DOCTORAL THESIS

Reactive oxygen species generation and gene expression linked to sources of atmospheric fine particulate matter ($PM_{2.5}$) in Hong Kong

Cheng, Yubo

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Abstract

Fine particulate matter ($PM_{2.5}$) is the leading public health risk factor of global disease burden, which has caused 4.2 million deaths in 2015. This thesis aims to improve the scientific understanding on the sources and health impacts of $PM_{2.5}$ in Hong Kong. Various chemical and biological analytical techniques were applied to characterize the chemical and toxicological properties of $PM_{2.5}$ samples collected in Hong Kong during 2011-2012. Positive matrix factorization (PMF), together with the quantified chemical markers and water-soluble $PM_{2.5}$-induced reactive oxygen species (ROS) activity as the input matrix, was performed to apportion the source-specific contributions to ambient organic carbon (OC) and the oxidative potential of water-soluble $PM_{2.5}$. Zebrafish was applied as in-vivo model to evaluate the $PM_{2.5}$-induced differential expression genes (DEGs). An L_2-normaliztion integrated PMF was developed and applied to quantitatively assess the ability of $PM_{2.5}$ to induced DEGs in relation to various sources and chemical compositions of $PM_{2.5}$. The main findings are summarized below:

(1) Thirty nine primary organic aerosol (POA) and secondary organic aerosol (SOA) markers of various anthropogenic (i.e. biomass burning (BB)) and biogenic sources (i.e. isoprene, monoterpenes and β-caryophyllene) were identified and quantified. High levels of OC and SOA markers were observed on regional pollution days than long regional transport (LRT) pollution and local emissions days. A kinetic model (Kintecus) was applied to explore the major formation channels of isoprene SOA, and it was found that isoprene SOA was mainly

formed through the ring-opening reaction of isoprene epoxydiols (IEPOX) in Hong Kong.

(2) PMF analysis, together with the chemical markers measured in Chapter 1 &2, was performed to evaluate the sources of OA in Hong Kong. Sea salt, marine vessels, vehicle emissions, BB/SOA, SOA, and secondary sulfate (SS) were apportioned as the major sources of ambient OC in Hong Kong. Secondary formation, including SOA, BB aging and SS sources, was found to be the major contributor to OC (~51%) throughout the whole year. BB was the major anthropogenic contributor to OC on regional days (28.8%); while marine vessel was the dominated primary source of OC on local days (33.2%). SOC concentrations were estimated using a tracer-based method (SOC_{TBM}) and PMF (SOC_{PMF}). Both SOC_{TBM} and SOC_{PMF} showed highest concentrations on regional days (SOC_{TBM}: 0.74 μg m^{-3}; SOC_{PMF}: 3.27 μg m^{-3}). Among all SOA precursors, monoterpenes had the most abundant contribution (40.9%) to SOC_{TMB} during the whole year. Moreover, sulfate has significant impacts on SS-related SOC and SOA from monoterpenes and naphthalene. Particle acidity (H^{P+}) showed correlation with SOC from BB aging. These results provide us a quantitative understanding on the SOA origins in the region, which lays a foundation for the source apportionment of $PM_{2.5}$-induced toxicity in the following chapters.

(3) Cell-free dithiothreitol (DTT) and ·OH generation assays were applied to measure the ROS activity induced by water-soluble $PM_{2.5}$ collected in Hong Kong during 2011-2012. Different levels of ROS activity were observed for different chemical

fractions of $PM_{2.5}$ and $PM_{2.5}$ from various sources. Six factors, i.e. SS, BB, SOA, vehicle emissions, marine vessels and metal factors were apportioned by PMF as the major sources of water-soluble $PM_{2.5}$ induced ROS potential. Metal factors was found to be the major contributor to both DTT activity (39.1%) and ·OH generation ability (84.5%) throughout the year, especially on LRT (DTT: 54.8%; ·OH generation: 91.1%) and regional days (DTT: 53.9%; ·OH generation: 87.7%). On local days, contribution of marine vessels to DTT oxidation become more significant (48.7%), however its contribution to ·OH generation is negligible. Metal factors is by far the most significant contributor to ·OH generation, even on local days (73.1%). It is interesting to note that all six PMF-resolved sources are associated with DTT oxidation, however only three sources (i.e. metal factor, vehicle emissions and SOA) showed contributions to ·OH generation. Moreover, among these six sources, marine vessels exhibited the highest intrinsic DTT ability; while metal factor was the most effective source in ·OH generation.

(4) Zebrafish embryo (AB strain) was applied as the *in-vivo* model to assess $PM_{2.5}$ toxicity in Hong Kong through genome-wide gene transcriptional analysis. The results showed that embryonic exposure to $PM_{2.5}$ could induce remarkable changes in gene expression patterns in zebrafish. DEGs between $PM_{2.5}$ extract treated and untreated zebrafish embryo samples were identified, and they were found mainly associated with responses to xenobiotic stimulus, and muscle and heart development and functions. The correlation analysis between co-expressed gene modules and chemical species of $PM_{2.5}$ implied the different chemical

compositions and sources of $PM_{2.5}$ have significant influences on the $PM_{2.5}$-induced biological responses.

(5) An L_2-normalizaiton integrated PMF was developed to analyze the high throughput biological and chemical data simultaneously, which quantitatively evaluated the ability of $PM_{2.5}$ to induce DEGs in relation to sources and compositions. In this chapter, nine sources associated with $PM_{2.5}$-induced DEGs were well apportioned, i.e. fresh sea salt, aged sea salt, SS, SOA, BB, coal combustion, vehicle emissions, marine vessels and metal factors. Among these sources, metal factors (annual mean: 26.5%, range: 17.6-39.3%) and vehicle emissions (annual mean: 16.3%, range: 0.0-25.3%) are the two leading contributors to $PM_{2.5}$-induced DEGs levels. $PM_{2.5}$ from combustion related sources (e.g. vehicle emissions, metal factors, BB) and sea salt exhibited stronger ability to induce DEGs than those from secondary sources. Although secondary formation (including SOA and SS) has a significant contribution to ambient $PM_{2.5}$ (12 μg m^{-3}, 40%), its capacity of DEGs induction is quite low. Moreover, several biological functions and pathways influenced by $PM_{2.5}$ from various sources have also been well evaluated.

In this study, large scales of biological and chemical data were analyzed for the first time by a L_2-normalizaiton integrated PMF to apportion the $PM_{2.5}$-induced DEGs, and this thesis work firstly reported the major sources of water-soluble $PM_{2.5}$-induced ROS in Hong Kong. Results from this study provide a scientific basis for the prediction of $PM_{2.5}$-associated adverse health outcomes and can help the policy

makers to formulate cost-effective and targeted $PM_{2.5}$ mitigation strategies to protect public health.

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