专栏·中国卓越国际论文

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非平面多环芳烃有望为肿瘤精准治疗提供新策略

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上海交通大学医学院附属仁济医院中心实验室刘培峰研究组和上海交通大学化工学院邱惠斌研究组首次证实非平面多环芳烃能够选择性杀伤多种肿瘤细胞。该研究成果以“Selective killing of cancer cells by nonplanar aromatic hydrocarbon-induced DNA damage”为题于2019年9月发表于国际著名学术期刊*Adv Sci*。主管技师周雁、博士研究生干富伟为论文的共同第一作者，刘培峰研究员、邱惠斌教授为论文的共同通信作者。上海交通大学医学院附属仁济医院和上海交通大学化工学院为论文的共同通信单位。

刘培峰研究组主攻微纳米技术与生物医学应用方面的研究，致力于开发高效及精准的肿瘤治疗方法与药物。多环芳烃因具有与DNA结合可激活其杀伤肿瘤细胞潜能的特性而备受关注，但该类化合物潜在的致癌性也为其应用于肿瘤治疗带来了挑战。刘培峰研究组通过对多环芳烃的分子结构进行改造发现，非平面多环芳烃小分子——氮杂螺烯季铵盐（[4]helicenium）在低浓度下能够选择性杀伤多种肿瘤（如肝癌、肺癌和白血病）细胞，而对相应组织来源的正常细胞无明显毒性作用。在此基础上，该研究组对[4]helicenium的作用机制进一步研究发现，其可通过诱导DNA损伤并抑制DNA修复实现肿瘤细胞周期的阻滞及细胞凋亡。

该项研究打破了多环芳烃因具有致癌性而被限制其在生物医药领域中应用的传统观念；同时，通过改造该类化合物的分子结构使“毒药”变“解药”的药物研发方法也将为肿瘤治疗领域提供新的研发方向。此外，与临床常用的化学治疗药物顺铂相比，[4]helicenium对肝癌细胞具有更好的杀伤效果，这也将为解决临床上顺铂的耐药问题提供新的思路。

该项工作由上海交通大学医学院附属仁济医院与上海交通大学化工学院的科研人员合作完成；在刘培峰研究员和邱惠斌教授的精心指导下，由研究组成员主管技师周雁和博士研究生干富伟等共同完成。刘培峰研究组长期致力于材料和生物医学应用的交叉研究，此次研究成果是小分子化合物应用于肿瘤治疗的又一重要发现。该项工作得到国家自然科学基金、上海市人才发展资金、上海交通大学转化医学交叉研究基金以及上海市教育委员会高峰高原学科建设计划等的支持。

Selective killing of cancer cells by nonplanar aromatic hydrocarbon-induced DNA damage

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Abstract:

A large number of current chemotherapeutic agents prevent the growth of tumors by inhibiting DNA synthesis of cancer cells. It has been found recently that many planar polycyclic aromatichydrocarbons (PAHs) derivatives, previously known as carcinogenic, display anticancer activity through DNA cross-linking. However, the practical use of these PAHs is substantially limited by their low therapeutic efficiency and selectivity toward most tumors. Herein, the anticancer property of a nonplanar PAH named [4]helicenium, which exhibits highly selective cytotoxicity toward liver, lung cancer, and leukemia cells compared with normal cells, is reported. Moreover, [4]helicenium effectively inhibits tumor growth in liver cancer-bearing mice and shows little side effects in normal mice. RNA sequencing and confirmatory results demonstrate that [4]helicenium induces more DNA damage in tumor cells than in normal cells, resulting in tumor cell cycle arrest and apoptosis increment. This study reveals an unexpected role and molecular mechanism for PAHs in selectively killing tumor cells and provides an effective strategy for precision cancer therapies.

学者介绍

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刘培峰（1980—），上海交通大学医学院上海市肿瘤研究所癌基因及相关基因国家重点实验室课题组组长，上海交通大学医学院附属仁济医院中心实验室常务副主任。2010 年获东华大学材料学博士学位。2017—2018 年于美国康奈尔大学从事博士后研究工作。现任中国抗癌协会青年理事会常务理事、上海市生物工程学会理事、上海市医药卫生青年联合会委员。

长期从事 DNA 功能材料、器官仿生、微纳米技术及其生物学应用等领域的研究。近 5 年，主持国家自然科学基金 3 项，以第一作者或通信作者于 *Acc Chem Res*、*Adv Sci*、*Chem Mater*、*Biomaterials* 等权威期刊发表论文 20 余篇。2017 年获上海市人才发展资金资助，2018 年入选上海市教育委员会高峰高原学科建设计划和上海市青年拔尖人才开发计划。

LIU Pei-feng (1980—), group leader of State Key Laboratory of Oncogenes and Related Genes of Shanghai Cancer Institute, Shanghai Jiao Tong University School of Medicine, and executive deputy director of Central Laboratory of Renji Hospital, Shanghai Jiao Tong University School of Medicine. He got his doctor's degree of Materials Science from Donghua University in 2010. From 2017 to 2018, he worked as a postdoctor at Cornell University, USA. Currently, he is executive director of Youth Council of Chinese Anti-Cancer Association, a member of Shanghai Society for Biotechnology, and a member of Shanghai Medical and Health Youth Federation.

LIU's research focuses on DNA functional materials, organ bionics, micro-nano technology and its biological applications. In the past 5 years, he has been supported by 3 National Natural Science Foundation of China, and published more than 20 papers as the first author or corresponding author in authoritative journals, such as *Acc Chem Res*, *Adv Sci*, *Chem Mater*, and *Biomaterials*. He was supported by "Shanghai Talent Development Fund" in 2017, and enrolled into "Shanghai Municipal Education Commission—Gaofeng Clinical Medicine Grant Support" and "Shanghai Youth Top Talent Program" in 2018.

微纳米技术与生物医学研究组

立足于材料与生物医学的国际发展前沿，研究组致力于将功能材料和微纳米技术有机结合，充分发挥二者集成后的协同效应以用于疾病的治疗和诊断。根据疾病的发生发展特点，研发设计一系列具有高灵敏性和高特异性的功能材料、递药系统、仿生器官，实现对肿瘤、心血管疾病等的有效诊治。

On the basis of the international development frontier of materials and biomedicine, LIU′s group is committed to combine and employ the synergistic roles of functional nanomaterials and micro-nano technologies for the treatment and diagnosis of diseases. According to the characteristics of the occurrence and development of the disease, LIU′s group develops and designs a series of functional materials, delivery drug system and bionic organ with high sensitivity and specificity to effectively diagnose and treat tumor and cardiovascular diseases.

5 篇代表性论文：

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