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疾病患者中常出现不可分型流感嗜血杆菌等细菌性病原体的定植，它们通过破坏气道上皮细胞和放大肺部炎症，促进慢性阻塞性肺疾病的进一步发展，再逐渐进展为肺癌。另外，不可分型流感嗜血杆菌感染还能诱导 IL-17C 产生，并通过促进中性粒细胞炎症进而调节肿瘤相关炎症，促进肿瘤生长[42-43]。

5.2 免疫反应 基于健康成人的支气管肺泡灌洗标本显示，肺微生物菌群的组成与上呼吸道（包括口咽和鼻腔）的细菌门组成类似，但组成比例存在差异。随着个体年龄增长，机体逐渐形成一个独特且相对稳定的肺微生态，细菌负荷增加，细菌组成由以革兰氏阴性杆菌和硬壁菌转变为以类杆菌为主，这种变化与程序性死亡蛋白-1 依赖的调节性 T 细胞增多有关，调节性 T 细胞能增强机体对环境过敏原的耐受性[44-46]。对于肺部微生物组群改变的反应性调控会使机体增加免疫细胞，微生物组群无法适应免疫改变就会被人体免疫系统清除。相关研究发现，具核梭杆菌会产生一种特殊蛋白即 FAP2 细胞表面蛋白，可参与到 T 细胞和自然杀伤细胞相互作用中产生抑制抗肿瘤效应[47]。长双歧杆菌所产生的的表面多糖也可抑制肺部选择性 T 辅助细胞 17 型细胞（Helper T cells 17，Th17）反应。此外，肠产毒性脆弱拟杆菌可通过 Th17 反应激活信号传导转录激活因子 3（signal transducer and activator of transcription 3，STAT3），表明人体共生细菌可通过 Th17 依赖性途径诱发癌症[48]。免疫系统在预防癌症发生中起重要作用。

5.3 代谢产物调节作用 除炎症反应及免疫反应外，代谢产物调节作用也是微生物组群促癌机制中重要的一部分。有研究报道，微生物在代谢胆汁酸和蛋白质时可产生致癌芳香胺和硫化物[49]。在中国宣威地区进行的一项与室内燃煤烟雾有关的小型研究中发现肺癌患者显著富集颗粒性球菌、非营养性球菌和链球菌，推测多环芳烃等致癌物的代谢由于受到呼吸道微生物组群的影响，也参与肺癌的发生及进展。在一项关于肺腺癌患者的微生物组成的研究中发现，肺腺癌蓝藻菌属阳性组织中由蓝藻菌属分泌的微囊藻毒素导致 CD36（Toll 样受体分子）水平降低，多腺苷二磷酸核糖聚合酶水平升高，表明蓝藻源性微囊藻毒素激活了导致肺癌发生的炎症途径，在细胞增殖和癌变中起重要作用[50]。

6 总结与展望

将微生物组群的动态变化看做癌症发生及进展的危险因素，为癌症的发病机制及诊疗提供了一个新视角。相对于肠道菌群而言，肺部微生物的研究起步较晚，但随着高通量测序的广泛应用，对于肺部微生物的研究取得显著进展。将微生物组群的动态变化与肺癌相联系，为肺癌的诊断及治疗提供了一个新思路。但是目前关于肺癌微生物组群的研究中，中小量样本居多。积极推行大样本量的纵向队列研究将更有利于对肺癌及下呼吸道微生物组群两者相关性的认识。未来有望通过更多的关于微生物组群及肺癌相关性的研究来改善肺癌患者的疗效及预后。

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