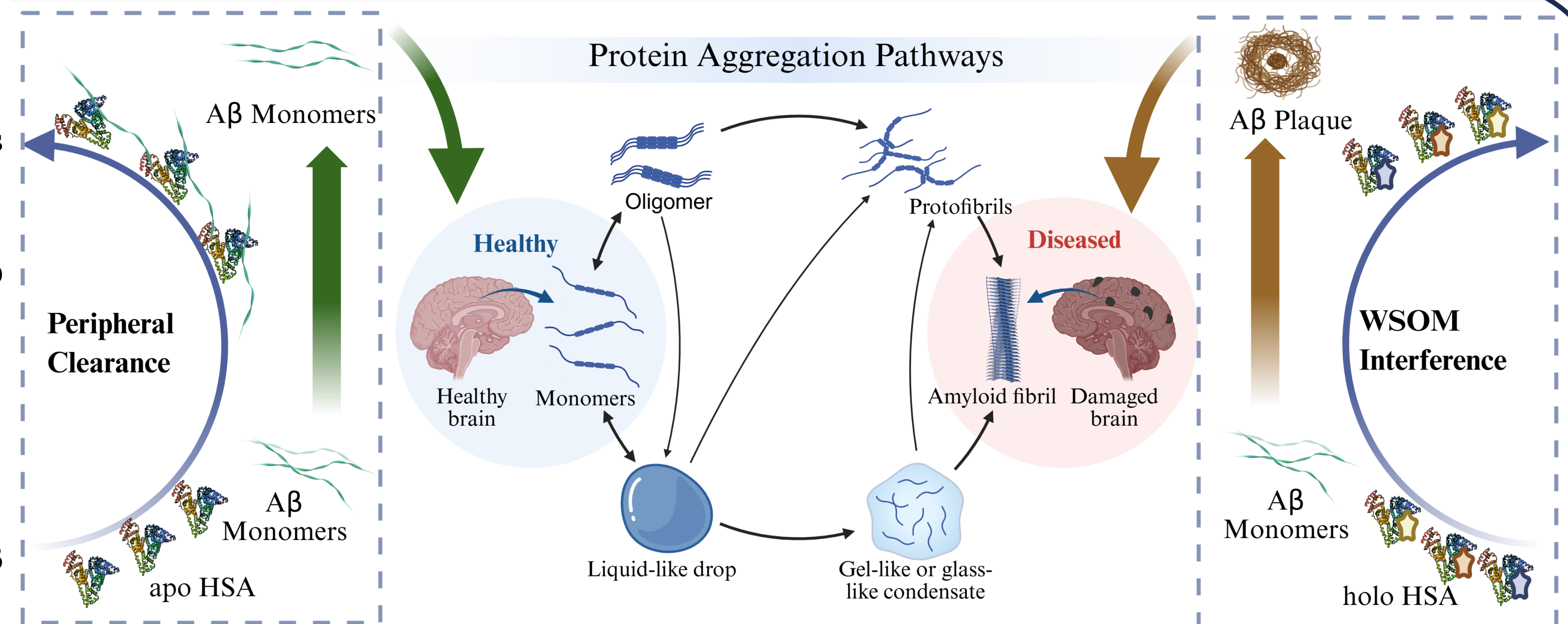
Yaling Zeng

Southern University of Science and Technology

E-mail: zengyl@sustech.edu.cn

Background

- ◆ Alzheimer's disease (AD) is a growing global burden, making modifiable risk factors critical for prevention.
- ◆ Long-term PM_{2.5} exposure is consistently linked to cognitive decline and higher AD risk.
- ◆ Impaired A β clearance is a key bottleneck in AD progression.
- ◆ HSA binds most circulating A β and regulates its peripheral transport and elimination.
- ◆ PM_{2.5} chemical complexity obscures the molecular pathway linking exposure to A β clearance.

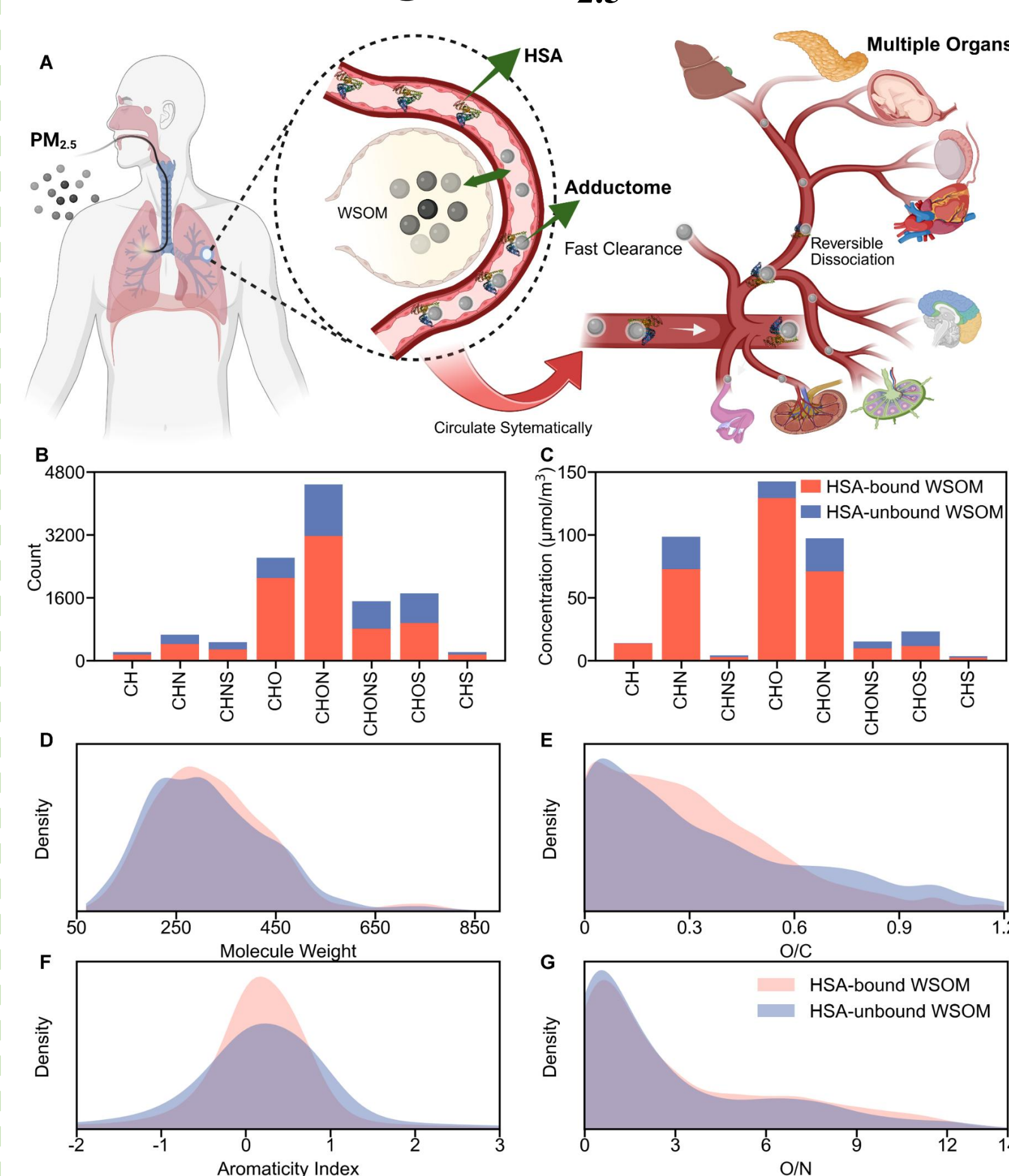


Methods

- ◆ Urban ambient PM_{2.5} samples were collected from representative sites in China.
- ◆ PM_{2.5} water-soluble molecular composition was characterized by non-targeted high-resolution mass spectrometry.
- ◆ SPR quantified WSOM-HSA binding and apo-HSA versus holo-HSA differences in A β binding, with PLSR attributing both responses to individual molecules.
- ◆ Molecular docking and 100-ns molecular dynamics simulations characterized WSOM-HSA binding poses and their effects on HSA-A β complexes.

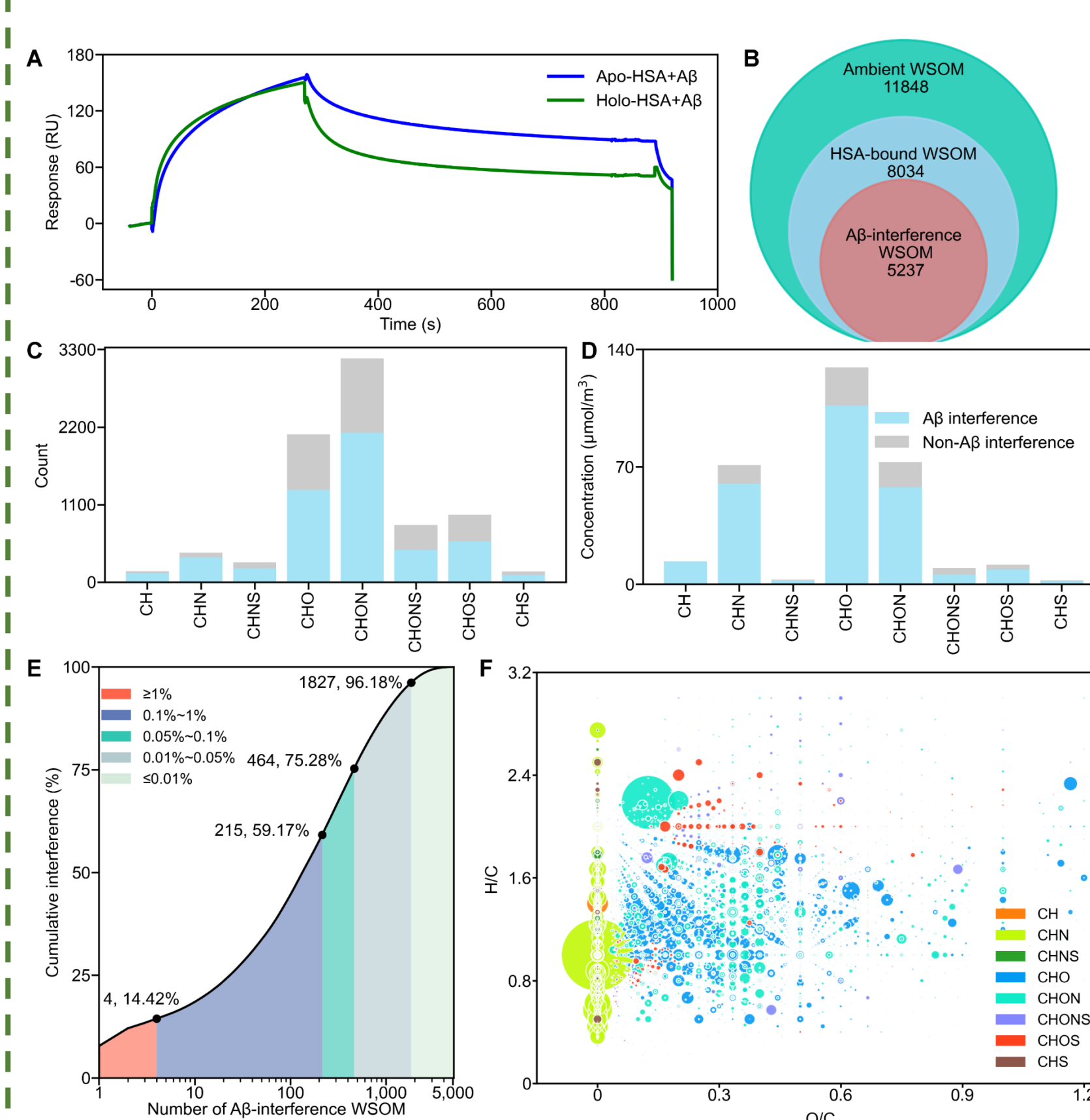
Findings

Selective binding of PM_{2.5} WSOM to HSA



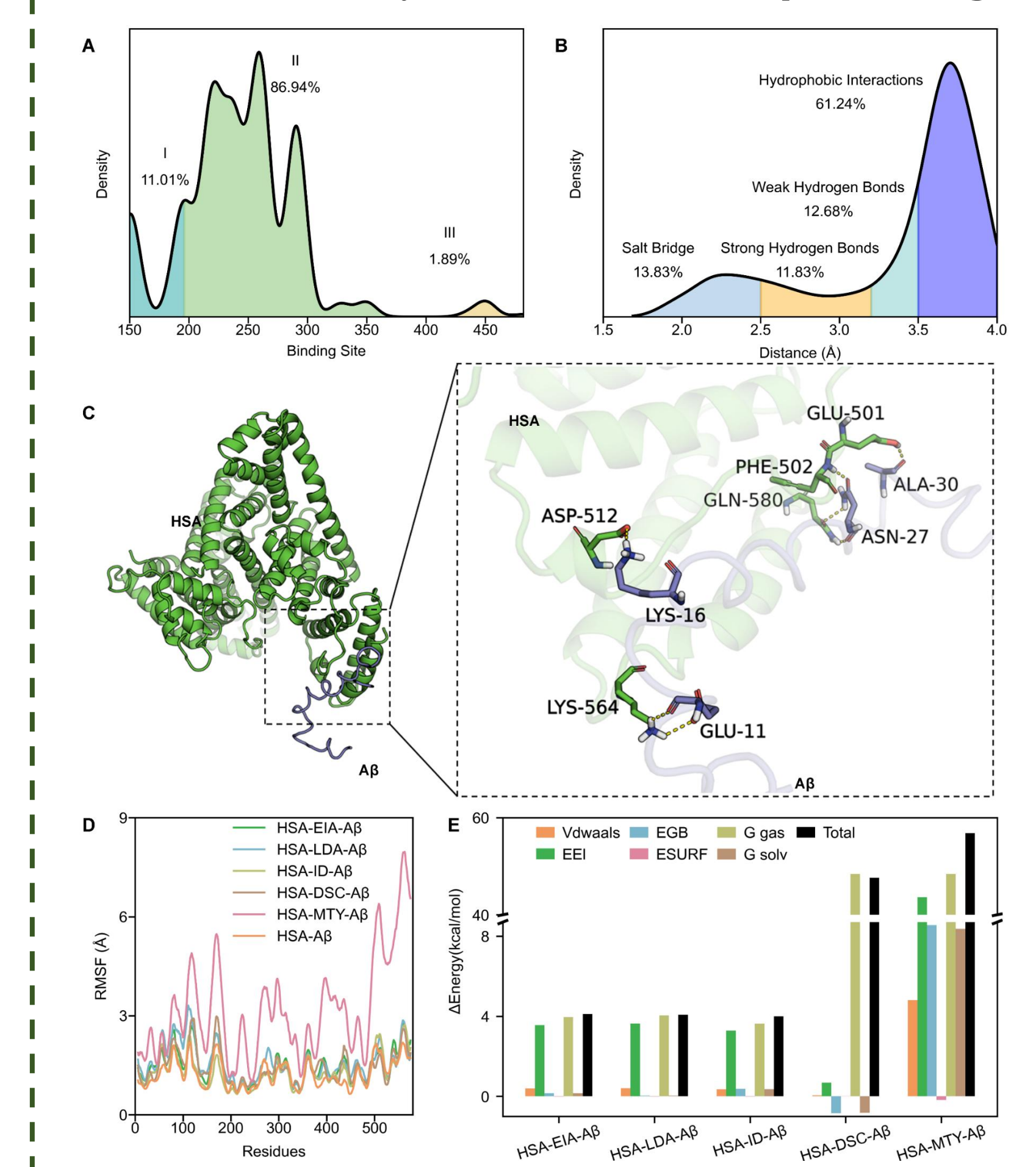
- PM_{2.5} profiling identified 11,848 WSOM, including 8,034 HSA-bound molecules.
- Oxygen-containing species dominated the HSA-bound molecular pool.
- HSA-bound WSOM favored moderate MW, low aromaticity, and low O/N.

Disproportionate control of HSA-A β binding



- WSOM interference showed dose-dependent reduction of HSA-A β binding.
- 5,237 HSA-bound molecules contributed to A β -binding interference.
- CHN and CHO dominated functional interference with skewed contributions.

WSOM remotely weaken HSA-A β binding



- WSOM bind mainly to HSA domain II, away from the A β -binding interface.
- WSOM interfere through allosteric effects rather than direct site competition.
- MD showed WSOM loosen HSA structure and destabilize HSA-A β binding.