科学通报 2018 年 第 63 卷 第 10 期: 968 ~ 978
《中国科学》杂志社
SCIENCE CHINA PRESS
香山科学会议 专栏 评 述
第600次学术讨论会 •生物气溶胶与人类健康、国家生物安全及大气污染

# 大气颗粒物生物化学组分的促炎症效应研究进展

申芳霞*, 朱天乐, 牛牧童

北京航空航天大学空间与环境学院, 北京 102206
* 联系人, E-mail: fxshen@buaa.edu.cn

2017-10-11 收稿, 2017-11-15 修回, 2017-11-15 接受, 2017-12-07 网络版发表
国家重点研发计划(2017YFC0702800)、环境模拟与污染控制国家重点联合实验室专项经费(17K07ESPCP)和北京航空航天大学卓越百人专项经费(ZG216S17A6)资助

**摘要** 大气污染物暴露与呼吸系统疾病、心脑血管疾病、神经退化性疾病之间的关系, 已被大量流行病学和基于动物、细胞的毒理学所确认. 促炎症效应是污染物尤其是颗粒物影响健康的重要机制之一. 然而, 颗粒物通过何种过程引起炎症效应, 哪些组分是促炎症效应的关键因子, 依然不清楚. 多环芳烃、重金属等化学组分对颗粒物促炎症效应的贡献已有大量报道. 细菌、真菌、病毒、花粉等微生物及其碎片构成的生物气溶胶, 基于其配体特征, 在激活免疫系统引起炎症反应方面有独有的"优势". 但由于对生物气溶胶进行在线监测分析有较大困难, 导致缺乏对其种类、浓度等特征的全面了解, 从而限制了对颗粒物中生物组分促炎症效应的认识. 本文简单总结了大气颗粒物的促炎症效应, 从炎症效应机制、不同组分的炎症效应及生物化学组分协同作用3个方面进行了归纳, 并提出了开展大气污染健康效应研究的几点新的研究思路和方向建议.

**关键词** 颗粒物, 生物气溶胶, 化学组分, 炎症效应, 协同炎症效应, 氧化损伤

20世纪30年代开始, 比利时马斯河谷烟雾、伦敦烟雾、洛杉矶光化学烟雾等公害事件不断爆发, 造成成千上万人死亡, 直接促进了世界各地清洁空气法案的通过和实施. 但是在此阶段人们对气污染健康效应的关注点主要集中于突发性的大规模污染事件. 20世纪90年代起美国的两项队列研究开启了气污染与人体健康研究的新阶段, 人们逐渐意识到较低水平的污染(相对于伦敦烟雾事件等)对健康也有不可忽视的影响. 心脑血管疾病(血管硬化、中风等)、呼吸系统疾病、肺癌、肝损伤等非呼吸系统疾病、寿命缩短的现状与气污染之间的因果关系越来越明确[1~7]. 以心血管疾病为例, 短到几小时至几周的$PM_{2.5}$(粒径小于2.5 μm的大气细颗粒物)暴露, 可导致死亡率上升, 长期暴露可导致寿命缩减多达几年, 而降低$PM_{2.5}$浓度可有效降低上述风险[8]. $PM_{2.5}$质量浓度每升高10 μg/m$^3$, 造成人体收缩压升高1.4 mmHg(1 mmHg= 1.013×10$^5$ Pa), 脉搏压升高1.0 mmHg, 动脉压升高0.8 mmHg, 同时10 ppb(20.53 μg/m$^3$)的二氧化氮($NO_2$)上升伴随着0.4 mmHg的脉冲压上升, 一定程度上解释了当前心脑血管疾病发病率和致死率不断上升的问题[9]. 儿童作为易感人群, $PM_{2.5}$, 二氧化硫($SO_2$), $NO_2$等污染物暴露造成的哮喘、心脑血管疾病患病风险上升[10~12]. 此外, 关于气污染与阿尔茨海默症等神经退化性疾病关系的研究也越来越多, 2015

**引用格式**: 申芳霞, 朱天乐, 牛牧童. 大气颗粒物生物化学组分的促炎症效应研究进展. 科学通报, 2018, 63: 968–978
Shen F X, Zhu T L, Niu M T. Pro-inflammatory effects of airborne particulate matters in relation to biological and chemical composition (in Chinese). Chin Sci Bull, 2018, 63: 968–978, doi: 10.1360/N972017-01063

年的一项研究表明长期暴露于$PM_{2.5}$可导致神经退化性疾病的第一次门诊时间提前[13~16]. 每年因$PM_{2.5}$暴露过早死亡的人数超过300万人[17].

基于呼吸道上皮细胞、肺部巨噬细胞、胶质细胞、动物等毒理学实验和流行病学研究开展了大量大气污染的健康影响机制研究, 结果表明局部炎症、系统性炎症、神经性炎症等是重要的病理学机制, 其中污染物的氧化能力及其在人体肺部造成的氧化压力对机体内氧化还原平衡和局部及系统性炎症免疫反应有重要影响[4,18~23]. 尽管如此, 当前对于大气污染导致不利健康效应的关键因子仍不清楚. 由于颗粒物组分复杂, 仅根据颗粒物粒径难以解释其健康效应, 来源及组分在颗粒物生物学效应中的重要性日益凸显[24~27]. 颗粒物根据其性质可分为化学组分和生物组分. 生物组分包括两部分, 一部分是生物源释放的挥发性有机污染物(volatile organic compound, VOC)等气态污染物在空气中经过二次转化生成的二次有机气溶胶, 如植物源异戊二烯; 另一部分包括细菌、真菌、病毒、花粉等微生物及其碎片、动植物源性蛋白等. 化学组分主要包括硫酸盐、硝酸盐、铵盐、无机碳、有机碳、金属、地壳元素、低挥发性有机物等. 哪些组分是导致颗粒物炎症效应的关键因素, 当前还没有一致答案.

免疫系统是机体识别和清除非己进而维持健康的保护网, 分为天然免疫系统和适应性免疫系统, 是人类在长期进化过程中形成的, 其免疫能力是通过感知元件“受体”识别抗原和各类环境因素等“配体”后实现的. 当受体分子和配体分子结合后, 才可实现信号转导, 从而将细胞外信号转化为胞内生化响应事件. TOLL样受体(toll-like receptor, TLR)是最早发现的模式识别受体, 其发现人比尤勒、霍夫曼教授在2011年被授予诺贝尔生理学或医学奖[28]. 炎症反应是免疫系统的受体识别配体后, 由不同类型的细胞分泌促炎症介质(类花生酸、细胞因子、趋化因子等)诱导启动的免疫防御行为. 来自于微生物的保守组分、损伤相关分子模式等, 是重要的配体分子[28]. 免疫系统的这种工作模式和生物组分的配体特征使得研究颗粒物中的生物组分进而解释颗粒物的健康效应显得尤为必要和迫切. 经过几十年的流行病学观察研究、人群实验、实验室研究等, 科学界仍未搞清楚大气污染威胁人类健康的关键因素, 这或许是由于对颗粒物中的生物组分认识不足, 导致不能完全解释其中的关键原因.

## 1 大气颗粒物生物化学组分的促炎症效应

人体免疫系统在受到外界刺激和组织损伤时会启动炎症反应, 其中参与诱导的炎症介质包括细胞因子(白细胞介素-6(interleukin 6, IL-6), IL-8, IL-1; 肿瘤坏死因子(tumor necrosis factor, TNF)等)、前列腺素(Prostaglandin, PG)和白细胞三烯(Leukotriene)等脂类介质、C-反应蛋白(C-reactive protein, CRP)等. 急性炎症反应典型症状包括红、肿、热、痛四种, 主要表现为白细胞上升, 慢性炎症反应主要是由于上述炎症介质等持久性存在而导致的.

### 1.1 颗粒物化学组分的促炎症效应

越来越多的研究表明不同类型的疾病均与炎症尤其是慢性炎症反应相关. 动物实验、细胞实验、流行病学研究等提供了丰富的关于大气污染物尤其是颗粒物在促进炎症介质信号分子上升方面的影响, 如表1所示. 糖尿病发病率近年来不断上升, 小鼠研究表明$PM_{2.5}$可通过影响内脏脂肪组织炎症、肝脂质代谢等途径调控小鼠的胰岛素抗性[12]. 颗粒物中的重金属、多环芳烃(polycyclic aromatic hydrocarbon, PAH)、总碳、纳米颗粒等可通过不同途径影响细胞, 包括损伤线粒体、生成活性氧、增加细胞因子等炎症介质[29~34].

人类作为需氧生物体, 每日在摄入氧的同时也不断生成很多活性氧类副产品, 在体内抗氧化系统的作用下, 机体维持着相对稳定的氧化还原平衡态. 氧化还原平衡失调后, 可对体内基因转录、信号转导、生物大分子活性等产生影响, 包括炎症反应通路中涉及到的蛋白、基因等, 从而导致炎症反应. 烟酰胺腺嘌呤二核苷酸磷酸氧化酶(NADPH oxidase)、线粒体等是胞内主要的活性氧来源. 加州大学Nel课题组[40~44]在颗粒物氧化损伤方面进行了很多相关研究, 以柴油车排放颗粒物(diesel exhaust particles, DEP)、超细颗粒物等作为研究对象, 发现其中的有机化学组分是激发活性氧产生的主要成分, 可引起血红素加氧酶(heme oxygenase-1, HO-1)、谷胱甘肽S转移酶(glutathione-S-transferase, GST)等氧化损伤相关基因的表达变化, 表现为线粒体膜电势下降、脱氧核糖核酸(DNA)损伤、炎症细胞因子升高、细胞程序性死亡等, 而抗氧化剂则可一定程度上降低上述指标, 表明

**表 1** 大气污染物化学组分的促炎症效应研究报道

**Table 1** Pro-inflammatory effects of ambient chemical pollutants

| 组分 | 实验类型 | 炎症介质 | 参考文献 |
|---|---|---|---|
| 臭氧(0.1~1 ppm,1 h)[a)] | 肺泡巨噬细胞、气道上皮细胞 | IL-6, IL-8, 纤维蛋白原 | [34] |
| 臭氧(0~500 ppb, 6 h)[a)] | 气道上皮细胞 | IL-8, GM-CSF, TNF, sICAM-1[b)] | [35] |
| 油飞灰颗粒物 | 气道上皮细胞 | IL-6, IL-8, TNF | [36] |
| $PM_{2.5}$有机提取物 | 人支气管上皮细胞 | IL-6, IL-1β | [33] |
| 吸烟颗粒物, 臭氧 | 动物实验 | IL-6 | [37] |
| $PM_{10}$ | 动物实验 | IL-1 β, COX-2[c)] | [31] |
| $PM_{2.5}$ | 人群实验 | CRP, 纤维蛋白原 | [4] |
| $PM_{2.5}$, $SO_2$, $NO_2$ | 哮喘儿童 | 脂质过氧化产物TBARS | [11] |
| $PM_{2.5}$(OC, $NO_3^-$, $SO_4^{2-}$) | 人群实验 | CRP, 纤维蛋白原, 白细胞 | [38] |
| $PM_{10}$ | 人群实验 | 8-iso-PGF2a, 8-OHdG[d)] | [39] |

a) 1 ppm $O_3$=1000 ppb $O_3$=2143 μg/m$^3$ $O_3$; b) GM-CSF, 粒细胞-巨噬细胞集落刺激因子; TNF, 肿瘤坏死因子; sICAM-1, 可溶性细胞粘附因子-1; c) COX-2, 环氧化酶2; d) 8-iso-PGF2a, 人8异前列腺素F2a; 8-OHdG, 8-羟基脱氧鸟苷

了氧化损伤在颗粒物促炎症效应的作用. 石棉、二氧化硅等颗粒物可激活NADPH氧化酶释放活性氧, 继而激活核苷酸结合寡聚化结构域样受体(NALP3)炎症小体(NACHT(神经元凋亡抑制蛋白(NAIP)、MHC类别2转录激活因子(C2TA)、异核体不相容性(HET-E)和端粒酶相关蛋白1(TP1), 富含亮氨酸重复序列(LRR)和茁蛋白之后的PYRIN结构域(PYD)), 导致炎症介质IL-1β等的释放[45]. 除了关于颗粒物化学组分和炎症细胞因子相关性的研究报道, 血液或尿液中的DNA损伤标志物8-OHdG, 丙二醛(MDA)等氧化损伤生物标志物和铁离子、黑炭等组分之间的显著关联也被证实[39]. 此外, 活性氮类物质也可引起胞内氧化损伤. 研究发现DEP和纳米颗粒物等通过刺激胞内一氧化氮释放引起蛋白硝基化, 导致了胞内炎症反应, 与呼吸系统疾病及帕金森症、阿尔茨海默病等神经退化性疾病有明确关联[46,47]. 在刺激胞内活性氧或者活性氮类物质生成的同时, 胞内抗氧化防御体系, 包括抗氧化酶(extracellular superoxide dismutase, EC-SOD)、小分子抗氧化剂(glutathione, GSH)等也受到颗粒物中的重金属、硝酸根离子$NO_3^-$, 氯离子$Cl^-$的明显影响[43,48,49]. 当前, 颗粒物氧化潜势主要通过基于细胞和非细胞的方法进行评价, 非细胞评价方法包括二硫苏糖醇(dithiothreitol, DTT)、荧光探针2′,7′-二氯荧光黄双乙酸盐(DCFA-DA)等, 尽管不同方法得到的颗粒物氧化潜势有所差别, 但炎症反应和颗粒物的氧化潜势在单污染物和多污染物模型下均显著相关[50]. 颗粒物水溶性的醌类有机物等和重金属是其DTT氧化潜势的主要贡献因子, 同时还可和模拟肺部流体生成过氧化氢[51,52]. 但也有部分研究认为颗粒物氧化潜势无法很好地预测颗粒物的急性炎症效应[53].

炎症反应中各种炎症介质的释放依赖于效应细胞的激活, 而该激活过程除了依赖于受体-配体分子的结合, 同时依赖于胞内的基因转录激活和产物表达, 受多重因素影响. 蛋白磷酸化和脱磷酸化是对细胞内信号转导至关重要的生化过程, 污染物可对激酶(促成蛋白磷酸化)、磷酸酶(促成蛋白脱磷酸化)等产生影响, 导致相应的下游信号通路变化, 从而产生炎症反应. 不同种类的重金属对于激酶有不同的影响, V, Zn等可抑制酪氨酸磷酸酶导致磷酸化酪氨酸累积, 进而激活丝裂原活化蛋白激酶(mitogen-activated protein kinase, MAPK), 引起炎症效应, 而As离子则没有类似效应[54]. Wu等人[55,56]发现As, Cu, V, Zn这些重金属可促进皮肤增长因子(epidermal growth factor, EGF)磷酸化, 进而激活丝裂原活化蛋白(MAP)激酶, 导致细胞炎症反应, 氧化锌纳米颗粒可以通过p65和IκBα的磷酸化和去磷酸化过程影响炎症介质IL-8的表达和释放, 引起急性肺部炎症. 信号转导过程的蛋白磷酸化和脱磷酸化受到影响后, 下游的基因转录和表达也会相应发生变化. 转录因子是通过和特定DNA序列结合控制基因转录过程实现基因表达调控目的的蛋白质. 颗粒物有机组分刺激细胞活性氧产生激活MAP激酶和激活蛋白1(AP-1)、核因子-κB(NF-κB)、核因子-相关因子2(Nrf2)等炎症相

关的转录因子，使得相关的炎症介质大量表达[41,57,58].

### 1.2 颗粒物生物组分的炎症效应

一方面，颗粒物化学组分的氧化还原活性直接影响机体氧化还原稳态、免疫系统炎症响应；另一方面，细菌、真菌等微生物组分由于其特有的配体特征，其促炎症效应也值得重视. 内毒素、葡聚糖等胞壁结构组分是源于微生物的保守组分，是结合免疫细胞表面受体的重要配体分子. 不同地区的空气中内毒素浓度水平有较大差异，每毫克$PM_{2.5}$中的内毒素浓度从0.3~5.52 EU不等，与臭氧、二氧化氮、总酸度、$PM_{2.5}$质量浓度等无明显关联，和大气温度显著正相关[59~62]，且粒径分布区间也不一致. Adhikari等人[63]发现1 μm以下的细颗粒物中含有高浓度的内毒素和葡聚糖，前者平均水平为22.7%，可高达63%；后者平均水平为22.6%，可高达96%.

部分研究认为颗粒物的来源及其组分对其毒性的影响要大于其质量浓度和粒径的影响，在研究化学组分促炎症效应的同时，也有研究探讨了生物组分内毒素的贡献，如表2所示，其中重金属和内毒素组分的促炎症效应较为突出[64~66]. 通过使用金属螯合剂分析重金属在炎症效应中的作用，发现重金属、颗粒物DTT氧化潜势等对颗粒物炎症潜势的作用机制不同于内毒素[67,68]. 人群实验结果表明颗粒物内毒素、葡聚糖水平和机体炎症反应相关性最强，即使是短到2 h的颗粒物暴露导致的白细胞上升症状也主要是由内毒素引起的[69,70]. Schins等人[71]的动物实验认为颗粒物中的Fe, Cu, V, Ni, Cr, Al 及颗粒物的羟基自由基生成能力等与其促炎症效应无显著关系，而内毒素浓度和其促炎症效应显著相关. 通过使用多黏菌素B(polymyxin B)或者脂多糖结合蛋白(LPS-binding protein, LBP)封闭内毒素结合位点开展的实验室研究发现，封闭后颗粒物的炎症效应均有显著下降，进一步证明了内毒素组分对颗粒物促炎症效应的重要性[61,72~79]. 除了内毒素这些特定的具有直接促炎症效应的生物组分，空气中的细菌、真菌也对老年人群和健康年轻人均有影响，其变化和人群血液中的CRP, IL-6, 白细胞计数等变化有显著相关性[80]. 有研究中发现年轻健康人体在暴露于污染大气5 h后白细胞数量明显上升，但是该变化与污染物特征无明显关联，推测部分原因是由于该研究中污染物特征仅包括$PM_{2.5}$, $PM_{10}$, 颗粒物数浓度(PNC), 有机碳/无机碳(OC/EC), 铜Cu, 镍Ni, 钒V, DTT氧化潜势、$NO_2$等化学特征，而没有包括颗粒物的生物组分特征. 尽管内毒素成分的季节变化可造成颗粒物促炎症效应的季节性变化趋势，但内毒素也不能完全解释颗粒物的促炎症效应[81]. 总体上目前关于生物组分的促炎症效应多集中于内毒素这一组分，未来需要对葡聚糖、壳糖等其他具有配体性质的生物组分开展充分研究.

除了颗粒物中的生物组分，颗粒物还可能通过影响呼吸道微生物环境产生影响. 研究中利用煤燃烧飞灰、火山灰进行动物和细胞实验发现，颗粒物可破坏抗微生物多肽功能损伤呼吸道的微生物清除能力，同时颗粒物中的铁可有效促进呼吸道细菌增长[88,89].

### 1.3 颗粒物生物化学组分的协同炎症效应

#### 1.3.1 化学组分在过敏性疾病中的佐剂效应

过敏反应是花粉、动物皮屑、尘螨等外源性蛋白过敏原颗粒诱导的病理反应之一. 一项研究中利用

**表 2 大气污染物生物组分的促炎症效应研究报道**

**Table 2** Pro-inflammatory effects of ambient biological pollutants

| 组分 | 实验类型 | 炎症介质 | 文献 |
|---|---|---|---|
| 内毒素 | 人群实验 | IL-6, IL-8, $FEV_1$[a)] | [82] |
| 内毒素，超细颗粒 | 动物实验 | IL-6，纤维蛋白原 | [83] |
| $PM_{10}$, $PM_{2.5}$(内毒素、重金属) | 细胞实验 | TNF, IL-6 | [84] |
| $PM_{10}$, $PM_{2.5}$(内毒素、重金属) | 细胞实验 | TNF，花生四烯酸 | [85] |
| $PM_{2.5}$(内毒素、重金属、PAH) | 细胞实验 | IL-1β, IL-10 | [86] |
| $PM_{10}$(内毒素、重金属、PAH) | 细胞实验 | TNF, IL-8 | [87] |
| $PM_{10}$, $PM_{2.5}$(内毒素、重金属、PAH等) | 细胞实验 | IL-6 | [66] |

a) $FEV_1$: 最大深吸气后做最大呼气，最大呼气第1 min呼出的气量的容积

调查问卷分别在1964和1989年对苏格兰的过敏性疾病发病率进行调查, 结果表明, 哮喘发病率从4.1%上升至10.2%, 花粉过敏性疾病从3.2%升至11.9%, 过敏性皮炎从5.3%升至12%, 引起了对大气污染物与过敏性疾病之间关系的关注, 过敏原在臭氧、二氧化硫、二氧化氮、DEP等作用下表现出了更强的致敏性, 尤其是气传过敏原, 如花粉、真菌毒素、动植物蛋白等[90]. 随着工业源、机动车排放等导致的室外大气污染越来越严重, 东南亚地区尤其是中国, 哮喘等过敏性疾病发病率逐渐攀升, 展现出和西方过去相似的趋势[91]. 除了特定的过敏原, 还需要共刺激信号, 即炎症信号, 两者相结合起到"双保险"的作用, 才可引起过敏反应[92]. 在疫苗学中, 氢氧化铝等组分多作为佐剂加入到疫苗中, 通过加强炎症信号增强疫苗的免疫保护作用[93]. 从1986年Muranaka等人[94]的第1篇文章开始, 大量动物实验揭示了DEP的类似于氢氧化铝的佐剂效应, 主要表现为DEP可和过敏源协同导致小鼠产生更多的免疫球蛋白E(Immunoglobulin E, IgE), 且再次暴露相同过敏原时, 前者的IgE持久性更强[94~97]. 此外, VOC, 颗粒物有机组分和无机组分、内毒素、葡聚糖等通过激活Toll样受体2(TLR2)、Toll样受体4(TLR4)等模式识别受体也有一定的佐剂效应[98~100]. 氧化损伤机制在上述污染物组分的佐剂作用中起到了重要作用[101~104]. 嗜碱性粒细胞是IL-4(白介素-4, 导致过敏反应的关键细胞因子)的重要来源, 研究发现抗氧化剂NAC(N-乙酰-半胱氨酸)可抑制由DEP造成的IL-4上升. DEP中的PAH等有机物和氧化性物质通过激活芳香烃受体(AhR)和Nrf2转录因子调控的信号通路起到了增强炎症信号的佐剂效应[105~108].

### 1.3.2 化学组分与生物组分的协同炎症效应

尽管至今仍未完全清楚大气污染对过敏性疾病的影响机制, 花粉等具有致敏性的生物组分和化学类颗粒物组分、气态污染物的佐剂协同效应对过敏性疾病的影响得到越来越多的共识[109]. 同理推测, 颗粒物内其他非致敏性的生物和化学组分之间也可能存在协同效应, 或可解释颗粒物的炎症效应. Long等人[110]在2001年开展了一项探索性研究, 将同时采集的室内、室外颗粒物以100 μg/mL暴露处理小鼠巨噬细胞, 发现室内颗粒物中高浓度的内毒素导致其促炎症效应强于室外颗粒物, 然而在依据内毒素浓度对颗粒物的促炎症效应标准化后, 发现室内颗粒物的促炎症效应依然强于室外颗粒物, 推测是由于室内颗粒物中的其他组分协同内毒素导致了更强的炎症效应, 但是文中并未进行进一步研究. $PM_{2.5}$和当量浓度的碳黑颗粒物的促炎症效应可差10倍左右, 意味着$PM_{2.5}$上吸附的相应组分对其促炎症效应有不可忽略的作用[111]. 利用标准超细颗粒物开展的细胞实验结果表明颗粒物单独暴露对炎症介质COX-2表达无显著影响, 然而在使用细颗粒物预暴露1 h后加入内毒素进行共同暴露处理时, 发现细胞调控脂类炎症介质的基因表达和蛋白分泌均有显著提高, 且高于单纯的内毒素对照组, 进一步证实了颗粒物化学组分与内毒素之间的协同炎症效应[112]. 另外一项研究使用模拟环境中生成的颗粒物开展了细胞实验, 发现该颗粒物抑制了上皮细胞释放的IL-8浓度, 推测与模拟生成颗粒物中无内毒素或内毒素浓度极低有关[113]. 此外, PAH在细胞实验中也表现出与内毒素的协同炎症效应[114]. 一项2015年的研究中, 通过抑制细胞吞噬、抑制TLR4, MAP激酶(细胞外信号调节激酶p38, 细胞外信号调节激酶ERK1/2)等实验设计, 发现纳米颗粒物和内毒素的协同炎症效应主要是由纳米颗粒物在胞内环境中促进磷酸化刺激TLR4受体相关的炎症信号通路而造成的[115].

越来越多的研究发现单单依靠颗粒物的化学组分或者内毒素等生物组分仍难以完全解释颗粒物的促炎症效应[116~118], 化学组分与生物组分之间的协同效应或许有助于解释其促炎症效应. 然而, 目前关于颗粒物生物、化学组分的协同炎症效应的研究仍然较少, 未来亟待通过学科间交叉结合, 综合研究颗粒物的各项特征进而解释其促炎症效应.

## 2 展望

炎症反应尤其是慢性炎症是引起不同类型疾病的重要病理学机制之一, 大气颗粒物及气态污染物的促炎症能力已被流行病学观察实验、人群实验、动物实验、细胞实验等证实, 然而对于颗粒物这种复杂的污染物类型, 其导致炎症效应的关键因子仍不明确, 病理学机制也不清楚. 在线监测技术的发展使得各项化学污染物监测变得简单易行, 而生物组分由于其特有的生物学特性, 仍然缺乏简单高效的监测手段, 导致对其时空分布特征等认识依然有限, 从而难以评估生物组分对颗粒物促炎症效应的贡献. 鉴于生物组分在激活免疫系统方面的独有"优势", 对

其种类、浓度等特征开展大量研究显得尤为必要. 生物组分和化学组分究竟哪一类是导致炎症因子的主要贡献者, 两者如何协同作用也还没有明确答案.

除了颗粒物本身含有的生物组分, 颗粒物对人体微生物的影响也是一个需要考虑的问题. 近年来人体微生物组学发展迅速, 其数量是人体自身细胞数量的10倍左右, 微生物和人组成的超级共存体已得到越来越多的共识, 微生物组在维持机体健康中的重要性不言而喻[119,120]. 呼吸道并不是无菌的, 含有丰富的微生物, 对于呼吸系统健康乃至机体健康也至关重要[121,122]. 颗粒物通过呼吸作用入肺后, 是否会和呼吸道的微生物组分相互作用影响呼吸道免疫平衡, 吸入的颗粒物等污染物是否会通过影响呼吸道内的微生物群落稳态间接影响呼吸道免疫系统平衡, 回答这些问题对于厘清大气污染物的健康效应机制有重要意义.

根据当前关于大气污染健康效应的研究现状, 建议如下: (1) 研究大气污染对空气中生物组分特征的影响, 尤其是在重污染天气期间细菌、真菌、病毒等微生物气溶胶及其组分如内毒素、葡聚糖、核糖核酸RNA等的变化, 为评估生物组分的促炎症效应的贡献提供基础数据. (2) 深入研究内毒素等生物组分和不同类型的化学组分(包括硝酸盐、硫酸盐、有机碳、无机碳、二次有机气溶胶、重金属、臭氧、氮氧化物、二氧化硫)共同作用下的促炎症效应和机制. (3) 研究呼吸道微生物群落在大气污染影响下的动态变化, 为研究颗粒物健康效应提供新的可能解释.

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Summary for “大气颗粒物生物化学组分的促炎症效应研究进展”

# Pro-inflammatory effects of airborne particulate matters in relation to biological and chemical composition

Fangxia Shen*, Tianle Zhu & Mutong Niu

*School of Space and Environment, Beihang University, Beijing 102206, China*
* Corresponding author, E-mail: fxshen@buaa.edu.cn

Exposure to air pollution has been linked to various adverse health effects, including respiratory diseases, cardiovascular diseases as well as neurological diseases by numerous epidemiological and toxicological studies. Pro-inflammatory effect is suggested to be one of the major mechanisms regarding the health risks posed by pollutants, especially particulate matter (PM). Although the impacts of particle sources and compositions on the discrepancy of elicited inflammation have gained growing attentions, the key determinants remain unclear. Chemical components, i.e., sulfates, nitrates, trace metals, polycyclic aromatic hydrocarbons, have been most closely associated with inflammatory effects. Bioaerosols (short for biological aerosols) including bacteria, fungi, virus, pollen as well as their debris, feature the unique “ligand” properties in activating the receptors of the innate immune cell and evoking inflammation. Nonetheless, with the challenge of identification and characterization of bioaerosols in a real-time manner remaining, there were still limited studies discussing the inflammation induced by bioaerosols. We present a short summary of the pro-inflammatory effects of airborne particles including bioaerosols and chemical composition. Studies on the indispensable role of oxidative stress in promoting cellular inflammatory cytokine production were summarized. Specifically, chemical compositions of PM could affect cellular inflammatory responses via affecting various phosphatase, kinase (e.g., mitogen-activated protein kinase, tyrosine phosphatase), as well as the transcription factors (e.g. NF-κB, Nrf2). Moreover, the role of the PM-borne biological components, e.g. lipopolysaccharide (LPS), was also summarized. Whereas, neither chemical components nor biological components could fully elucidate the PM-induced inflammation. Notably, synergistic effects between PM and allergens were largely discussed with respect to the high prevalence and severity of allergic diseases. Particularly, PM could function as “adjuvant” in elevating the allergic potential of allergens. By taking advantage of this adjuvant function concept, we summarized the past studies on the synergistic effects between chemical and microbial components of particles. Several suggestions are offered for future researches on air pollution-associated health effects: (1) characterize bioaerosols under various weather conditions, aiming to figure out the effects of air pollutants on the airborne microbes; (2) investigate the effects of the interplay between microbial components (e.g., LPS, 1,3-β-glucan) and chemical pollutants (i.e., nitrates, sulfates, organic carbon, elemental carbon, secondary organic aerosols, trace metals, $O_3$, $NO_x$, and $SO_2$) on the development of individual inflammation; (3) study the dynamic change of respiratory microbiota, especially under distinct pollution levels, which might give a new clue to uncover the air pollutants-related adverse health effects.

**particulate matter, bioaerosols, chemical composition, inflammatory effects, synergistic effects, oxidative stress**

doi: 10.1360/N972017-01063