放射医学与辐射防护国家重点实验室

State Key Laboratory of Radiation Medicine and Protection

年度工作报告

ANNUAL REPORT

2021

苏州大学

Soochow University

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目　录

前　言

放射医学与辐射防护国家重点实验室是江苏省人民政府和科学技术部共同批准建设的江苏省首个省部共建国家重点实验室（国科发基[2018]161号），也是苏州市和苏州大学的第一个国家重点实验室。

放射医学与辐射防护国家重点实验室是为了满足我国人民健康、国家安全和核能可持续发展等重大需求而建立的。苏州大学放射医学是我国该领域中唯一的国家重点学科。实验室依托苏州大学放射医学与防护学院和核工业总医院，拥有一支由院士、国家重大专项首席科学家、杰青、长江学者等组成的放射医学及交叉科学研究的人才队伍，团队专业结构合理，涵盖放射医学、辐射防护、血液学、临床医学、药学、材料学、化学、核科学技术等多个学科。

放射医学与辐射防护国家重点实验室的定位是“**以放射生物效应为基础、以放射诊治和辐射防护为目标**”。围绕国家中长期发展规划和区域发展的战略布局，面对核技术在医学领域中的广泛应用，瞄准国际放射医学与辐射防护的重大科学问题，围绕放射生物效应及机理、先进放射诊断和治疗、辐射防护等3个重点研究方向开展高水平前沿研究，通过平台建设以及体制机制创新，建设和完善高水平研究团队，加强基础研究，努力提高研发能力，通过科技创新，促进区域经济社会发展，促进放射医学及相关学科可持续发展。

2021 年实验室在科学研究、人才队伍、对外交流、开放服务和实验室科学规范管理等方面均取得了一定成绩。 “放射医学专业”入选国家级一流本科专业建设点。本年度新增固定成员何亦辉等 6 人，现有成员 100 人，其中中国科学院院士 1 人、中国工程院院士 1 人、欧洲科学院院士 1 人、国际宇航科学院院士 2 人、杰青 7 人、优青 6 人。柴之芳院士、时玉舫、钟志远、杨凯和邓超教授入选 2021 年全球高被引科学家榜单。第五娟教授获教育部青年长江学者。畅磊教授获得江苏省特聘教授。王殳凹教授获第 25 届“中国青年五四奖章”，张乐帅教授获中国认证毒理学家资质认定（DCST），

何亦辉教授获 NPSS（核与等离子科学学会）辐射仪器青年科学家奖，高明远教授团队完成的“肿瘤多模态诊疗一体化探针相关基础研究”项目荣获 2020 年度教育部高等学校科学研究优秀成果奖（科学技术）自然科学一等奖。戴克胜教授团队获江苏省科技进步一等奖。胡士军教授获国家科学技术进步奖二等奖（排名第 4）。田野教授团队获国防科学技术进步奖三等奖。与中国疾控中心辐射医学与健康研究所合作主办的英文期刊《Radiation Medicine and Protection》获得国家新闻出版署创刊批复，并正式被 Scopus 收录。2021 年国重室被评为江苏省教育系统先进集体。

在科研方面，2021 年实验室新增包括国家重点研发计划、国家自然科学基金等科研课题 73 项，总金额超 1.35 亿元。值得指出的是，王殳凹教授和何亦辉教授分别牵头主持了科技部重点研发计划资助，高明远教授和第五娟教授获得国家自然科学基金委重点项目资助，黄玉辉教授获得国家自然科学基金原创探索计划项目，陈华兵教授获得国家自然科学基金杰出青年基金项目资助，汪勇教授获得国家自然科学基金优秀青年基金项目资助。实验室共发表 SCI 研究论文 246 篇，其中影响因子大于 10 的 52 篇，大于 5 的 174 篇，SCI 引用逾万次。获得授权发明专利 50 项，其中外国发明专利 5 项。

今年实验室在研发合作和成果转化方面继续保持良好势头。获得了国防科工局、航天员中心、国家核应急办等军民合作项目；与中广核、好医生医药集团、中陕核、鞍山肿瘤医院、华克、华益等公司的合作稳步向前。2021 年 6 月，国重室荣获中国同位素与辐射行业协会表彰

2021 年国家重点实验室举办了系列会议和科普活动。举办了“建党百年创伟业，大国底气从核来—系列科普”—全国科技创新周等一系列大型科普活动。在庆祝建党百年诞辰之际，国重室全面贯彻落实《全民科学素质行动计划纲要》精神　在“全国科普日”等重要节点，围绕“与核同行”主题，开展了一系列科普活动，累计线上线下参与人数达 96 万余人次，收到社会广泛好评。目前，实验室正在申报国家级科普平台。

2021 年，苏大放医国重室继续主动作为，开展“助力企业，共渡难关”系列活动，包括：委派专家对接企业解决技术难题、合作项目研发、平台免

费向企业开放、科技成果转化发布会、学术交流会、技术培训讲座、科普知识宣讲会等，采用“走出去”和“请进来”、“线上+线下相结合” 多措并举——“助力企业，共渡难关”。2021 年 6 月，国重室荣获中国同位素与辐射行业协会表彰。

同时实验室共有 93 人次被邀请在国际国内学术会议上作报告或者交流；共有 22 人次被邀请来作学术报告。另外，实验室成功举办了航天医学与空间生命科学高峰论坛（2021.1.21），中华医学会第十四次全国实验诊断血液学学术会议（2021.4.23）和聚集发光，共谋发展——第一届苏港澳“聚集诱导发光”研讨交流会（2021.10.21）等学术会议。

学术委员会成员名单

职务	姓　名	职称	单位	研究方向
顾问	陈洪渊	院士	南京大学	生命分析
顾问	阮长耿	院士	苏州大学	血液学
主任	詹启敏	院士	中国医学科学院/北京大学	肿瘤学
副主任	陈凯先	院士	上海中医药大学	药物化学
副主任	于金明	院士	山东省肿瘤医院	放射医学
副主任	赵宇亮	院士	国家纳米中心	纳米毒理学
委员	王红阳	院士	上海交通大学	肿瘤与细胞信号转导
委员	欧阳晓平	院士	西北核技术所	核技术
委员	田　禾	院士	华东理工大学	材料化学
委员	叶朝辉	院士	中国科学院武汉物理与数学研究所	核磁共振技术
委员	柴之芳	院士	苏州大学	放射医学
委员	吴宜灿	院士	中科院合肥物质科学研究院核安全所	核技术
委员	Tom K.Hei	教授	美国哥伦比亚大学医学中心	放射医学
委员	汪小琳	教授	中国工程物理研究院	核安全
委员	常学奇	教授	中国辐射防护研究院	辐射防护
委员	周平坤	教授	军事医学科学院	放射医学
委员	邵春林	教授	复旦大学	放射生物学
特邀委员	郭子建	院士	南京大学	生物无机化学
特邀委员	魏于全	院士	四川大学	肿瘤免疫学

一、研究队伍

实验室研究队伍建设的总目标：建设一支素质优良、结构合理、精干高效的科研队伍。实验室人员由三部分组成：专职研究团队、技术人员团队和管理团队。目前，实验室有固定人员 100 人，其中中国科学院院士 1 人、中国工程院院士 1 人、欧洲科学院院士 1 人、国际宇航科学院院士 2 人、杰青 7 人、优青 6 人，已建立了年龄层次和知识结构合理的研究团队。

实验室人员组成情况

序号	姓　名	性别	出生年月	专　业	技术职务
研究人员					
1	柴之芳	男	194209	放射化学/放射医学	主任、中国科学院院士、教授
2	时玉舫	男	196010	肿瘤学	副主任、欧洲科学院院士、教授、杰青
3	高明远	男	196703	分子影像与核医学	副主任、教授、杰青
4	华道本	男	197404	放射化学/辐射防护	副主任、教授、青蓝工程
5	戴克胜	男	196508	血液学	副主任、国际宇航科学院院士、教授
6	阮长耿	男	193908	血液学	中国工程院院士、教授
7	张学光	男	195111	免疫学	教授、杰青
8	钟志远	男	197404	药物化学	特聘教授、杰青
9	王殳凹	男	198506	放射化学	杰青、长江学者、优青
10	张正彪	男	197411	化学	教授、杰青
11	陈华兵	男	197811	纳米毒理学	教授、杰青
12	吴庆宇	男	195710	血液与血管生物学	教授、高层次人才
13	周光明	男	197007	放射医学/特种医学	特聘教授、国际宇航科学院院士
14	邵常顺	男	196210	遗传学	特聘教授、海外杰青
15	陈新建	男	197905	分子影像学	特聘教授、优青
16	杨　凯	男	198308	放射医学	特聘教授、优青

17	葛翠翠	女	198311	辐射纳米毒理学	特聘教授、优青
18	汪　勇	男	198309	放射医学	特聘教授、优青
19	谌宁	男	198010	化学	特聘教授、青长
20	第五娟	女	198604	放射化学	教授、青长、省杰青
21	李　桢	男	197608	分子影像与核医学	高层次人才、省双创人才
22	史海斌	男	197803	分子影像与核医学	特聘教授、高层次人才
23	李瑞宾	男	198209	辐射纳米毒理学	特聘教授、高层次人次、省杰青
24	畅磊	男	198705	生物与医药	特聘教授、高层次人才
25	何亦辉	男	198705	材料与化工	特聘教授、高层次人才
26	苗庆庆	女	198907	化学	特聘教授、高层次人才
27	何玉龙	男	196701	淋巴管与肿瘤	教授、新世纪人才
28	黄玉辉	男	197212	病理学与病理生理学	教授、省特聘教授
29	杨　林	男	196408	免疫学	教授、省“双创”
30	李培山	男	198407	生物学	特聘教授、省杰青
31	崔家斌	男	198908	化学	特聘教授、海外优青
32	吴德沛	男	195802	血液学	教授、主任医师
33	刘玉龙	男	196608	放射损伤临床	教授、主任医师
34	胡士军	男	198002	细胞生物学	特聘教授
35	武　艺	男	196503	血栓与血管生物学	特聘教授
36	周泉生	男	195505	病理学与病理生理学	特聘教授
37	王建荣	男	196205	细胞生物学	特聘教授
38	徐鹏	男	198904	生物学	特聘教授
39	杨光保	男	198911	化学	特聘教授
40	余自强	男	196311	血液学	主任医师
41	韩　悦	女	197002	血液学	主任医师
42	朱秀林	男	195510	材料化学	教授
43	路建美	女	196010	材料化学/辐射防护	教授
44	曹建平	男	196205	放射医学/特种医学	教授

45	王　畅	女	197601	放射医学	教授
46	许玉杰	男	196311	放射医学与核医学	教授
47	涂　彧	男	196507	放射医学/辐射防护	教授
48	郭正清	男	198105	放射医学	教授
49	张乐帅	男	198002	毒理学	教授
50	刘芬菊	女	195412	放射医学/特种医学	教授
51	杨红英	女	197211	放射医学	教授
52	陈　秋	女	197608	辐射免疫学	教授
53	孙　巧	女	197407	定量生物医学	教授
54	崔凤梅	女	197510	放射毒理学	教授
55	杨巍	男	197609	特种医学	教授
56	田野	男	196501	特种医学	教授
57	宋耀华	男	196103	化学	教授
58	邓超	男	197511	化学	教授
59	刘志勇	男	198101	放射化学	教授
60	焦　旸	女	197711	放射医学	教授
61	曾剑峰	男	198706	化学	教授
62	董宁征	女	197001	临床医学	研究员
63	王艳龙	男	198604	化学	副教授、省优青
64	胡　亮	男	198402	核科学与技术	特聘副教授
65	杨再兴	男	198209	定量生物医学	副研究员
66	孟烜宇	女	198306	定量生物医学	副研究员
67	代星	男	198710	物理学	副研究员
68	赵　利	男	198302	放射医学	副教授
69	俞家华	男	198102	放射医学/特种医学	副教授
70	朱　巍	男	197009	放射医学	副教授
71	朱　然	女	197508	放射医学	副教授
72	万　骏	男	196411	放射医学/辐射防护	副教授

73	孙　亮	男	197410	放射医学/辐射防护	副教授
74	王杨云	女	198610	放射医学	副教授
75	胡文涛	男	198408	物理学	副教授
76	屈卫卫	男	198808	物理学	副教授
77	田欣	男	198506	生物学	副教授
78	何伟伟	男	198710	高分子化学与物理	副教授
79	赵　琳	女	198710	放射医学	副教授
80	刘汉洲	男	198505	化学	副教授
技术人员					
81	徐加英	女	197201	肿瘤放射生物	研究员
82	白　霞	女	196809	血液学	高级实验师
83	王敬东	男	197004	放射医学	实验师
84	吴安庆	男	198706	放射免疫学	实验师
85	商冰雪	女	198612	免疫学	助理研究员
86	陈永井	男	197712	免疫学	副研究员
87	聂　晶	女	197304	生物化学	实验师
88	盛道鹏	男	198507	放射化学	助理研究员
89	封　琼	女	198710	放射医学	助理研究员
90	王春宏	女	198001	生物学	助理研究员
91	陈兰花	女	198707	放射化学	实验师
92	吴　艳	女	198107	免疫学	高级实验师
93	刘胜堂	男	198702	放射医学	助理实验师
94	闫思齐	女	198905	核物理	实验师
管理人员					
95	王成奎	男	197108	心理学	副教授
96	朱本兴	男	197012	机关管理办公自动化	实验师
97	易　剑	女	196403	机关管理办公自动化	主管技师
98	彭　蓉	女	197704	机关管理办公自动化	科员

99	燕　倩	女	199409	商务管理	财务秘书
100	佟　鑫	女	199108	新闻与传播	行政秘书

二、重要学术组织及期刊任职

1、重要学术组织任职

序号	人员	学术组织名称	职务	任职开始时间	任职结束时间
1	周光明	COSPAR	Vice-Chair of Sub-Commission F2	2018	2022
2	钟志远	中国材料研究学会高分子材料与工程分会	常务理事	2014	至今
3	刘芬菊	中国核医学辐射研究与技术分会	常务理事	2019	2022
4	涂彧	中国计量协会医学计量专业委员会	常务委员	2019	2024
5	刘玉龙	中国辐射防护学会常委	常务委员	2016	2021
6	韩悦	中国老年医学会血液学分会	常务委员	2017	至今
7	陈华兵	中国医药生物技术协会造影技术分会	常务委员	2019	2023
8	胡士军	中国生物工程学会干细胞工程技术分会	常务委员	2019	2023
9	涂彧	中华预防医学会放射卫生专业委员会	副主任委员	2016	2021
10	涂彧	中国医学装备协会医用辐射装备防护与检测专业委员会	副主任委员	2017	2022
11	刘玉龙	国际原子能机构（IAEA）核应急救援专家	副组长	2016	2021
12	韩悦	中华医学会血液学分会血栓止血学组	副组长	2017	至今

2、重要学术期刊任职

姓　名	学术期刊名称	职务	任职开始时间	任职结束时间
柴之芳	Radiochimca Acta	主编	2012	至今
柴之芳	Radiation Medicine and Protection	名誉主编	2019.12	至今
曹建平	Radiation Medicine and Protection	主编	2019.12	至今
时玉舫	Cell Death & Disease	主编	2010	至今
时玉舫	Oncogene	副主编	2008	至今
时玉舫	Cell Death and Differentiation	Receiving Editor	2015	至今
时玉舫	Advanced Science	Executive Board	2020	至今
时玉舫	Cell Regeneration	副主编	2020	至今
时玉舫	Stem Cell Research & Therapy	副主编	2013	至今
时玉舫	Cell& Bioscience	副主编	2010	至今
钟志远	Journal of Controlled Release	副主编	2019.07	至今
邵常顺	Frontiers in Oncology	副主编	2019.1	至今
周光明	Life Sciences in Space Research	副主编	2019	至今
武艺	Thrombosis Journal	副主编	2018	至今
陈新建	IEEE Transactions on Medical Imaging	副主编	2016.01	至今
陈新建	IEEE Journal of Translational Engineering in Health and Medicine	副主编	2016.03	至今
刘芬菊	辐射研究与辐射工艺 学报	副主编	2014.01	至今

三、研究方向

实验室以放射生物效应为基础、以放射诊治和辐射防护为目标，开展高水平的基础研究和应用基础研究。具体如下：

（1）**放射生物效应及机理：**探讨不同 LET 辐射生物效应、辐射对干细胞的作用及机理、空间辐射生物效应，不仅可以阐明电离辐射损伤的分子机制，还可以为提高放射治疗的精准性和载人航天的的安全性奠定科学理论基础；

（2）**先进放射诊断和治疗：**开展放射诊疗一体化分子影像、核医学影像组学、纳米诊疗药物和质子/重离子辐射治疗的研究，为恶性肿瘤、心脑血管病、神经退行性疾病的精准放疗提供三维空间影像数据和图谱，实现恶性肿瘤等重大疾病的早期诊断、转移预警、疗效评估；

（3）**辐射防护：**进一步开展辐射防护新原理、新机理和新方法研究，构建新型辐射防护药物体系，实现辐射剂量的精确测定和核能放射性污染的有效治理，为辐射防护和核应急提供科学依据和技术保障。

四、代表性科研成果

（一） 放射生物效应及机理

1、微环境中间充质细胞是肿瘤转移灶形成的“推手”

肿瘤转移是癌症治疗的一大难题，然而肿瘤细胞向远端扩散和定植的条件与机制，一直困惑着肿瘤研究人员。肿瘤细胞定植于其他组织的局部微环境，进而实现肿瘤向远端器官转移并形成转移灶，也称为预转移微环境（pre-metastatic niche, PMN）。与肿瘤微环境相似，PMN 涉及多种细胞组分与分子，如免疫细胞、基质细胞、内皮细胞、细胞外基质、生长因子、细胞因子、趋化因子和代谢产物等，它们之间的交互作用影响 PMN 塑造和演变，其作用和机制一直是医学科学界研究的前沿热点。

通过比对和分析乳腺癌肺转移动物模型不同病理阶段的肺间充质基质细胞（LMSCs）调控乳腺癌细胞肺部转移和定植的能力，研究发现，乳腺癌肺转移前期和肺转移期小鼠的 LMSCs 可以显著促进乳腺癌细胞向肺部的转移。RNA- seq 分析揭示肺转移前期和肺转移期的 LMSCs 均高表达补体 C3。前期研究也发现放射的增长微环境也产生大量 C3。利用 C3 缺失 MSCs 以及 C3a 受体缺失小鼠，研究揭示 LMSCs 调控转移灶的形成依赖于其分泌的 C3 以及其借以 C3aR 对中性粒细胞的募集。此外，C3 能够促进中性粒细胞胞外陷阱（NETs）形成，从而帮助乳腺癌细胞在肺组织中的定植。利用 DNA 酶破坏 NETS 形成可以明显消除 LMSCs 介导的促乳腺癌细胞肺转移的现象。

究竟何种原因推动 LMSCs 演变为具有营造乳腺癌细胞肺部定植的微环境的“推手”。通过解析乳腺癌肺部转移过程中肺脏免疫细胞及炎症因子的变化特征，研究发现，乳腺癌病理进程伴随肺部 IL-4 和 IL-13 水平的明显增加，而 IL-4 和 IL-13 可以通过 STAT6 信号通路促进 LMSCs 表达 C3。该研究阐释了在乳腺癌肺部转移 PMN 形成过程中 Th2 细胞、LMSCs 和中性粒细胞在功能上连接并形成调控网络，通过“LMSCs-STAT6-C3-中性粒细胞-NETS”的途径，对肿瘤细胞定植所需的 PMN 进行塑造，成为推动乳腺癌向肺部转移的“幕后推手”。“Th2 炎症因子-STAT6-C3-NETs”通路是控制乳腺癌肺部转移的新靶点，可能成为改善中晚期癌

症患者肿瘤转移的潜在治疗策略。该研究重点阐明了肺部间充质基质细胞（mesenchymal stromal cells, MSCs）在 II 型炎症反应作用下，通过分泌补体 C3 调控中性粒细胞的浸润与功能，塑造适合肿瘤细胞定植的 PMN，促进乳腺癌向肺组织的转移。相关成果发表在 **Nature Communications**, 2021 Oct 27;12(1):6202。

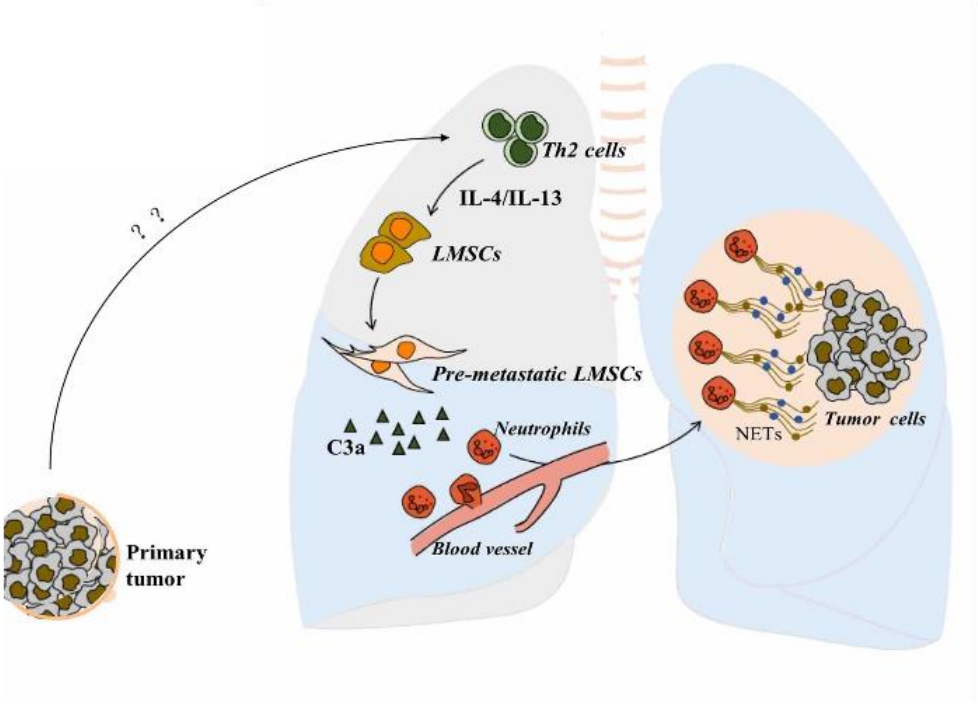


图 1.1 肺部 MSCs 通过分泌补体 C3 调控中性粒细胞塑造预转移微环境促进乳腺癌肺转移

2、电离辐射诱导的长链非编码 RNA 调控基因组不稳定的新机制

非整倍体是基因组不稳定性的标志，与肿瘤发生、发展和转移密切相关。由 CDC20、Bub1 和 Bub3 形成的有丝分裂检查点复合体，以及与之结合的有丝分裂中后期促进复合体（APC/C），是纺锤体组装检查点（SAC）的重要组成部分，对于确保所有姐妹染色体的正常分离以及基因组的稳定性具有十分重要的意义。然而，在有丝分裂过程中，有丝分裂检查点复合体（MCC）如何被精确调控以确保正常有丝分裂正常进行的机制仍不清楚。

在最新的研究中，我们发现碳离子辐射诱导的 LNC CRYBG3 可以与 Bub3 结合，干扰 Bub3 与 CDC20 的相互作用，从而导致 MCC 的功能紊乱，最终导致非整倍体的发生，诱发基因组不稳定。该项成果从电离辐射诱导非编码 RNA 表达和其对非整倍体调控的角度阐述了肿瘤的发生机制，解释了非小细胞肺癌的发生、

发展和恶性程度，为非小细胞肺癌的诊断、治疗和预后提供了潜在的靶点。相关成果发表在 **Oncogene**, 2021, 40, 1821–1835 。

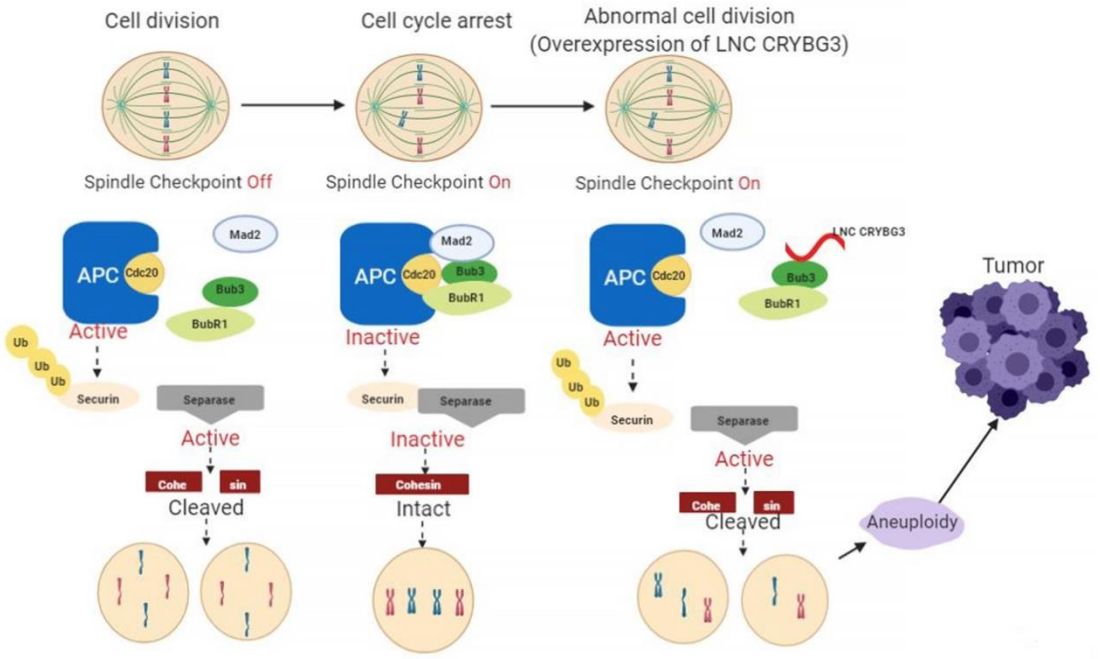


图 1.2 lncRNA 通过靶向纺锤体组装检验点导致细胞检验点逃逸的分子机制。

3、基于重离子放疗特异性非编码 RNA 的基因疗法研究新进展

肺癌是目前世界范围内死亡率和发病率较高的癌症之一，严重威胁人类健康。放疗作为肿瘤的三大疗法之一，在肺癌的治疗中扮演着重要角色，然而，传统放疗所使用的光子射线不仅对乏氧肿瘤治疗效果较差，而且具有对肿瘤周围正常组织损伤较大、放疗后肿瘤易复发和转移等缺点。重离子的应用大大改善了这一现状，具有相对生物学效应高、氧增比低、束流易于控制从而毒副作用小等特点，因此被誉为 21 世纪最优良的放疗射线。周光明教授课题组的前期研究发现，LNC CRYBG3 是一种在肺癌细胞中特异性响应重离子辐照的长链非编码 RNA，它能够通过与 G-actin 互作导致肌动蛋白细胞骨架解聚、细胞凋亡以及肿瘤生长受到抑制。因此，在重离子治疗设施有限、治疗费用高昂的今天，能否将 LNC CRYBG3 应用于模拟重离子放疗效果的基因疗法是一个值得探索的课题。纳米制剂是一种广泛用于生物研究以输送药物的纳米材料，多孔氧化铁纳米剂（PIONs）作为其中之一，因其特殊的磁性和光热特性而被用作基因疗法的优良载体。那么，PIONs 作为重离子放疗特异性基因疗法递送载体将结合 PIONs 优良的光热性能和重离子放疗特异性基因的高杀伤效果，从而克服传统基因疗法低杀伤力的缺点。

我们研究了结合 PIONs 介导的光热治疗（PTT）和 LNC CRYBG3 介导的基因疗法（GT）来杀灭非小细胞肺癌细胞（A549）的可能性。为此，我们构建了质粒 pcDNA3.1-LNC CRYBG3，并通过 PIONs 将其递送至 A549 细胞以过表达 LNC CRYBG3。结果表明，PIONs 可以有效地将 pcDNA3.1-LNC CRYBG3 携带到癌细胞中，并且 LNC CRYBG3 在肺癌细胞中成功过表达。在联合治疗中，一方面，近红外辐射后 PIONs 产生的热量可以提高 pcDNA3.1-LNC CRYBG3 释放的效率。光热转换过程中产生的热量可以通过将组织局部加热到 42℃以上来无创消融肿瘤组织。另一方面，响应重离子照射的 LNC CRYBG3 可在肿瘤细胞中降解肌动蛋白细胞骨架，造成细胞有丝分裂障碍，引起细胞凋亡，模拟重离子照射的肿瘤杀伤作用，但不会引起类似于放疗那样的副作用。PIONs 介导的光热消融的和 LNC CRYBG3 介导的细胞毒性共同发挥作用，并展现出协同的癌症抑制作用，为临床开展肿瘤的精准诊治提供了新思路。相关成果发表在 ***Bioactive Materials,*** 9 (2022), 157-167。

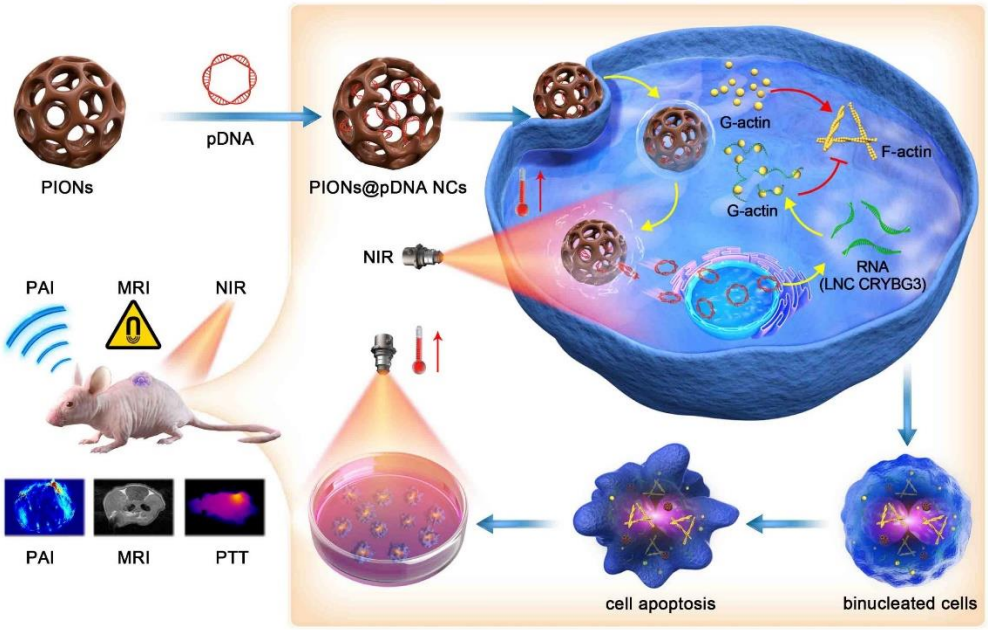


图 1.3 PIONs 介导光热治疗协同基因治疗的机制。

（二） 先进放射诊断和治疗

1、DLL1 诱导长效肿瘤血管正常化和提高放射与免疫治疗效果

放射与免疫治疗是常用的癌症治疗方法，为人类治愈恶性肿瘤带来了希望，但目前仅一部分癌症患者获得了持久疗效。异常的肿瘤血管及由此产生的缺氧、免疫抑制性的肿瘤微环境是阻碍肿瘤放射与免疫治疗的一个主要因素。所以，通过诱导肿瘤血管正常化来重塑肿瘤微环境，有望克服这些障碍，从而改善肿瘤放射与免疫治疗效果。目前通过抑制促血管形成因子，如内皮细胞生长因子（VEGF）等，可以诱导肿瘤血管正常化，但其正常化的持续时间较短，导致其对同步放化疗和免疫治疗的改善有限。因此，急需寻找新的策略在更广泛的肿瘤中长期重塑肿瘤血管及其微环境。

Notch 信号通路在细胞分化、血管生成、个体发育等方面都发挥着重要作用。哺乳动物有 4 个 Notch 受体和 5 个配体：Delta-like 1（DLL1）、DLL3、DLL4、Jagged 1 和 Jagged 2。其中，DLL1，DLL4 和 Jagged1 已被证明在内皮细胞中表达，参与肿瘤血管生成调控。前期研究表明长期阻断 DLL4/Notch 信号通路虽可抑制肿瘤生长，但会诱发血管瘤。所以，我们独辟蹊径，通过选择性激活 DLL1/Notch 信号通路来诱导长效肿瘤血管正常化，该作用还伴随 $CD8^+$ T 细胞的瘤内聚集，巨噬细胞的 M1 型极化和抗肿瘤免疫反应的增强。体内去除 $CD8^+$ T 细胞或者敲除小鼠的干扰素γ（IFNγ）可逆转 DLL1 诱导的肿瘤生长抑制和长效血管正常化。因此，我们首次发现 DLL1 可诱导长效肿瘤血管正常化，持续改善肿瘤微环境中的缺氧和免疫抑制作用，并显著提高肿瘤放射与免疫治疗效果（图 1）。本研究的发现为开发靶向 DLL/Notch 信号通路的药物提供了一种新思路。相关成果以 Direct Submission 方式发表在 ***Proc Natl Acad Sci U S A,*** 2021, 118(22): e2020057118。

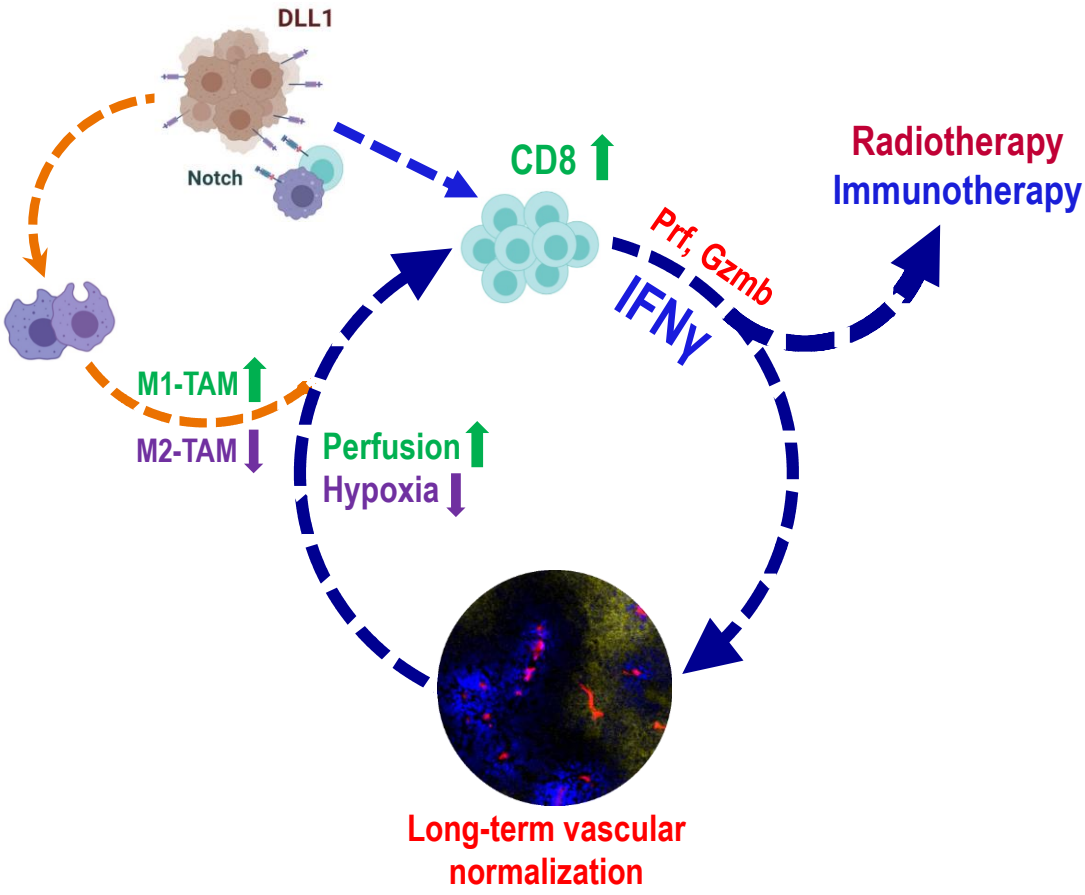


图 2.1 DLL1 通过激活 $CD8^+$T 细胞诱导长效肿瘤血管正常化和提高放射与免疫治疗效果

2、放射性核素标记的金纳米团簇增强肿瘤放射免疫治疗研究

由于患者肿瘤的复杂性、异质性和易转移性，临床上常需采用多种手段联合的综合治疗方式，其中基于放射性同位素的内放疗已成为原发性肿瘤不可缺少的治疗策略之一。但对于转移性肿瘤，同位素内放疗的治疗效果并不理想。在最新的研究中，我们通过将谷胱甘肽与放射性核素的简单螯合，设计了放射性核素标记的谷胱甘肽修饰金纳米团簇（锝-99m 标记的金纳米团簇（^{99m}Tc@Au NCs）和镥-177 标记的金纳米团簇（^{177}Lu@Au NCs））。这种放射性核素标记的金纳米团簇不仅可以增强放射性同位素内放疗的治疗效果，还可以通过激活树突状细胞（DC）来诱导抗肿瘤免疫反应。在将 ^{177}Lu@Au NCs 与免疫检查点抑制剂（α PD-L1）联合后，其可有效清除原发肿瘤，同时抑制远端肿瘤的生长。此外，在放射性同位

素标记的金纳米团簇治疗后，还可观察到长期的免疫记忆效应。值得注意的是，在临床相关的乳腺癌自发转移的转基因小鼠模型上，这种治疗策略显著抑制自发转移瘤的生长，并延长了转基因小鼠的生存时间。总的来说，本研究为肿瘤放射免疫治疗提供了一种新的方法，同时也为临床治疗自发转移性肿瘤提供了新的思路。相关成果发表在 **Nano Today**, 2021, 38, 101144.

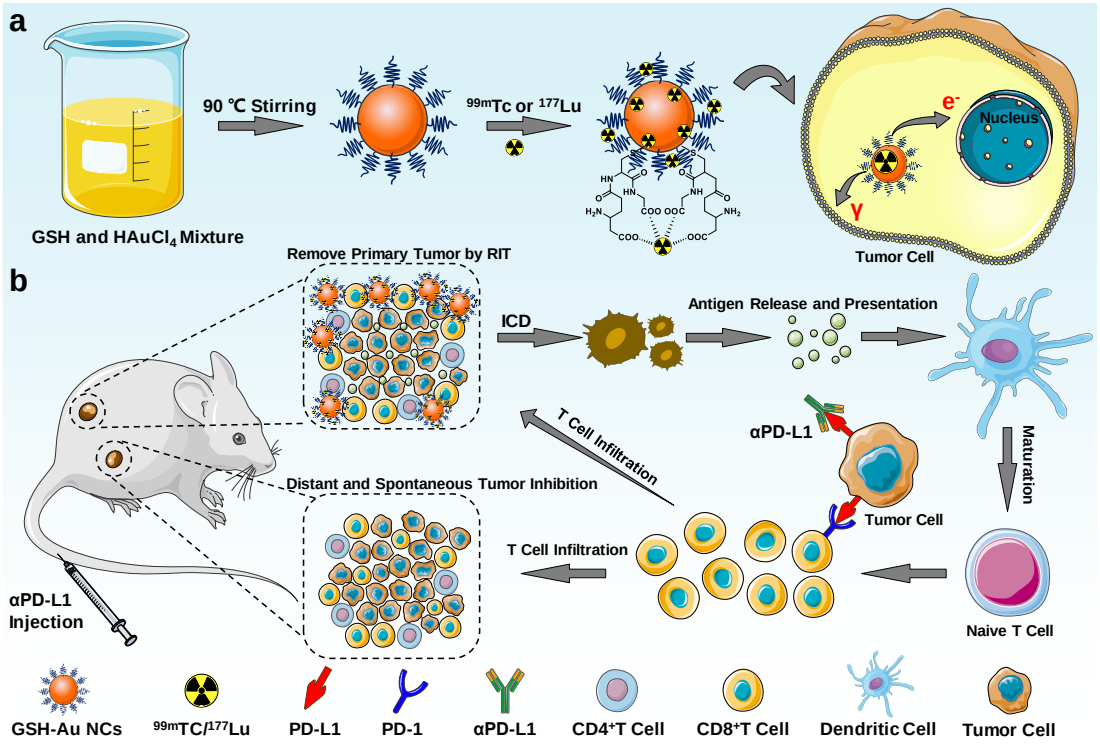


图 2.2 基于放射性核素标记的金纳米团簇增强肿瘤放射免疫治疗研究

3、超小 Cu2-xSe 纳米颗粒极化肿瘤相关巨噬细胞增强抗肿瘤免疫的新机制

调节抑制性肿瘤免疫微环境(TIME)重建免疫监测系统是非常有前景的肿瘤免疫疗法。肿瘤相关巨噬细胞（TAMs）是实体瘤中较为丰富的免疫抑制细胞，约占肿瘤内细胞总数的 50%，通常表现为促进肿瘤生长的 M2 型巨噬细胞，对肿瘤生长、转移、侵袭发挥重要作用。此外，它们还降低抗肿瘤 T 细胞的活性抑制适应性免疫。相反地，M1 型巨噬细胞具有较强的肿瘤杀伤和抗原提呈能力，可通过激活抗肿瘤 $CD8^+$ T 细胞（细胞毒性 T 淋巴细胞，CTL）反应而增强抗肿瘤效应。因此，将 M2 型巨噬细胞极化为抑制肿瘤生长的 M1 型巨噬细胞是较为有效的增强抗肿瘤免疫策略。目前，大多数研究聚焦于利用纳米颗粒递送极化 TAMs 的药物，

然而纳米颗粒本身，尤其是无机纳米颗粒，极化 TAMs 的机制尚不明确，而且直接重塑 TAMs 表型的研究鲜有报道。

铜（Cu）和硒（Se）是维持机体健康所必需的微量元素，由其组成的无机纳米颗粒在肿瘤治疗中也显示出巨大的潜力。在前期工作之中，我们构建了“富含空位”的超小 $Cu_{2-x}Se$ 纳米颗粒，“空位”使其在近红外一区及二区（NIR I 及 NIR II）具有较强的吸收，可以将近红外光高效地转化为热，用于肿瘤的光声成像和光热治疗（*Adv. Mater.* 2016, 28, 8927–8936），此外，空位还为纳米颗粒的掺杂和多功能化提供了广阔空间（*ACS Nano*, 2017, 11, 5633-5645; *Nanoscale*, 2018, 10, 3130-3143；*ACS Nano*, 2019, 13, 1342-1353；*ACS Appl. Mater. Interfaces*, 2020, 12, 4231-4240）。其中，超小 $Cu_{2-x}Se$ 纳米颗粒具有优异的生物可降解性和良好的生物相容性（*Nano Lett*, 2018, 18, 4985-4992）。在近红外光照下，$Cu_{2-x}Se$ 纳米颗粒可以与肿瘤内部 H_2O_2 和 O_2 反应，通过电子转移和能量转移两种机理产生活性氧（ROS），实现光动力肿瘤治疗（*Nanoscale*, 2019, 11, 7600–7608; *ACS Appl. Mater. Interfaces* 2019, 11, 16367−16379）。在无光照的情况下，超小 $Cu_{2-x}Se$ 纳米颗粒可释放出 Cu^+离子（*Nanoscale*, 2019, 11, 11819-11829），与肿瘤内的 H_2O_2 通过类芬顿反应产生 O_2 及 ROS，实现化学动力治疗肿瘤。此外，还可以通过提高肿瘤内部 H_2O_2 浓度以及产生 ROS 的化学反应速率，在肿瘤内部产生大量 ROS 而提高抗肿瘤疗效（*Adv. Funct. Mater.*, 2020, 30, 1906128）。

鉴于肿瘤中含有大量的 M2 型肿瘤相关巨噬细胞，而 ROS 可以使巨噬细胞极化，因此，探究超小 $Cu_{2-x}Se$ 纳米颗粒对 TIME 中巨噬细胞表型的影响和潜在机制具有重要意义。我们发现 $Cu_{2-x}Se$ 纳米颗粒可有效地诱导巨噬细胞产生 ROS，促进肿瘤坏死因子受体相关因子 6（TRAF6）发生泛素化，进一步激活促进 M1 型巨噬细胞极化的重要转录因子干扰素调节因子 5（IRF5），促进其下游信号因子白细胞介素 23（IL-23）的表达，从而显著降低 M2 型巨噬细胞标志物 CD206 和 Arginase1（Arg1）的表达，增强 M1 型巨噬细胞标志物 CD80 和 CD86 的表达，进而有效地将黑色素瘤（B16F10）内的 TAMs 极化为 M1 型。同时还意外地发现，$Cu_{2-x}Se$ 纳米颗粒虽然激活了促进 M1 型巨噬细胞极化的重要转录因子 NF-κB，但未影响其下游诱导型一氧化氮合酶（iNOS）的表达。因此，超小 $Cu_{2-x}Se$ 纳米颗粒极化巨噬细胞的 ROS-TRAF6-IRF5-IL-23 新机制明显不同于传统的 ROS-NF-κB-iNOS 机制。

此外，$Cu_{2-x}Se$ 纳米颗粒还增强了特异性的抗肿瘤 $CD8^+$ T 细胞活化和免疫记忆反应，从而高效地抑制了 B16F10 肿瘤的生长及复发，显著延长小鼠生存周期。该研究为 $Cu_{2-x}Se$ 纳米颗粒抗肿瘤免疫治疗奠定了基础，相关研究成果于近期发表在 **Advanced Functional Materials**, 2021, DOI: 10.1002/adfm.202108971。需要指出，$Cu_{2-x}Se$ 纳米颗粒不仅可以极化肿瘤相关巨噬细胞，还可以调控小胶质细胞表型，对治疗氧化应激引起的帕金森疾病具有显著疗效（*J. Am. Chem. Soc.*, 2020, 142, 21730-21742）。

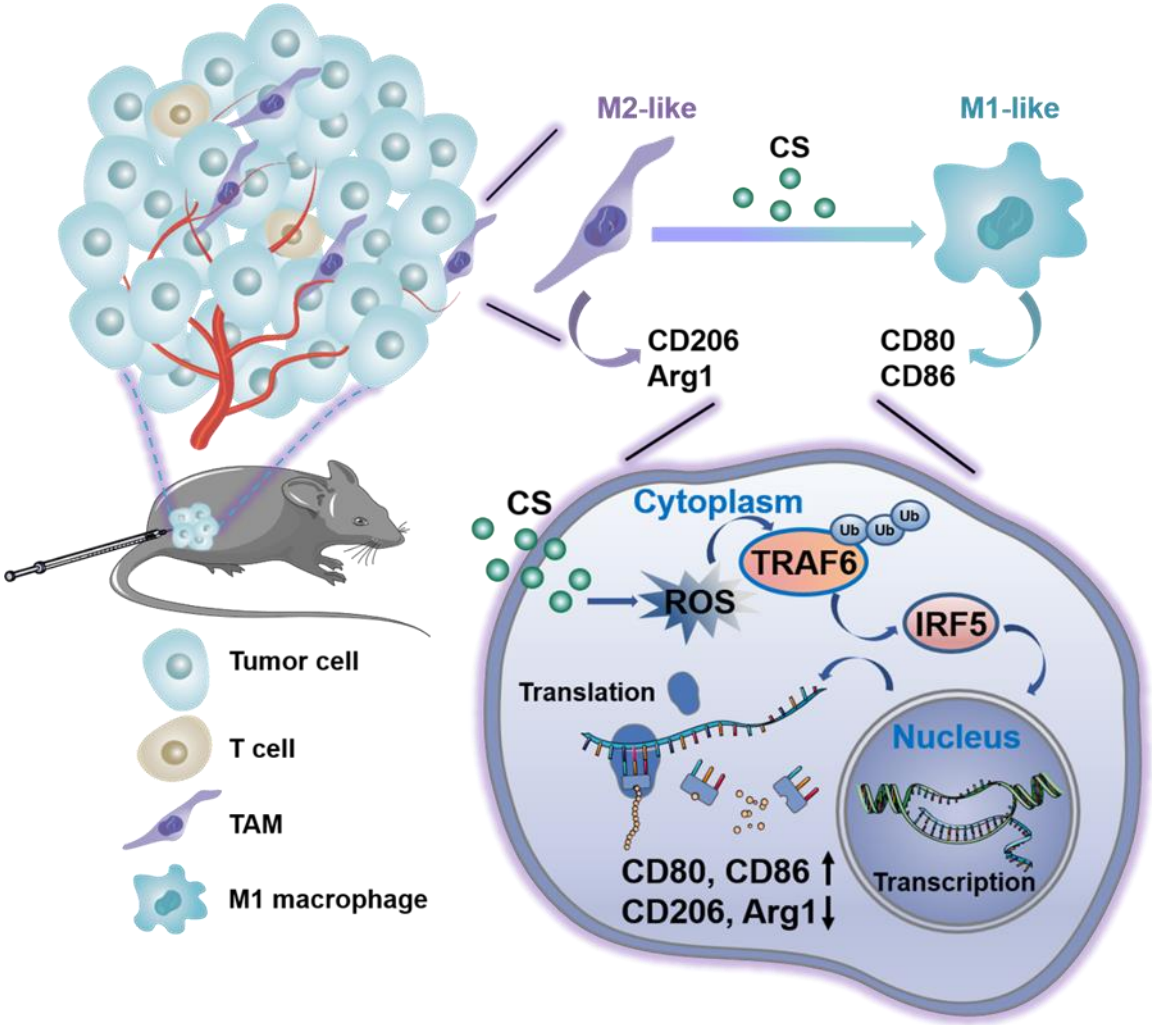


图 2.3 $Cu_{2-x}Se$ 纳米颗粒通过极化肿瘤相关巨噬细胞（TAMs）为 M1 表型抑制肿瘤生长。

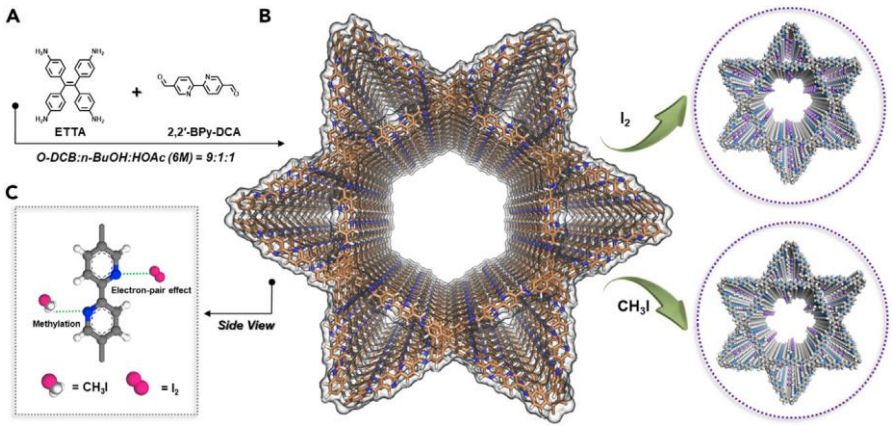
（三） 辐射防护

1、新型 COF 材料用于 I_2 及 CH_3I 共同捕获

碘是长寿命的放射性裂变元素之一。核燃料循环中铀-235 裂变产物中碘同位

素约占 0.69%，是核废料中产生的主要放射性废物之一。后处理过程中，核燃料（UNF）溶解在浓硝酸中会导致大量放射性碘从后处理设施中释放出来。此过程中产生的溶解废气（dissolver off-gas，DOG）流中的主要化学物质是高挥发性的双原子元素碘单质（I2）和少量的有机碘（如甲基碘和乙基碘）。碘的主要同位素 129I 具有极长的半衰期（1.6×107 年），另外一种同位素 131I 因其比活性高，而具有更短的半衰期短（8.02d）。气态的放射性碘的会在大气中积累并会被人体吸入沉积在甲状腺内，具有极强的生物毒性和放射毒性。因此，在核燃料后处理和核事故发生过程中，从尾气中捕获高挥发性的放射性碘，对核安全、环境保护、公众健康，进而实现核能的可持续发展至关重要。研究开发各种功能材料以有效控制放射性碘蒸汽的排放具有重要意义，但由于燃料后处理废气的复杂情况，比如体系温度高，环境湿度大，辐照强度高，碘的浓度极低且体系分压小，且存在大量共存酸性气体（如 NOx、HNO3）等，如何有效的去除后处理体系中的放射性碘仍然是一个挑战。

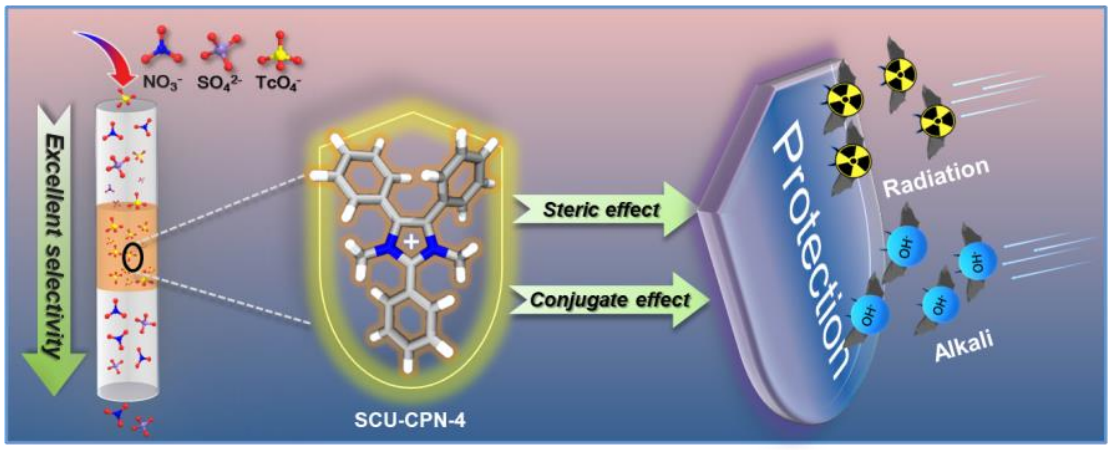
该工作率先研究了共价有机框架（COFs）材料在模拟的真实后处理废气环境下，同时对低浓度碘单质、甲基碘的吸附去除效果。在目前已报道的材料中，SCU-COF-2 具有在静态条件下对 CH_3I 最高的吸附容量（1.45 g g^{-1}）和动态穿透条件下对 I_2 最高的吸附容量（0.98 g g^{-1}），且几乎不受大量竞争水汽和高辐照剂量的影响，表明该类新型 COFs 材料在核事故应急或乏燃料后处理中对放射性碘或有机碘的紧急泄漏方面具有极大的实用价值。*Chem*, **2021**, 7, 699–714. **(ESI Highly Cited Paper)**



2、放射性阴离子 TcO4-的高效分离

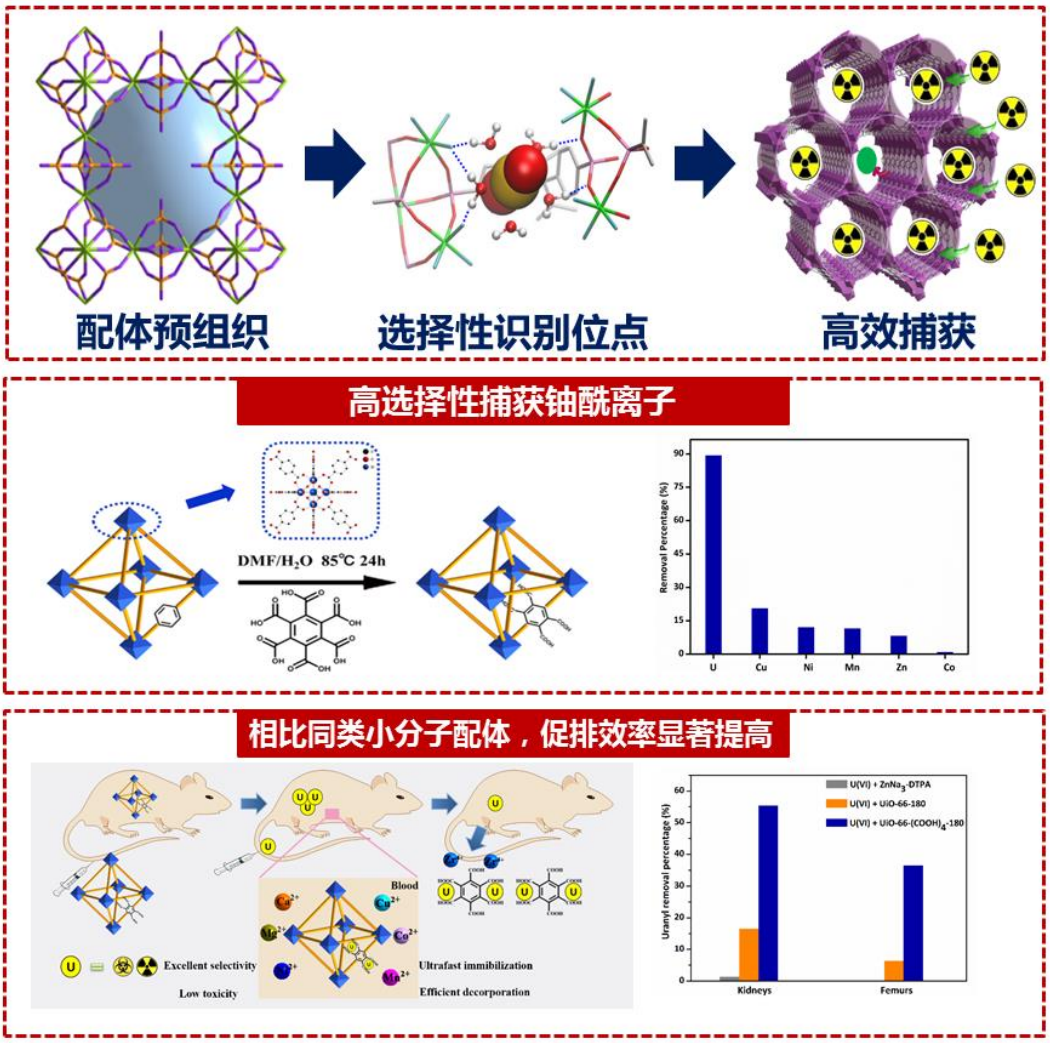
99Tc 是乏燃料后处理流程中重点关注的放射性核素之一，其半衰期长（2.13×105 年）、裂变产额高（6%）、且在水溶液中主要以最稳定的 99TcO4−阴离子形式存在。99TcO4−具有难络合的特点，很难被深度去除。从高放废液中直接去除 99TcO4−具有重要意义。然而，在高放废液的极端环境下(强放射性、高离子强度和强酸/强碱性)，传统材料很难保持稳定，尤其是强碱性高放废液体系。由于多数的阳离骨架材料的阳离子成分来源于季铵盐类官能团，而该官能团对碱极其敏感。针对这一问题，苏州大学王殳凹教授课题组于 2020 年报道了一例罕见的耐强碱的阳离子 MOF 材料（SCU-103），首次实现了真实强碱性废液体系中 99TcO4−的选择性去除（Nat. Commun. **2020**, *11*, 5571.）。SCU-103 在短期接触的静态吸附中对 99TcO4−具有良好的去除性能，但在长期动态吸附实验过程中随着结构的破坏，吸附性能有所降低，在极端真实条件下的稳定性还有较大的提升空间。因此，如何高效地去除强碱性高放废液体系中的放射性 99TcO4−仍是极具挑战性的课题。

该工作通过在咪唑鎓盐的周围接枝大齿疏水性共轭基团合成了一例耐强碱、耐辐照和高选择性的阳离子有机聚合物（SCU-CPN-4）。克服了传统吸附材料碱稳定性差、选择性低和辐照稳定性差的缺点。SCU-CPN-4 对 $^{99}TcO_4^-$表现出优异的静态吸附效果，包括具有非常快的吸附动力学、较高的吸附容量(437 mg/g)以及非常高的吸附选择性。此外，SCU-CPN-4 材料还具有非常优异的碱稳定性，在 1 M 的 NaOH 溶液和模拟的强碱性塞瓦纳河(SRS)高放废液中对 $^{99}TcO_4^-$表现出优异的动态吸附效果，有望解决强碱性放射性废液中 $^{99}TcO_4^-$污染物难去除的问题。(*ACS Cent. Sci.* 2021, 7, 1441–1450)



3、功能化的金属有机框架（MOFs）用于内污染铀促排

由 FDA 唯一批准用于临床的羧酸类锕系促排药物——DTPA 类药物，由于离子选择性较差，导致对铀的促排效果有限，限制了其在锕系促排领域中的应用。本工作率先提出了纳米 MOF 材料用于体内锕系元素促排的研究思路，制备了一例羧酸类配体修饰的纳米 MOF 材料——UiO-66-$(COOH)_4$。通过利用金属节点和有机配体通过配体预组装形成对铀具有选择性识别能力的位点，结合框架材料的立体效应和孔道限域效应，显著提高了对铀的络合能力和选择性，进一步实现了体内铀的选择性吸附促排。实验结果表明该材料对铀酰离子表现出超快的吸附动力学和极强的离子选择性，并且能够进一步有效降低小鼠肾脏中的铀含量，促排效果远优于 DTPA，成功拓展出一类崭新且高效的铀促排剂。(*Angew. Chem. Int. Edit.*, **2021**, 133(3), 1670-1674.）



五、新增科研项目

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
1	国家重点实验室	省部共建放射医学与辐射防护国家重点实验室	SS12800119	柴之芳	3000
2	省协同创新中心	省放射医学协同创新中心	SX12800117	柴之芳	940
3	省优势学科	省特种医学优势学科	YX12800211	柴之芳	590
4	国家重点研发计划	有机框架材料及气体传感技术	2021YFB3200400	王殳凹	1100
5	国家重点研发计划子课题	特定谱系颅颌干细胞和免疫微环境交互调控	2021YFA1100602	邵常顺	586
6	国家自然科学基金杰青项目	生物医用高分子材料	52125304	陈华兵	400
7	国家自然科学基金重大项目	航天极端环境致机体损伤的风险评价与健康监测研究	82192883	周光明	370
8	国家重点研发计划子课题	生物大分子药物输送聚合物载体材料	2021YFB3800902	钟志远	367.5
9	国家重点研发计划青年项目	用于核医学成像的钙钛矿半导体探测基元研究	2021YFF0502600	何亦辉	350
10	国家自然科学基金重点项目	超小磁性氧化铁纳米多功能对比剂相关基础研究	82130059	高明远	290
11	国家自然科学基金原创项目	肿瘤内皮细胞免疫检查点的作用机制与精准免疫治疗策略	82150106	黄玉辉	260
12	国家自然科学基金联合重点项目	新型双功能铀促排剂研究	U2167222	第五娟	255
13	国家级其他项目	海外高层次人才青年项目	无	畅磊	200
14	国家级其他项目	海外高层次人才青年项目	无	何亦辉	200
15	国家级其他项目	海外高层次人才青年项目	无	苗庆庆	200
16	国家自然科学基金优青项目	活体成像分析	22122407	汪勇	200

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
17	国家重点研发计划子课题参与	牙颌组织发育和再生中颅颌干细胞谱系演变	2021YFA1100601	李培山	190
18	国家重点研发计划子课题参与	生物界面蛋白质冠主动精准调控与高效递送载体构建	2020YFA0710701	张正彪	180.8
19	国家自然科学基金	Redox Regulation in Tissue Microenvironment	32150710523	邵常顺	160
20	国家重点研发计划子课题参与	心脑血管再生修复机制及其物种差异	2021YFA0805000	何玉龙	70
21	国家自然科学基金面上项目	电离辐射诱导胶质瘤干细胞免疫原性细胞死亡激活CAR-T细胞免疫治疗胶质瘤	32171234	杨巍	58
22	国家自然科学基金面上项目	辐射响应性聚前药纳米载体的肿瘤放射免疫治疗研究	12175162	王杨云	64
23	国家自然科学基金面上项目	基于神经网络的微剂量学径迹结构分析模型构建及其初步应用研究	12175161	孙亮	61
24	国家自然科学基金面上项目	基于分子模拟和大数据分析的氡捕获MOFs材料的理性筛选与设计及实验验证研究	22176137	杨再兴	60
25	国家自然科学基金面上项目	基于细菌载体的肿瘤放射免疫联合治疗的应用基础研究	32171382	杨凯	59
26	国家自然科学基金面上项目	新型锕系镧系混合金属内嵌富勒烯的合成,价键结构与材料特性研究	52172051	谌宁	58
27	国家自然科学基金面上项目	心脏蛋白酶corin在糖脂代谢中的作用及机制研究	32171112	董宁征	58
28	国家自然科学基金面上项目	基于微接触印刷技术的细胞背包设计及其在肿瘤免疫治疗中的应用	32171403	张乐帅	58
29	国家自然科学基金面上项目	中性粒细胞脂代谢重编程重塑免疫抑制性肿瘤微环境的作用和机制研究	82173108	李培山	55

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
30	国家自然科学基金面上项目	FBXO11 靶向转录因子 GTF2A1 对红细胞生成的调控作用及机制研究	82170119	徐鹏	55
31	国家自然科学基金面上项目	纤维蛋白原介导血栓形成的功能性二硫键的调控机制	8217011021	武艺	55
32	国家自然科学基金面上项目	电离辐射通过 YAP/TAZ 和 SWI/SNF 复合物调控早期胚胎发育的研究	82173465	畅磊	55
33	国家自然科学基金面上项目	易损性动脉粥样硬化斑块的早期预警及动态可视化评估	82172003	曾剑峰	55
34	国家自然科学基金面上项目	线粒体自噬调控血小板保存寿命的作用和机制研究	82170227	王建荣	54
35	国家自然科学基金面上项目	利用患者特异 iPSC 模型研究 TNNT2 突变引发线粒体动态失衡的扩张型心肌病分子机制	82170364	胡士军	53
36	国家自然科学基金青年项目	新型近红外响应性纳米酶的设计及其肿瘤多模态成像研究	22104105	崔家斌	30
37	国家自然科学基金青年项目	阳离子型金属有机框架材料去除 $^{99}TcO_4^-$ 构效关系的理论研究	22106114	刘胜堂	30
38	国家社科基金一般项目	我国核应急管理政策优化及快速响应机制研究	21BGL300	刘玉龙	20
39	省部级项目	造血干细胞移植后血小板重建不良的治疗策略及其机制 探索	BE2021645	韩悦	200
40	省部级项目	中性粒细胞脂代谢重编程在呼吸系统炎性反应中的作用及机制	BK20211543	李培山	100
41	省部级项目	纳米-生物界面作用规律的解析及类酶催化性能的研究	BK20211545	李瑞宾	100
42	省部级项目	组织再生与功能重塑国际合作联合实验室	无	时玉舫	100
43	省部级项目	多功能近红外纳米探针的设计及肿瘤微环境的可视化成像	BK20210702	崔家斌	20

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
44	省部级项目	新型卤化物钙钛矿材料的制备及其器件的高能伽马射线能谱测量	BK20210711	何亦辉	20
45	省部级项目	磷酸化修饰抑制 BAHD1 降解对红细胞生成作用及意义	BK20210714	徐鹏	20
46	省部级项目	大尺寸新型金属有机框架闪烁体的制备及性能研究	BK20211318	刘汉洲	10
47	省部级项目	《南京铱-192 源放射事故应急救治经验》编著项目	ZYY20210839	刘玉龙	10
48	市厅级项目	苏州市放射治疗临床医学中心	Szlcyxzx202103	田野	1000
49	市厅级项目	调控 HMGB1 介导的巨噬细胞免疫效应改善放射性肠炎的研究	21KJB310006	赵琳	5
50	市厅级项目	兼具肿瘤靶向和近红外荧光成像的 BNCT 纳米硼药研制与临床应用研究	SKJY2021047	赵利	5
51	省特聘教授	--	--	畅磊	100
52	姑苏创新创业领军人才	中性粒细胞脂代谢重编程在呼吸系统炎性反应中的作用及机制	苏财教【2021】195号	李培山	100
53	姑苏创新创业领军人才	重离子射线对肿瘤治疗以及预防肿瘤转移的分子机制研究	2XL2022454	畅磊	100
54	姑苏创新创业领军人才	高性能卤化物半导体核辐射探测器材料的制备及表征	2XL2022455	何亦辉	100
55	姑苏创新创业领军人才	预靶向核医学探针用于肿瘤的精准诊疗	ZXL2022457	苗庆庆	100
56	企业合作项目	PSQ 对血小板功能的影响及机制研究		戴克胜	200
57	企业合作项目	放射治疗中质量控制系统研发及信号数据采集卡研发	p112801121	屈卫卫	100
58	企业合作项目	新型高性能辐射屏蔽材料的研发及应用课题 1、课题 2 委托研发	0309cmp0721030801	刘汉洲	70

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
59	企业合作项目	定向注射 PVP 在治疗胸腰椎老年骨质疏松性骨折的研究	H210117	王杨云	40
60	企业合作项目	玻璃基材及核素替代材料关键性质研究技术服务合同	4500175670	第五娟	38.3
61	企业合作项目	数字高分子在油墨中的防伪应用	44201	张正彪	25
62	企业合作项目	化合物在 CDX 模型鼠的生物分布	H211420	刘志勇	21
63	企业合作项目	钇 90 委托检验	H211318	刘志勇	20
64	企业合作项目	新型高性能辐射屏蔽材料的研发及应用课题 1、课题 2 委托研发补充协议	0309cmp0721030802	刘汉洲	19.5
65	企业合作项目	液态氚辐射生物标志物的筛选及分析	P112801921	孙亮	15
66	企业合作项目	K/BxN 诱导的小鼠关节炎模型药效研究（2021-2022, 12 万）	P121100221	武艺	12
67	企业合作项目	AMT754 凝血筛选研究（2021-2022, 11.45 万）	P121100121	武艺	11.5
68	企业合作项目	ROS 响应性高分子药物载体用于药物 DFO 递送系统的研发	H210202	王杨云	10
69	企业合作项目	益生菌通过机体免疫调节辅助肿瘤放化疗的评价研究	H210058	王杨云	10
70	企业合作项目	碳同位素分离技术优化	H211262	刘汉洲	8
71	企业合作项目	放射性核素标记的多功能纳米探针用于口腔癌的诊断与治疗研究	H211264	史海斌	5
72	企业合作项目	口腔锥形束 CT 扫描的剂量分布及防护优化研究	P112801321	孙亮	5
73	企业合作项目	GD-K01 材料辐射防护性能分析和评价	H211085	胡文涛	3.55
合计					**13551.1**

六、国内外学术交流

1、主办、承办会议

序号	会议名称	会议类型	主办/承办	会议日期	参会人数	会议地点
1	中华医学会第十四次全国实验诊断血液学学术会议	全国性	承办	2021-04-23	800	杭州
2	航天医学与空间生命科学高峰论坛	全国性	主办	2021-01-21	40	苏州
3	聚集发光，共谋发展——第一届苏港澳“聚集诱导发光”研讨交流会	区域性	主办	2021-10-21	200	苏州

2、专家来访

序号	时间	报告人	主题	单位
1	2021-06-24	苏文明	喷墨印刷显示与发光关键材料与技术	中科院苏州纳米技术与纳米仿生研究所
2	2021-09-16	邱敏	器官靶向性脂质纳米颗粒用于 mRNA 的递送及基因编辑	复旦大学
3	2021-09-16	陈景	Multifunctional biomaterials for protein delivery in biomedicine and food security field	南京中医药大学
4	2021-10-08	王广基	精准医学背景下药代动力学新技术在新药及临床研究中的探索	中国医学科学院
5	2020-06-23	吴君心	开设放射医学本科专业	福州医科大学
6	2020-06-17	加固项目组专家	加固项目现场验收	21 基地
7	2020-04-14	王世恩主任、刘登参谋	实验室指导	装备发展部
8	2020-04-11	宋明涛	加速器参数探讨	中科院兰州近代物理研究所
9	2021-10-26	董晓臣	光敏剂结构调控及肿瘤多模态光治疗	南京工业大学
10	2021-10-26	张瑞平	基于黑色素纳米颗粒在肿瘤诊疗一体化的研究	山西白求恩医院

序号	时间	报告人	主题	单位
11	2021-07-05	嵇富海	吸入麻醉药对发育期大脑的影响及其机制研究	苏州大学附属第一医院
12	2021-06-03	凌代舜	动态变构诊疗探针与智能诊疗	上海交通大学
13	2021-10-27	袁荃	基于核酸适体的分子识别设计及生物分析应用	湖南大学
14	2021-06-04	安众福	有机超长磷光材料与性能研究	南京工业大学
15	2021-04-20	沈行	HDDA 芳炔的插入反应以及氮杂环卡宾加合物的高分子机械力化学研究	苏州大学
16	2021-05-06	董学会	精确与分散:链长不均一性对聚合物自组装的影响	华南理工大学
17	2021-10-18	万文明	巴比耶聚合方法	中国科学院福建物质结构研究所
18	2021-03-21	夏云生	纳米生物动态成像分析	安徽师范大学
19	2021-05-11	俞洋	Eukaryotic CRISPR: a piRNA-guided "innate immune" system in genome defence	中国科学院生物物理所
20	2021-06-23	王仲亚	AAV 基因技术	苏州克睿基因生物科技有限公司
21	2021-09-22	荆清	抑制细胞衰老小分子化合物的筛选及其作用机制	中国科学院上海营养与健康研究所
22	2021-09-22	陈丰原	NSFC 申请原则与要素	上海交通大学

3、参加会议

序号	会议类别	报告人	会议名称	会议地点
1	全国性	时玉舫	Immune Orchestration in the Stem Cell Microenvironment	昆明市
2	全国性	时玉舫	Immune Regulatory Properties of Mesenchymal Stromal / Stem Cells	合肥市
3	全国性	时玉舫	皮质激素和基质干细胞相互作用的临床启示	嘉兴市
4	全国性	时玉舫	T cells and glucocorticoid-induced osteoporosis	桐庐市
5	全国性	时玉舫	Steroid MSC and Immunity	重庆市
6	全球性	邵常顺	Redox Homeostasis and Cellular Senescence	成都市

序号	会议类别	报告人	会议名称	会议地点
7	全国性	黄玉辉	The immune-vascular crosstalk	海门
8	全球性	黄玉辉	The immune-vascular crosstalk	南京
9	全国性	黄玉辉	肿瘤免疫治疗新伙伴：抗肿瘤血管新生	上海
10	全国性	畅磊	电离辐射与肿瘤力学微环境	长春市
11	全国性	畅磊	Mechanotransduction in Radiation Oncology	温州市
12	全国性	崔家斌	From artificial atom to artificial molecules with multimodal imaging for biological applications	深圳市
13	全国性	李瑞宾	纳米生物学构效关系研究	珠海市
14	全国性	李瑞宾	针对有机底物分子的新型纳米酶及其应用研究	长春市
15	全国性	李瑞宾	Top-down Detection of Nanotoxicity	北京
16	全国性	李瑞宾	纳米类酶及类抗生素活性	长春市
17	全国性	李瑞宾	Top-down 策略解析纳米毒理学的化学本质	无锡市
18	全国性	李瑞宾	纳米生物界面相互作用分析	深圳
19	全国性	周光明	空间辐射致癌效应及 lncRNA 调控机理	衡阳
20	区域性	周光明	Radiation-inducible LNC CRYBG3 promotes tumorigenesis by targeting three proteins	在线
21	全国性	周光明	空间辐射致癌的新机制——一条 lncRNA 多重调控	温州
22	全国性	周光明	重离子高效杀灭肿瘤细胞的生物学机制	成都
23	全国性	周光明	肺癌进化的环境辐射依从性研究	在线
24	全国性	周光明	放射医学一流本科专业建设的模式创新与实践	南京
25	全国性	周光明	机体辐射敏感性的节律性变化及其分子机制	长沙
26	区域性	周光明	苏州大学医学物理专业人才培养体系简介	香港在线
27	全国性	周光明	深空辐射的健康风险及非编码 RNA 调控	衡阳
28	全国性	周光明	Cancer Risk of Space Radiation environment and its regulation by lncRNAs	杭州

序号	会议类别	报告人	会议名称	会议地点
29	全国性	周光明	航天极端环境对神经认知系统的影响	海口
30	全国性	周光明	重离子对肿瘤细胞的致死作用及非编码 RNA 调控	长春
31	国际会议	陈华兵	Self-assembled Nanomedicine for cancer phototherapy	杭州市
32	全国性	崔凤梅	促进核沾染创面愈合的水凝胶 PCECA plus 的研制和功能研究	
33	全国性	高明远	--	珠海市
34	双边性	高明远	--	
35	全国性	高明远	--	上海市
36	全国性	高明远	--	北京市
37	双边性	高明远	--	
38	全国性	高明远	--	太原市
39	全国性	高明远	--	上海市
40	全国性	高明远	--	上海市
41	全国性	高明远	--	
42	全国性	高明远	--	上海市
43	全国性	李桢	超小纳米探针治疗脑疾病	苏州市
44	国际性	李桢	Nanotheranostic Agents for Imaging and Therapy of Brain Diseases	线上
45	全国性	李桢	分子影像与脑疾病	合肥市
46	全国性	李桢	多模态诊疗一体化分子影像	上海市
47	全国性	李桢	纳米酶在脑疾病治疗中的应用	长春市
48	全国性	史海斌	智能响应探针构建及肿瘤诊疗基础研究	太原市
49	全国性	史海斌	基于有机智能响应型探针的生物成像分析研究	长沙市
50	全国性	史海斌	分子影像探针与肿瘤诊疗	上海
51	全球性	吴庆宇	Protease function in uterine spiral artery remodeling	
52	全国性	胡士军	心血管类器官与疾病研究	长沙市

序号	会议类别	报告人	会议名称	会议地点
53	全国性	胡士军	心脏类器官与疾病研究	重庆市
54	全国性	胡士军	心脏类器官与疾病研究	西安市
55	全国性	胡士军	多能干细胞、类器官和心血管疾病	杭州市
56	全国性	胡士军	多能干细胞、类器官 和心血管疾病研究	哈尔滨市
57	全国性	胡士军	多能干细胞在心血管疾病研究中的转化应用	广州市
58	全国性	胡士军	多能干细胞、类器官与心血管 疾病研究	北京市
59	全国性	胡士军	利用 iPSCs 研究 GATA4 突变家族先天性心脏病	北京市
60	全国性	时玉舫	中欧科学院天然免疫与慢性疾病重点实验室第一届学术委员会第七次会议	线上会议
61	全国性	时玉舫	浙江省科学技术奖候选成果论坛	浙江，杭州
62	全国性	时玉舫	第四届中国出生缺陷干预救助基金会科学技术奖评审	线上会议
63	全球性	时玉舫	‘New perspectives on COVID-19’ 网络研讨会	线上会议
64	全国性	时玉舫	放射防护国家重点实验室第四届学术委员会第二次会议	江苏，苏州
65	全国性	时玉舫	“发育编程及其代谢调节”重点专项项目 2020 年度总结汇报会议	线上会议
66	全国性	李培山	第四届中国生物物理学会代谢生物学分会学术研讨会	广西桂林
67	全国性	许玉杰	第六届核工业教育学会常务委员会年会	成都市
68	许玉杰	许玉杰	第六届《中国辐射卫生》杂志编委会	济南市
69	全球性	周光明	59th PTCOG	美国
70	区域性	周光明	苏大夏令营科普	苏州
71	全国性	周光明	中西医结合学会 40 周年	北京
72	全国性	李桢	第十届中国医药生物技术论坛暨第二届绍兴生命健康产业峰会	绍兴
73	全国性	李桢	第四届江苏省医学生物光子专业委员会会员代表大会	南京
74	全国性	史海斌	中国化学会第 32 届学术年会	珠海

序号	会议类别	报告人	会议名称	会议地点
75	全国性	史海斌	2021 中国生物材料大会	上海
76	全国性	史海斌	第二十一届全国有机分析及生物分析学术研讨会	长沙
77	全国性	史海斌	中国化学会第十五届生物无机化学会议暨金属化学生物学学术会议	太原
78	全国性	史海斌	第五届荧光探针与成像青年学者研讨会	长沙
79	全国性	杨光保	中国化学会第 32 届学术年会	珠海
80	区域	徐加英	江苏省高校实验室研究会 2020 年学术年会	江苏徐州
81	全国性	柴之芳	中国同位素与辐射行业协会	北京
82	全国性	徐加英、赵琳	中国同位素与辐射行业协会	北京
83	全国性	徐加英	中国环境诱变剂学会辐射与健康专业委员会成立大会暨 2021 年首届学术交流会	南阳（线上）
84	全国性	张正彪	第十届先进纤维与聚合物材料国际会议	上海市
85	全国性	张正彪	2021 年全国高分子学术报告会	北京市
86	全国性	张正彪	第四届国际生态环境高分子材料大会	贵阳市
87	全国性	俞家华	全国辐射生物效应与辐射防护学术研讨会	吉林市
88	全国性	汪勇	微纳米技术与医疗健康创新大会	上海
89	全国性	汪勇	第十三届全国生物医药色谱及相关技术学术交流会	上海
90	全国性	焦旸	全国辐射生物效应与辐射防护学术研讨会	长春市
91	全国性	王殳凹 第五娟	全国核燃料后处理专业学术交流会	山东青岛
92	全国性	第五娟	2021 年中西部地区无机化学化工学术研讨会	甘肃兰州
93	全国性	第五娟	全国分析毒理第二届青年论坛	江苏无锡

七、授权专利目录

序号	专利号	专利名称	授权公告日	国家	完成人(固定人员)
1	ZL 2019 1 0551216.X	透明质酸-g-叶酸两亲性聚合物及其应用	2021-08-27	中国	钟志远
2	ZL 2019 1 0780914.7	末端含硫辛酰基的星型聚合物的制备方法及聚合物纳米粒子的制备方法	2021-06-16	中国	钟志远
3	ZL 2018 1 0172582.X	基于末端含硫辛酰基星型聚合物的纳米药物	2021-04-27	中国	钟志远
4	ZL 2017 1 0237726.0	基于主动反应型一步法的交联纳米药物的制备方法	2021-06-18	中国	钟志远
5	ZL 2018 1 1185536.X	具有不对称膜结构的可逆交联生物可降解聚合物囊泡及其制备方法	2021-08-27	中国	钟志远
6	ZL 2017 1 0496784.5	生物可降解交联纳米药物冻干粉的制备方法	2021-03-02	中国	钟志远
7	US11009476B2	Squaraine-polymer-based ammonium/nitrogen monoxide Two-component sensor, as well as preparation method and Application thereof	2021-05-18	美国	路建美
8	US11084027B2	Three-dimensional composite material, preparation method Thereof and application thereof in removal of water Pollutants by visible light catalytic degrading	2021-08-10	美国	路建美
9	US11111605B2	Iodine Doped Bismuthyl Carbonate Nanosheet And Molybdenum Disulfide Modified Carbon Nanofiber Composites, Preparation Method And Application Thereof	2021-09-07	美国	路建美
10	ZL 2018 1 0317460.5	金掺杂纳米氧化锌复合材料及其制备方法与在光催化降解四环素中的应用	2021-01-01	中国	路建美
11	ZL 2018 1 1527697.2	负载微生物的酸改性海泡石生物纳米复合材料及其制备方法与应用	2021-02-09	中国	路建美

序号	专利号	专利名称	授权公告日	国家	完成人(固定人员)
12	ZL 2018 1 1467962.2	黑磷/钨酸铋纳米复合材料及其制备方法与在废气处理中的应用	2021-02-12	中国	路建美
13	ZL 2019 1 0351490.2	四氧化三钴十二面体/氮化碳纳米片复合物及其在废气处理方面的应用	2021-03-19	中国	路建美
14	ZL 2019 1 0411836.3	一种具有可见光催活性的 In-NH2/g-C3N4 复合材料及其应用	2021-05-24	中国	路建美
15	ZL 2019 1 1089784.9	碘氧化铋/氧化锌复合材料及其制备方法与在压电-光催化去除有机污染物中的应用	2021-09-28	中国	路建美
16	ZL 2019 1 0507730.3	方酰胺聚合物、基于方酰胺聚合物的 VOC 传感器及其制备方法	2021-09-28	中国	路建美
17	ZL 2020 1 1449869.6	多孔聚合物修饰的金属碳纳米管复合膜及其制备方法与应用	2021-09-28	中国	路建美
18	ZL 2019 1 0165584.0	掺磷管状氮化碳微纳米材料及其在废气催化处理中的应用	2021-09-28	中国	路建美
19	ZL 201911358302.5	肌肉干细胞在制备抗炎药物中的应用	202-07-27	中国	时玉舫,陈永井,邵常顺
20	ZL 201910415089.0	一种诱导造血干细胞向 T 系细胞分化的方法和试剂盒	2021-10-08	中国	时玉舫,陈永井
21	ZL 2019 1 0483092.6	靶向光热治疗联合免疫治疗抗肿瘤复合制剂的制备方法	2021-11-02	中国	陈华兵
22	ZL2019 1 0780919.X	一种抗肿瘤铂类药物矿化蛋白纳米粒及其制备方法和应用	2021-11-09	中国	陈华兵
23	ZL 2019 1 0197934.1	一种促进人多能干细胞定向分化为内皮细胞的方法	2021-06-01	中国	胡士军
24	ZL 2018 1 0123408.6	一种提高多能干细胞分化为心肌细胞的诱导方法	2021-04-30	中国	胡士军

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26	ZL 2016 1 0081875.8	FSTL1 在肝脏等组织抗纤维化的稳态调节中的保护作用与应用	2021.05.18	中国	何玉龙
27	US11072740B2	Use of uranium-containing compound as scintillator	2021-06-27	美国	王殳凹,王亚星,尹雪苗
28	US11145850B2	Soft neural electrode based on three-dimensional porous graphene foam material and use of three-dimensional porous graphene foam material to prepare bone deffect filler	2021-10-12	美国	曹建平
29	ZL 2018 1 1234721.3	特拉唑嗪在治疗放射性认证功能障碍药物中的应用	2021-07-09	中国	杨红英
30	ZL 2019 1 0299092.0	多碘修饰的氟硼二吡咯类衍生物及其制备方法和应用	2021-08-24	中国	郭正清,陈华兵,史梦柯
31	ZL 2019 1 0405248.9	RPRM 基因敲出小鼠模型及其构建方法与应用	2021-10-15	中国	杨红英,王敬东
32	ZL 2019 1 0473842. 1	改性内嵌金属富勒烯及其制备方法与应用	2021-08-27	中国	刘胜堂,杨再兴
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34	ZL 201910609503.1	磁性类普鲁士蓝材料及其制备和吸附铯离子的应用	2021-12-01	中国	华道本
35	ZL 2020 1 0652378.5	一种提高 CRISPR-Cas9 基因编辑中同源重组修复效率的方法	2021-08-17	中国	俞家华，丁伯洋，刘芬菊，张昊文
36	ZL 2020 1 1051025.6	共价纳米片材料的应用	2021-10-26	中国	王殳凹,第五娟
37	ZL 2020 1 1324191.9	一种半导体聚合物纳米颗粒及其制备方法和应用	2021-06-04	中国	朱然,苗庆庆
38	ZL 2020 1 1338372.7	一种砹 211 标记的半导体聚合物纳米及其制备方法和应用	2021-06-04	中国	朱然
39	ZL 202010803249.1	红外 II 区荧光金纳米团簇及其制备和应用	2021-07-29	中国	李瑞宾
40	ZL 2021 1 0142477.3	一种医用放射性二氧化硅微球及其制备方法与应用	2021-11-09	中国	高明远

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44	ZL201910508151.0	碱性磷酸酶响应型分子探针及其应用	2021-04-27	中国	史海斌
45	ZL201910895364.3	高稳定性近红外二区小分子荧光探针及其制备方法和应用	2021-04-13	中国	史海斌，赵梦
46	ZL 2019 1 0714401.6	碳基纳米材料及其应用	2021-12-03	中国	杨再兴
47	ZL 2017 1 0953735.X	硬脂酸/软脂酸组合作为 aGVHD 疾病诊断标志物的应用	2021-08-10	中国	吴德沛,韩悦
48	ZL 2018 1 1080814.5	一种基于改进 Faster R-CNN 的黄斑定位方法	2021-06-15	中国	陈新建
49	ZL 2018 1 1042548.7	一种基于条件生成对抗网络的 OCT 成像中散斑去噪的方法	2021-10-22	中国	陈新建
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11	Inflammasomes as therapeutic targets in human diseases	Signal Transduction and Targeted Therapy	Yangxin Li, Hui Huang, Bin Liu, Yu Zhang, Xiangbin Pan, Xiyong Yu, Zhenya Shen, Yaohua Song	2021 Jul 2;6(1):247.
12	FLT4/VEGFR3 activates AMPK to coordinate glycometabolic reprogramming with autophagy and inflammasome activation for bacterial elimination	Autophagy	Li Ma, Weiyun Li, Yanbo Zhang, Linlin Qi, Qi Zhao, Na Li, Yao Lu, Luqing Zhang, Fei Zhou, Yichun Wu, Yongning He, Hongxiu Yu, Yulong He, Bin Wei, Hongyan Wang	2021 Oct 10;1-16.
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16	Emerging targeted drug delivery strategies toward ovarian cancer	Adv. Drug Deliv. Rev.	Zhe Wang , Fenghua Meng, Zhiyuan Zhong	2021 Nov;178:113969.
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Detecting ionizing radiation using halide perovskite semiconductors processed through solution and alternative methods

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The direct detection of high-energy radiation such as X-rays and γ-rays by semiconductors at room temperature is a challenging proposition that requires remarkably pure and nearly perfect crystals. The emergence of metal halide perovskites, defect-tolerant semiconductors, is reviving hope for new materials in this field after an almost 20 year hiatus. Metal halide perovskites, which combine exceptional optoelectronic properties, versatile chemistry and simple synthesis, are challenging traditional approaches for the development of novel semiconductors for detecting hard radiation. We discuss the relevant physical properties, promising materials, fabrication techniques and device architectures for high-performance, low-cost detectors by targeting next-generation semiconductors for radiation detection. We also present a perspective on the impact of such advances in future medical imaging applications.

X-rays and γ-rays with energies ranging from tens of kilo- to megaelectronvolts (keV, MeV) are used in various photonics applications, such as medical imaging, industrial inspection, astronomy, the nuclear energy industry, high-energy physics and radioisotope identification in homeland security[1–4]. The direct detection of X- and γ-rays by semiconductor materials at room temperature is of great interest, as such devices are anticipated to offer unparalleled performance in terms of image quality, energy resolution and system volume. However, semiconductor detectors have so far been deployed commercially in only a few specific fields and applications.

These applications are primarily based on two semiconductor materials: amorphous Se (a-Se) films in large-area radiography imaging and bulk $Cd_{1-x}Zn_xTe$ (CZT, $x \approx 0.1$) single crystals in homeland security and nuclear medical imaging[5,6]. These materials are limited by either their sensitivity (a-Se) or processability (CZT). Progressively more demanding requirements in precision medicine and nuclear threat reduction have imposed higher standards on the development of room-temperature radiation detectors. Semiconductor materials capable of achieving superior performance, but at a substantially lower cost, are therefore in demand and have been sought for decades.

Solution-processed metal halide perovskites (MHPs), which have the general formula AMX_3 (where $A = CH_3NH_3^+$ (MA), $HC(NH_2)_2^+$ (FA), Cs^+; $M = Ge^{2+}$, Sn^{2+}, Pb^{2+}; and $X = Cl^-$, Br^-, I^-), have emerged in recent years as a promising class of semiconductor materials for optoelectronic applications[7–12]. MHPs were first used as absorbers in photovoltaic devices and quickly achieved high efficiency comparable to that of state-of-the-art traditional semiconductors such as Si and CdTe (refs. [12–15]). These advances have ignited great efforts in research of MHPs, which have clarified their unique and desirable characteristics and quickly led to their implementation in applications such as light emission and detection[16].

On the basis of these studies, MHPs were also considered for the challenging task of X- and γ-ray photon detection. The superior carrier transport properties of MHPs, which are based on a special type of defect tolerance that derives from the idiosyncrasies of their chemical bonding and electronic structure, together with their high effective atomic number (enabling high stopping power, suitable bandgap energies to achieve low dark current and versatile synthesis routes) make MHPs ideal candidates for these applications. This so-called defect tolerance in these materials, however, though much better than classical semiconductors, it is not unlimited. The first example of MHP-based X- and γ-ray radiation detection was introduced in 2013 using a melt-grown $CsPbBr_3$ semiconductor[17]. The successful use of $CsPbBr_3$ for radiation detection has brought other MHP counterparts to the forefront, as they were substantiated both as direct detectors (semiconductors) and indirect detectors (scintillators)[3,18,19].

This Review focuses on the application of MHPs as semiconductor detectors for high-energy X- and γ-ray detection. We present the primary application-oriented material requirements, discuss the two detection schemes (the charge-integration and single-photon modes) and present current approaches for defining and obtaining these criteria. We discuss the unique features of the family of MHPs, specifically in dimensionality reduction and their influence on detection in the charge-integration mode. Versatile fabrication routes for achieving different device geometries are also discussed. We then review the MHP semiconductors used for X- and γ-ray spectroscopy in the single-photon mode. Finally, we present an outlook on the unresolved issues and future approaches for detectors and applications based on MHP semiconductors. We anticipate that this Review will direct the attention of other members of the MHP community towards materials development for X- and γ-ray detection and encourage researchers focused on detectors to explore and further develop advanced devices based on MHPs.

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Daratumumab Immunopolymersome-Enabled Safe and CD38-Targeted Chemotherapy and Depletion of Multiple Myeloma

Na Yu, Yifan Zhang, Jiaying Li, Wenxing Gu, Shujing Yue, Bin Li, Fenghua Meng, Huanli Sun, Rainer Haag, Jiandong Yuan, and Zhiyuan Zhong**

Multiple myeloma (MM) is a second ranking hematological malignancy. Despite the fast advancement of new treatments such as bortezormib and daratumumab, MM patients remain incurable and tend to eventually become relapsed and drug-resistant. Development of novel therapies capable of depleting MM cells is strongly needed. Here, daratumumab immunopolymersomes carrying vincristine sulfate (Dar-IPs-VCR) are reported for safe and high-efficacy CD38-targeted chemotherapy and depletion of orthotopic MM in vivo. Dar-IPs-VCR made by postmodification via strain-promoted click reaction holds tailored antibody density (2.2, 4.4 to 8.7 Dar per IPs), superb stability, small size (43–49 nm), efficacious VCR loading, and glutathione-responsive VCR release. $Dar_{4.4}$-IPs-VCR induces exceptional anti-MM activity with an IC_{50} of 76×10^{-12} M to CD38-positive LP-1 MM cells, 12- and 20-fold enhancement over nontargeted Ps-VCR and free VCR controls, respectively. Intriguingly, mice bearing orthotopic LP-1-Luc MM following four cycles of i.v. administration of $Dar_{4.4}$-IPs-VCR at 0.25 mg VCR equiv. kg^{-1} reveal complete depletion of LP-1-Luc cells, superior survival rate to all controls, and no body weight loss. The bone and histological analyses indicate bare bone and organ damage. Dar-IPs-VCR appears as a safe and targeted treatment for CD38-overexpressed hematological malignancies.

The development of actively targeted nanotherapeutics to realize specific homing and augmented retention in the tumor site as well as boosted internalization by tumor cells is a primary goal of nanomedicine for revolutionizing cancer treatment.[1] Installing affinity ligands such as peptides, small molecules, antibodies and their fragments onto the surface of liposomes and polymeric nanosystems has been a major strategy and obtained booming development.[2] Amidst them, antibody and antibody fragment decorated immuno-nanomedicines have gained particular attention due to their high specificity and affinity, as evidenced by marketed antibody–drug conjugates[3] and undergoing clinical trials of several immunoliposomes (e.g., MCC-465, MM-302, C225-ILs-DOX, and MM-310).[4] The immuno-nanomedicines based on liposomes and polymeric nanoparticles (e.g., poly(lactic-*co*-glycolic acid)) though have shown enhanced tumor cell uptake and good safety brought about only moderate therapeutic benefits,[5] partly due to their large size, insufficient stability, suboptimal ligand density, and premature drug leakage. The lack of robust and small-sized nanosystem that allows stable drug loading and facile and controllable antibody conjugation is a major hurdle for clinical translation of targeted immuno-nanomedicines.

Multiple myeloma (MM), the second most common hematological malignancy, remains incurable and tends to eventually become relapsed and drug-resistant.[6] Daratumumab (Dar), the first-in-class CD38-specific IgG1κ monoclonal antibody, has recently emerged as a new treatment regime for relapsed/refractory and newly diagnosed MM patients due to the relatively specific overexpression of CD38

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Heavy-Atom-Modulated Supramolecular Assembly Increases Antitumor Potency against Malignant Breast Tumors via Tunable Cooperativity

*Zhengqing Guo, Hui He, Yi Zhang, Jiaming Rao, Tao Yang, Ting Li, Lu Wang, Mengke Shi, Mengya Wang, Shihong Qiu, Xue Song, Hengte Ke, and Huabing Chen**

Triple-negative breast cancer (TNBC) remains with highest incidence and mortality rates among females, and a critical bottleneck lies in rationally establishing potent therapeutics against TNBC. Here, the self-assembled micellar nanoarchitecture of heavy-atom-modulated supramolecules with efficient cytoplasmic translocation and tunable photoconversion is shown, for potent suppression against primary, metastatic, and recurrent TNBC. Multi-iodinated boron dipyrromethene micelles yield tunable photoconversion into singlet oxygen and a thermal effect, together with deep penetration and subsequent cytoplasmic translocation at the tumor. Tetra-iodinated boron dipyrromethene micelles (4-IBMs) particularly show a distinctly enhanced cooperativity of antitumor efficiency through considerable expressions of apoptotic proteins, potently suppressing subcutaneous, and orthotopic TNBC models, together with reduced oxygen dependence. Furthermore, 4-IBMs yield preferable anti-metastatic and anti-recurrent efficacies through the inhibition of metastasis-relevant proteins, distinct immunogenic cell death, and re-education of M2 macrophages into tumoricidal M1 phenotype as compared to chemotherapy and surgical resection. These results offer insights into the cooperativity of supramolecular nanoarchitectures for potent phototherapy against TNBC.

Breast cancer is a complex and heterogeneous disease with the leading incidence and mortality among females,[1] in which triple-negative breast cancer (TNBC) with low expressions of progesterone receptor, estrogen receptor, and human epithelial growth receptor type 2 (HER2) is considered as a highly aggressive subtype with increased risk of recurrence, metastasis, and resistance.[2] Typically, a combination of diverse therapeutic modalities such as chemotherapy, phototherapy, radiation therapy, and immunotherapy is considered as an effective approach to treat TNBC,[3] arousing an intense interest in the explorations of various nanoscale vehicles such as liposomes, micelles, dendrimers, and polymeric nanoparticles that can achieve enhanced targeting and co-delivery for combinational treatments against TNBC.[4] For instance, photodynamic therapy (PDT) as a selective and non-invasive modality that relies on the apoptosis from singlet oxygen of photoactive dyes can combine with other therapeutic modalities such as immunotherapy and chemotherapy to yield enhanced antitumor efficacy against malignant tumors such as breast cancers.[4a,5] However, PDT-based strategies usually suffer from a few limitations such as sophisticated compositions of vehicles, restricted singlet oxygen generation, and severe oxygen dependence, inherently poor suppression on recurrence and metastasis, and inadequate spatiotemporal accessibility to subcellular organelles such as nucleus,[6] thus being urgent to explore a facile nanoparticle strategy to establish potent phototherapeutics against TNBC, together with favorable prognosis.

Various strategies to improve singlet oxygen quantum yields of photoactive agents have been applied to improve PDT-based cell injury through the regulations of apoptotic or anti-apoptotic proteins including heavy-atom effect, spin converter, resonance energy transfer and semiconducting structures.[7] However, the current dilemma is that photoactive agents are rationally incorporated into nanoparticles for higher tumor accumulations,[5b,6a,b] but failed to controllably modulate their photoconversions via chemical modifications to optimize tumor treatment and prognosis.[8] Supramolecular self-assembly as a bottom-up approach to fabricate nanoarchitectures of molecular components via the non-covalent interactions such as hydrophobic interaction, π–π stacking and hydrogen bonding, has been widely applied to address sophisticated cascade delivery, namely a circulation–penetration–endocytosis–cytoplasmic translocation pathway.[8a,9] In particular, the interplay of a few

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Highly Efficient Far-Red/NIR-Absorbing Neutral Ir(III) Complex Micelles for Potent Photodynamic/Photothermal Therapy

Bingqing Liu, Jian Jiao, Wan Xu, Miya Zhang, Peng Cui, Zhengqing Guo, Yibin Deng, Huabing Chen,* and Wenfang Sun**

A critical issue in photodynamic therapy (PDT) is inadequate reactive oxygen species (ROS) generation in tumors, causing inevitable survival of tumor cells that usually results in tumor recurrence and metastasis. Existing photosensitizers frequently suffer from relatively low light-to-ROS conversion efficiency with far-red/near-infrared (NIR) light excitation due to low-lying excited states that lead to rapid non-radiative decays. Here, a neutral Ir(III) complex bearing distyryl boron dipyrromethene (BODIPY-Ir) is reported to efficiently produce both ROS and hyperthermia upon far-red light activation for potentiating in vivo tumor suppression through micellization of BODIPY-Ir to form "Micelle-Ir". BODIPY-Ir absorbs strongly at 550–750 nm with a band maximum at 685 nm, and possesses a long-lived triplet excited state with sufficient non-radiative decays. Upon micellization, BODIPY-Ir forms *J*-type aggregates within Micelle-Ir, which boosts both singlet oxygen generation and the photothermal effect through the high molar extinction coefficient and amplification of light-to-ROS/heat conversion, causing severe cell apoptosis. Bifunctional Micelle-Ir that accumulates in tumors completely destroys orthotopic 4T1 breast tumors via synergistic PDT/photothermal therapy (PTT) damage under light irradiation, and enables remarkable suppression of metastatic nodules in the lungs, together without significant dark cytotoxicity. The present study offers an emerging approach to develop far-red/NIR photosensitizers toward potent cancer therapy.

1. Introduction

With minimal invasiveness and intrinsic spatiotemporal selectivity, photodynamic therapy (PDT) has been proven to be an effective adjuvant for cancer treatment and succeeded in improving the quality of patients' lives.[1] PDT utilizes the interactions of light, photosensitizer (PS), and oxygen to produce toxic reactive oxygen species (ROS), which directly kill tumor cells, damage the blood vessels in tumors, and elicit the immune responses to destroy tumor cells without injuring adjacent normal tissues.[2] The efficacy of PDT is mainly determined by the ROS generation efficiency of PS, which depends not only on their intrinsic properties, such as its ability to absorb light and its triplet excited state (T_1) characteristics (i.e., energy level, quantum yield, and lifetime), but also on the tissue oxygen tension. It is well known that the high metabolic level of tumor cells causes tumor hypoxia, which is aggravated by the oxygen-consuming PDT processes. Thus, the PDT efficiency is compromised

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Stimuli-Responsive Polymers for Sensing and Reacting to Environmental Conditions

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ABSTRACT

As we enter the age of artificial intelligence (AI), new technologies will be needed to "sample" environmental conditions to provide data to AI systems that will yield a specific response. This review focuses on stimuli-responsive polymers (SRPs), and their ability to react to changes in external environmental conditions by undergoing a physical and/or chemical change. We first describe various methods for SRP synthesis, which leads into a discussion of the mechanism of SRPs response to external conditions, and finally we highlight examples of their use for sensing, biosensing, and actuation. The aim of this review is to familiarize readers with some of the most recent developments in SRP design and application, which we hope will encourage further research in this field that can help overcome some of the current challenges and inspire new and creative applications for these materials.

1. Introduction

SRPs can change their physical and/or chemical properties in response to a variety of stimuli, for example: temperature [1,2],

Abbreviations: AI, Artificial Intelligence; SRPs, Stimuli-responsive Polymers; PDI, Polydispersity Index; ATRP, Atom Transfer Radical Polymerization; RAFT, Reversible Addition-fragmentation Chain Transfer; NMP, Nitroxide-mediated "living" Free-radical Polymerization; LCST, Lower Critical Solution Temperature; TPL, Triphenylmethane Leucohydroxide; TRPs, Thermoresponsive Polymers; UCST, Upper Critical Solution Temperature; PNVCL, Poly(N-vinylcaprolactam); THF, Tetrahydrofuran; CPTC, Critical Phase Transition Concentration; POEGMA, poly(oligo (ethylene glycol) methyl ether methacrylat); PMVE-, Poly(methyl vinyl ether)-; PEP-, Poly(phosphoester)-; SPZs, Sulfobetaine-based polyzwitterions; PAA, Poly(acrylic acid); PMAAc, Poly(methacrylic acid); PDMA, Poly(N, N′- diethylaminoethyl methacrylate); PDMAEMA, Poly(N,N-dimethylaminoethyl methacrylate); LRPs, Light-responsive polymers; NIR, Near Infrared; SP, Spiropyran; MC, Merocyanine; SPEA, Spiropyran Ethyl Acrylate; MMA, Methyl methacrylate; CNCs, cellulose nanocrystals; DTE, Dithienylethene; ERPs, Electroresponsive Polymers; p(VDF-TrEF), Poly(vinylidene fluoride-trifluoroethylene); LCEs, Liquid Crystalline Elastomers; IPMCs, Ionic Polymer-metal Composites; PPy, polypyrrole; ENRPs, Enzyme-responsive Polymers; ECMs, Enzymes cleavable moieties; ROMP, Ring-opening Metathesis Polymerization; MMP-7, Matrix Metalloproteinase-7; PLA, Polylactic Acid;PCL, Polycaprolactone; PBAT, Polybutylene Adipate-co-terephthalate; DOX, doxorubicin; AP, Alkaline Phosphatase; Pi, Phosphate; pHEMA, poly(hydroxyethyl methacrylate); PVA, Poly(vinylalcohol); PVAc, poly(vinyl acetate); PANI, polyaniline; PE, Polyethylene; PEO, Poly(ethylene oxide); ODMR, Optically Detected Magnetic Resonance; RGO, Reduced Graphene Oxide; C60, Fullerene; PMEO^{2}MA, poly(2-(2-methoxy ethoxy)ethyl methacrylate); RCA, Ractopamine; HAV, Hepatitis A Virus; RLS, Resonance Light Scattering; GR, Graphene; P2VP, Poly(2-vinyl pyridine); HyUPS, Hybrid Ultra-pH-sensitive; PET, Photoinduced Electron Transfer; d-TPE, Tetraphenyl Ethylene Derivatives; PCs, Photonic Crystals; FPIs, Fabry-Perot Interferometers; IDEs, Interdigitated Electrodes; RH, Relative Humidity; PBA, Phenylboronic Acid; NBR, Nitrile Butadiene Rubber; PEDOT, Poly(3,4-ethylenedioxythiophene); ON, Oligonucleotide; SRHs, Stimuli-responsive Hydrogels; CDs, Carbon Dots; GOx, Glucose Oxidase; HRP, Horseradish Peroxidase; CLC, Cholesteric Liquid Crystal; QCM, Quartz Crystal Microbalance; LSPR, Localized Surface Plasmon Resonance; SERS, Surface-enhanced Raman Scattering; PAH, Poly(allylaminehydrochloride); OFETs, Organic Field-effect Transistors; PDMS, Polydimethylsiloxane; GF, Gauge Factor; CCA, Coumarin-3-carboxylic Acid; TAMRA, 5(6)-carboxytetramethylrhodamine; BSEPs, Bistable Electroactive Polymers; Na-4-VBS, Na-4-vinyl benzenesulfonate; AN, Acrylonitrile; CNTs, Carbon Nanotubes; CTE, Coefficent of Thermal Expansion; CHE, Coefficient of Hygroscopic Expansion; CMC, Carboxymethylcellulose; RSF, Regenerated Silk Fibroin; PEtOx, poly(2-ethyl-2-oxazoline); pNIPAm, poly(N-isopropylacrylamide); PMA, poly(methacrylamide) (PMA); PNAAGA, poly(N-acryloylasparaginamide); pH-RPs, pH-responsive Polymers; PGMA, poly(glycidyl methacrylate); PVDF, Polyvinylidene Fluoride; PAAm, Polyacrylamide; PEG, poly(ethylene glycol); Boc, tert-butyl carbonate; HRPs, Humidity Responsive Polymers; MIP, Molecularly Imprinted Polymer; PS, Polystyrene; LOD, limit of detection; IPN, interpenetrated polymer network; PDGI, Poly(dodecylglyceryl itaconate); ONB, ortho-nitrobenzyl; PMA, poly(methyl acrylate); ERHs, eletro-responsive hydrogels.

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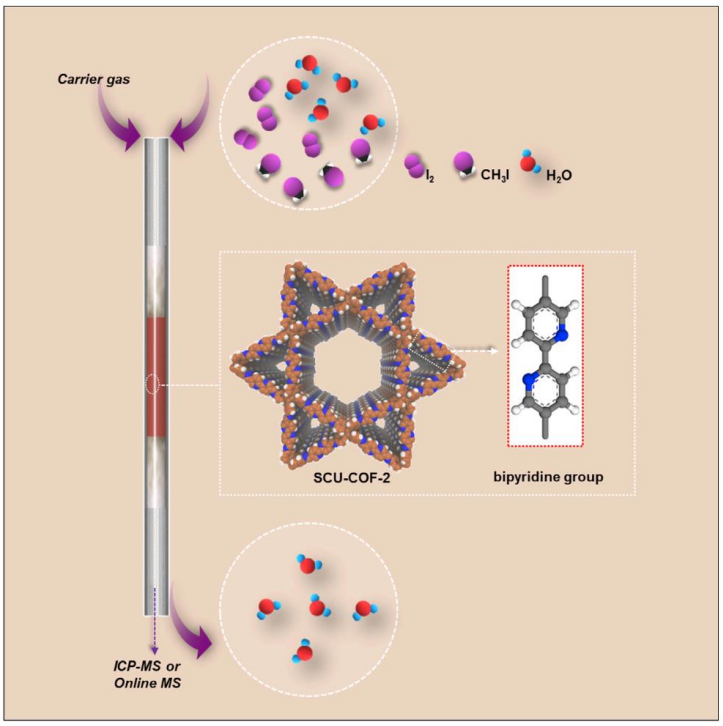
A nitrogen-rich covalent organic framework for simultaneous dynamic capture of iodine and methyl iodide



A 2D dual-pore covalent organic framework (SCU-COF-2) is constructed to efficiently capture iodine gas and methyl iodide simultaneously through the incorporation of 2,2′-bipyridine group introducing exceptionally strong host-guest interactions. This gives rise to new records of static methyl iodide uptake capacity and dynamic iodine uptake capacity, both far beyond those of state-of-art silver-zeolites, MOF materials, and active carbon, showing powerful application potentials.

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HIGHLIGHTS

A new design philosophy for iodine uptake material is presented

SCU-COF-2 exhibits record-high dynamic iodine uptake amount (0.98 g g^{-1})

SCU-COF-2 exhibits record-high static methyl iodide uptake amount (1.45 g g^{-1})

Moisture has a negligible influence on iodine uptake of SCU-COF-2

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Chem
Catalysis

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Reaction: Semiconducting MOFs Offer New Strategy for Uranium Extraction from Seawater

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Hui Li received his PhD from Xinjiang University, after which he worked as a postdoctoral fellow at South China University of Technology and Soochow University. He is currently a research assistant in Prof. Shuao Wang's group at Soochow University, where he studies uranium extraction from seawater using MOFs and COFs. Shuao Wang received his PhD from the University of Notre Dame and then worked as a postdoctoral fellow at Lawrence Berkeley National Laboratory and the University of California, Berkeley. He is currently a distinguished professor at Soochow University. His research interests include coordination, environmental, and material chemistry of critical radionuclides in the nuclear fuel cycle.

Uranium extraction from seawater (UES) is considered one of the seven chemical separations that could change the world.[1] One-round extraction capacity of sorbent materials in the real seawater test of higher than 30 mg/g is a critical research target for showing the potential for commercialization.[2] A common question is why the extraction capacity of sorbent materials in the real seawater test (overwhelming majority < 5 mg/g) is significantly lower than their theoretical extraction capacity obtained by the sorption isotherm experiment (for some materials, this could reach higher than 1,000 mg/g).[3,4] This is because in the sorption isotherm experiment, the sorption capacity is often extrapolated from the sorption experiment where the uranium concentration is extremely high (>1,000 ppm). In this case, uranium can be located at any possible site in the sorbent materials regardless of the binding strength. In sharp contrast, in real seawater, the uranium concentration is extremely low at 3.3 ppb, and its coordination is saturated with carbonate anions, which are known to be strong binding ligands for uranyl ions. Principally, UES capacity is determined when the thermodynamic equilibrium is established between the sorbed uranyl ion in the solid sorbent material and the uranyl carbonate in seawater. The equilibrium constant is designated by the difference of binding strength between uranyl-sorbent interaction and uranyl-carbonate interaction in addition to the number of such sites with strong binding strength. From here, it is very clear that grand challenges are present in reaching a high UES capacity when coordination is utilized as the sole thermodynamic driving force.

Fortunately, uranium is a redox-active metal, where highly soluble uranyl(VI) ion can be reduced to almost insoluble uranium(IV) (U(IV)) in a number of ways. Semiconductor-based photocatalytic reduction of uranyl(VI) offers an alternative way to make a breakthrough in the field of UES. With the introduction of the redox reaction path, the UES capacity can be improved, which is no longer determined by the sorption equilibrium. In addition, the energy input in this method is not an issue because solar light can be utilized.[5] However, although some photocatalysts have been studied for the extraction of U(VI), none of them show real utility in the real seawater test. It seems that the efficiency of sole photoreduction of U(VI) is also quite limited, which is most likely because none of these photocatalysts can pre-enrich uranyl from seawater, and the local concentration of photoreduced U(IV) species is too low to be separated from aqueous solution.

In recent years, semiconducting metal-organic frameworks (MOFs) have been regarded as new types of photocatalysts and, unlike most traditional photocatalysts, possess high structural designability and chemical functionalizability.[6,7] We have proposed a new uranium-extraction strategy with combined specific coordination and photocatalytic reduction based on subtly designed functionalized MOFs (PN-PCN-222 and SCU-19). Pre-enriched into the strong-coordination sites by the introduction of U(VI)-recognizing ligands, U(VI) was simultaneously reduced efficiently by the photoinduced electrons from the photoactive MOF host under visible-light irradiation, affording neutral U(IV) species that were stored in the open space. This also regenerated the coordination sites readily for the next round of uranium extraction.[8,9] This auto-recycled process offers an ultrahigh uranium-extraction capacity that will not be limited by the number of adsorption sites. More importantly, elevated uptake selectivity of uranium can be achieved over competing ions that are not redox active. Especially for PN-PCN-222, U(VI) can almost be completely separated in high or low concentration over an extremely wide pH range, which is impossible to achieve by sorbent materials relying solely on coordination or photocatalytic reduction.

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Review

Advances in oxidase-mimicking nanozymes: Classification, activity regulation and biomedical applications

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ABSTRACT

While oxidases play crucial roles in the cell metabolism by efficient and selective utilization of O_2, the practical applications of natural oxidases are limited due to their intrinsic shortcomings (high cost in purification and poor stability). Recently, great varieties of engineered nanostructures have been demonstrated to display oxidase-mimetic activity, which can serve as ideal candidates for oxidase-mimicking nanozymes. In view of the significant progress of nanozymes, we, in this review, systematically illustrate the classification of oxidase-mimicking nanozymes in terms of the acting group of representative substrates and discuss their possible catalytic mechanisms. We also summary the activity modulation of oxidase-mimicking nanozymes by tuning the physicochemical property of nanomaterials and surrounding environments, as well as their potential biomedical applications in biosensing, antibacteria and cancer treatment. Finally, the current opportunities and challenges are discussed to stimulate the research of understanding and development of nanozymes.

Contents

Abbreviations: ATBS, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); BSA, Bovine serum albumin; Cu_2O, Cuprous oxide; DOPA, 3,4-dihydroxy-phenylalanine; DAB, Diazoaminobenzene; ds-DNA, Double-stranded DNA; ELISA, Enzyme-linked immunosorbent assay; ESR, Electron spin resonance; g-C_3N_4, Graphitic carbon nitride; GMP, Guanosine monophosphate; GOx, Glucose oxidase; H_2O_2, Hydrogen peroxide; HRP, Horseradish peroxidase; IgG, Immunoglobulin G; IL-2, Interleukin 2; LOD, Limit of detection; MOF, Metal-organic framework; MSN, Mesoporous silica; MoO_3, Molybdenum trioxide; NCs, Nanoclusters; NPs, Nanoparticles; NRs, Nanorods; $O_2{}^1$, Singlet oxygen; OH, Hydroxyl radicals; OPD, O-phenylenediamine; PVP, Polyvinyl pyrrolidone; Ph-OH, Phenolic hydroxyl; ROS, Reactive oxygen species; SDS, Sodium dodecyl sulfate; SOD, Superoxide dismutase; ss-DNA, Single-stranded DNA; TBA, Thrombin-binding aptamer; TMB, 3,3′,5,5′-tetramethylbenzidine

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Radionuclide labeled gold nanoclusters boost effective anti-tumor immunity for augmented radio-immunotherapy of cancer

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ABSTRACT

Given the complexity, heterogeneity and metastasis of patient tumors, the combined therapy is usually applied in clinical applications. Internal radioisotope therapy has been an indispensable treatment strategy for primary tumor nowadays. However, the therapeutic effect of internal radioisotope therapy is dissatisfactory for distant tumors or spontaneously metastatic tumors. Herein, we design radionuclide labelled glutathione modified gold nanoclusters (technetium-99m labelled gold nanoclusters (^{99m}Tc@Au NCs) and lutecium-177 labelled gold nanoclusters (^{177}Lu@Au NCs)) by simple chelation between glutathione and radionuclide. Such radionuclide labelled gold nanoclusters could not only enhance the therapeutic outcomes of internal radioisotope therapy but also induce anticancer immunity by activation of dendritic cells (DCs). In addition, ^{177}Lu@Au NCs could effectively eliminate primary tumors and suppress the growth of distant tumors when combined with immune checkpoint inhibitors. Furthermore, a long-term immunological memory effect is also observed after internal radioisotope therapy. Importantly, on a clinical-relevant transgenic mice model, we for the first time use such therapeutic strategy to significantly suppress the growth of spontaneously metastatic tumors and lengthen the survival time of the transgenic mice. Our study presents a novel approach for tumor radio-immunotherapy and meanwhile provides a new idea for spontaneously metastatic tumors in clinic.

Introduction

The death of tumor patients is often caused by tumor metastasis, rather than the primary tumor [1–3]. Therefore, how to achieve solid tumor treatment and inhibit tumor metastasis is a key point in the field of clinical treatment [4,5]. For patients with cancer at an early stage, the use of imaging technology, tumor markers and other biologic methods to achieve the early lesion detection and timely scientific treatment are beneficial for radical treatment [6–8]. For advanced stages of cancer especially metastatic tumors, however, it is hard to achieve effective radical cure [9,10]. The current clinical treatment methods for spontaneously metastatic tumors include chemotherapy, molecular targeted therapy or combined therapy, *etc.* [11–17]. Unfortunately, the systemic side effects and nonspecific distribution further limit the therapeutic efficacy of those therapeutic modalities in a certain extent [18–20]. With the blooming of cancer immunotherapy in recent years, which can train the immune system of patients to assault distant or metastatic tumors and produce a certain immune memory effect, tumor treatment strategies are further expanded [21,22]. In immunotherapies for cancer, the use of immune checkpoint inhibitors such as anti-PD1/anti-PD-L1 or anti-CTLA-4 has achieved inspiring clinical effects in curing of some specific tumors [23–25]. Nevertheless, the response rate of immunotherapy is still relatively low for patients with tumor, which less than 30% on average. In order to further improve the response rate of immunotherapy, chemotherapy, radiotherapy or other treatments, which can induce the immunogenic cell death of tumor cells and enhance tumor immunogenicity, are also applied to combine with immune checkpoint inhibitors [26,27]. Among them, radiation therapy (RT) including external beam radiotherapy (EBRT) and internal radioisotope therapy have been indispensable treatments strategy in clinical trials [28–30]. However, the therapeutic effect of radiotherapy, especially internal radioisotope therapy, is still restricted by some certain mechanisms, such as off-targeted radionuclides, physiological toxicity and radiation resistance caused by tumor hypoxic microenvironment [31,32].

With the flourishing development of nanotechnology, nanomedicine strategies have been applied to improve the efficacy of

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Reprogramming Tumor-Associated Macrophages via ROS-Mediated Novel Mechanism of Ultra-Small $Cu_{2-x}Se$ Nanoparticles to Enhance Anti-Tumor Immunity

*Yanhui Zheng, Yaobao Han, Tingting Wang, Hanghang Liu, Qiao Sun, Shijun Hu, Jianquan Chen, and Zhen Li**

Reprogramming tumor-associated macrophages (TAMs) from tumor-supportive M2 phenotype to anti-tumor M1 phenotype holds great promise in tumor immunotherapy. However, there are few reports on the remodeling of TAMs by inorganic nanoparticles due to their unclear intrinsic polarization mechanism. In this article, a novel signaling pathway of repolarizing TAMs into M1-like macrophages is reported to boost anti-tumor immunity using ultra-small $Cu_{2-x}Se$ nanoparticles (CS NPs). The mechanism is totally different from the conventional ROS-mediated polarization mechanism. It is revealed that CS NPs can effectively generate ROS in the macrophages to trigger auto-ubiquitination of tumor necrosis factor receptor-associated factor 6 (TRAF6), which activates the interferon regulatory factor 5 (IRF5) to facilitate the expression of its downstream gene interleukin-23 (IL-23), and eventually remodels the TAMs into M1-like macrophages. It is shown that CS NPs can significantly inhibit the growth of melanoma tumor (B16F10) by repolarizing TAMs into M1-like macrophages, and enhance the adaptive anti-tumor immunity by inducing the infiltration of $CD8^+$ T cells. Moreover, it is found that CS NPs can also effectively inhibit the recurrence of distal tumor. The study shows the novel macrophage polarization mechanism for TAMs-targeted cancer immunotherapy, and demonstrates the great potential of ultra-small $Cu_{2-x}Se$ nanoparticles in cancer immunotherapy.

1. Introduction

It has been well known that tumor cells can recruit and control immune cells to escape immunological surveillance and to promote tumor progression.[1,2] Immunosuppressive cells, including regulatory T lymphocytes (Tregs), myeloid-derived suppressor cells (MDSCs) and tumor-associated macrophages (TAMs), usually overexpress specific receptors to communicate with the corresponding chemokines released by tumor cells and immune cells. They travel into the tumor microenvironment (TME), and transform into "accomplices" of tumor cells, which facilitate tumor growth and tumor metastasis.[1–3] In recent years, inspired by the immune escape of malignancies, tumor immunotherapy has opened a new gate for treatment through utilizing the innate and adaptive immunity of tumor patients.[4] Modulating the immunosuppressive tumor immune microenvironment (TIME) to reconstruct immune surveillance system is one of the most promising ways for tumor immunotherapy.[5] Training of macrophages to be immunosuppressive TAMs by abnormal TME is an impactive immune escape pattern during the tumor progression, because TAMs are the major tumor-infiltrating immunosuppressive cells in the TIME.[6–8]

Macrophages are highly plastic and can be divided into two phenotypes, i.e., proinflammatory or tumoricidal M1-like, and anti-inflammatory or tumor-supportive M2-like macrophages.[9] The abnormal TME contains multiple stimulating factors, such as colony stimulating factor-1 (CSF-1), interleukin-4 (IL-4), interleukin-13 (IL-13), lactic acid and prostaglandins,[6,7,10,11] which polarize TAMs to be tumor-supportive M2-like macrophages. The M2-like TAMs contribute to the tumor progression, metastasis, and invasion by inducing angiogenesis and remodeling the extracellular matrix.[4,7,12,13] They also inhibit adaptive immunity by suppressing T cells activity.[4,13] Due to the prominent role of TAMs in tumor-promotion and immune suppression, they have become a fascinating target for modulating the immunosuppressive TIME to enhance anti-tumor therapy.

As a class of professional phagocytes, which constitute the innate immune system to form the first line for nonspecific

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REVIEW ARTICLE OPEN

Inflammasomes as therapeutic targets in human diseases

Yangxin Li[1], Hui Huang[2], Bin Liu[3], Yu Zhang[1], Xiangbin Pan[4], Xi-Yong Yu[5], Zhenya Shen[1] and Yao-Hua Song[6]

Inflammasomes are protein complexes of the innate immune system that initiate inflammation in response to either exogenous pathogens or endogenous danger signals. Inflammasome multiprotein complexes are composed of three parts: a sensor protein, an adaptor, and pro-caspase-1. Activation of the inflammasome leads to the activation of caspase-1, which cleaves pro-inflammatory cytokines such as IL-1β and IL-18, leading to pyroptosis. Effectors of the inflammasome not only provide protection against infectious pathogens, but also mediate control over sterile insults. Aberrant inflammasome signaling has been implicated in the development of cardiovascular and metabolic diseases, cancer, and neurodegenerative disorders. Here, we review the role of the inflammasome as a double-edged sword in various diseases, and the outcomes can be either good or bad depending on the disease, as well as the genetic background. We highlight inflammasome memory and the two-shot activation process. We also propose the M- and N-type inflammation model, and discuss how the inflammasome pathway may be targeted for the development of novel therapy.

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INTRODUCTION

Inflammasomes are intracellular multimeric complex molecules that recognize either pathogen-associated molecular patterns (PAMPs) or danger-associated molecular patterns (DAMPs).[1,2] The nucleotide-binding oligomerization (NOD)-, leucine-rich repeat (LRR)-, and pyrin domain-containing 3 (NLRP3) and the NOD-, IRR-, and CARD-containing 4 (NLRC4) inflammasomes belong to the NOD-like receptor (NLR) family.[3,4] Non-NLR proteins, such as absent in melanoma 2 (AIM2), form inflammasomes that can sense cytosolic double-stranded DNA.[5,6]

The canonical inflammasomes (NLRP3, NLRC4, and AIM2) serve as a platform to engage pro-caspase-1 (Figs. 1–3 and Box 1), which becomes active caspase-1 through the oligomerization of pro-caspase-1 proteins.[7] Activated caspase-1 processes pro-interleukin-1β (IL-1β) and pro-IL-18 to generate their active forms, which induce pyroptosis, a pro-inflammatory form of cell death.[2,8–10] The non-canonical inflammasomes activate caspase-11 (mouse) or caspase-4/5 (human) in response to Gram-negative bacteria-derived lipopolysaccharide (LPS) without cleaving pro-IL-1β (Fig. 4).[1,11,12]

NLRs have three functional domains: the amino-terminal domain includes a pyrin domain (PYD), or a caspase-recruitment domain (CARD); the central nucleotide-binding and oligomerization domain (NACHT) is present in all NLR proteins; and the carboxy-terminal domain is an LRR domain that binds to ligand.[13] The PYD interacts with apoptosis-associated speck-like protein containing a CARD (ASC) which in turn binds pro-caspase-1 (Fig. 1).[14,15] ASC is an adaptor protein used by many cytoplasmic pattern recognition receptors (PRRs) such as NLRs to recruit pro-caspase-1 to the inflammasomes via its CARD domain. PRRs are sensor proteins that detect signals to activate an inflammatory response.

The membrane-bound PRRs such as Toll-like receptors (TLRs) and cytosolic PRRs such as NLRs recognize PAMPs and host-derived DAMPs, respectively.[16] Activation of PRRs by PAMPs leads to the production of type I interferons and chemokines, whereas activation of PRRs by DAMPs activates caspases that eventually lead to the production of pro-inflammatory cytokines. DAMP-induced inflammation is referred to as sterile inflammation because it occurs in the absence of invading microbes.[10,13,17] DAMP-triggered sterile inflammation can exaggerate pathology either as a causative or contributing factor in response to host-derived factors such as intracellular molecules released from damaged cells. When the inflammation persists for a long period of time, it becomes a chronic process, leading to sterile inflammatory diseases such as atherosclerosis, myocardial infarction, diabetes, neurodegenerative disease, depression, and cancer.

DISCOVERY AND MECHANISMS OF ACTIVATION OF INFLAMMASOMES

Different types of inflammasome are briefly discussed in order to understand the role of their activation in disease states.

History of inflammasomes

The term "inflammasome" was first coined in 2002 by Dr. Jurg Tschopp and colleagues.[2] They described the inflammasome as a

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Blastocyst-Inspired Hydrogels to Maintain Undifferentiation of Mouse Embryonic Stem Cells

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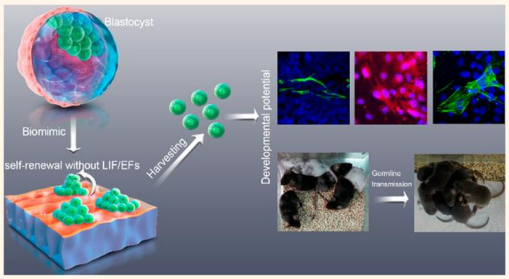
ABSTRACT: **Stem cell fate is determined by specific niches that provide multiple physical, chemical, and biological cues. However, the hierarchy or cascade of impact of these cues remains elusive due to their spatiotemporal complexity. Here, anisotropic silk protein nanofiber-based hydrogels with suitable cell adhesion capacity are developed to mimic the physical microenvironment inside the blastocele. The hydrogels enable mouse embryonic stem cells (mESCs) to maintain stemness *in vitro* in the absence of both leukemia inhibitory factor (LIF) and mouse embryonic fibroblasts (MEFs), two critical factors in the standard protocol for mESC maintenance. The mESCs on hydrogels can achieve superior pluripotency, genetic stability, developmental capacity, and germline transmission to those cultured with the standard protocol. Such biomaterials establish an improved dynamic niche through stimulating the secretion of autocrine factors and are sufficient to maintain the pluripotency and propagation of ESCs. The mESCs on hydrogels are distinct in their expression profiles and more resemble ESCs *in vivo*. The physical cues can thus initiate a self-sustaining stemness-maintaining program. In addition to providing a relatively simple and low-cost option for expansion and utility of ESCs in biological research and therapeutic applications, this biomimetic material helps gain more insights into the underpinnings of early mammalian embryogenesis.**



KEYWORDS: *hydrogels, embryonic stem cells, pluripotency, hierarchy, physical cues*

Stem cells, which can self-renew and have multipotent differentiation potential, are critical determinants in tissue engineering,[1,2] regenerative medicine,[3−5] and tissue/disease models.[6,7] Embryonic stem cells (ESCs), an important member of the stem cell family, are critical resources for deriving tissue-specific stem cells for regeneration and for understanding processes involved in early embryonic development.[1,3,8,9] Expansion of ESCs without differentiation *in vitro* is a prerequisite for long-term maintenance.[10] ESCs can maintain stemness *in vitro* under the control of a complex of exogenous growth factors in combination with embryonic fibroblasts (EFs).[11−13] While laborious and time-consuming protocols involving cytokine leukemia inhibitory factor (LIF) and mouse embryonic fibroblasts (MEFs) have been developed to maintain the long-term stemness of mESCs *in vitro*, potential pathogenic/xenogeneic contaminations raise safety concerns.[14] Although the long-term pluripotency of ESCs can be achieved, recent studies revealed the loss of biological features of ESCs under the reported culture procedures.[15] Moreover, the intrinsic features of the niche necessary for ESCs' self-renewal remain elusive. Recent studies have clarified the contributions of various cues,[16,17] and it is increasingly evident that MEF-free niches can maintain long-term pluripotency of mESCs, suggesting a decisive role for chemical and physical cues in this process.[18−21] LIF-free culture systems were also developed recently to tune the fates of mESCs, but only supported inferior long-term stemness to the standard LIF/MEF

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Postchronic Single-Walled Carbon Nanotube Exposure Causes Irreversible Malignant Transformation of Human Bronchial Epithelial Cells through DNA Methylation Changes

Jin Wang,[#] Xin Tian,[#] Jie Zhang, Lirong Tan, Nan Ouyang, Beibei Jia, Chunying Chen, Cuicui Ge,* and Jianxiang Li*

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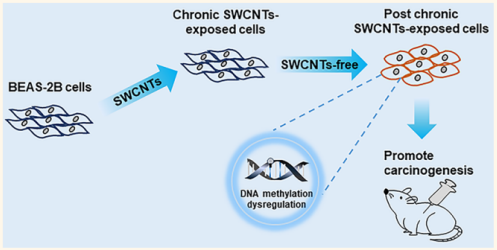
ABSTRACT: As environmental pollutants and possible carcinogens, carbon nanotubes (CNTs) have recently been found to induce carcinogenesis and tumor metastasis after long-term pulmonary exposure. However, whether CNT-induced carcinogenesis can be inherited and last for generations remains unclear. Herein, postchronic single-walled carbon nanotubes (SWCNTs) exposed human lung cell model (BEAS-2B cells) are established to investigate SWCNT-induced carcinogenesis. At a tolerated sublethal dose level, postchronic SWCNT exposure significantly increases the migration and invasion abilities of BEAS-2B cells, leading to malignant cell transformation. Notably, the malignant transformation of BEAS-2B cells is irreversible within a 60 day recovery period after SWCNT exposure, and the malignant transformation activities of cells gradually increase during the recovery period. Moreover, these transformed cells promote carcinogenesis *in vivo*, accompanied by a raised level of biomarkers of lung adenocarcinoma. Further mechanism analyses reveal that postchronic exposure to SWCNTs causes substantial DNA methylation and transcriptome dysregulation of BEAS-2B cells. Subsequent enrichment and clinical database analyses reveal that differentially expressed/methylated genes of BEAS-2B cells are enriched in cancer-related biological pathways. These results not only demonstrate that postchronic SWCNT-exposure-induced carcinogenesis is heritable but also uncover a mechanism from the perspective of DNA methylation.



KEYWORDS: *carbon nanotubes, postchronic exposure, human bronchial epithelial cells, malignant transformation, DNA methylation*

Carbon nanotubes (CNTs) are rolled-up graphene sheets that have been widely applied in industrial and biomedical fields.[1−3] With their large-scale production and extensive applications, there are already numerous toxicity studies about CNTs concerning their toxic effects on environmental exposure and human health.[4−8] Recent studies have suggested CNTs can induce inflammation and fibrosis of granuloma formation, contributing to lung cancer risk.[9−11] It has been reported that CNT-exposed human lung cells exhibit an aggressive, neoplastic-like phenotype, which has toxicity similar to that of asbestos fibers, a kind of human carcinogen.[12−15] In addition, Chen and co-workers have demonstrated that pulmonary exposure to multiwalled carbon nanotubes (MWCNTs) significantly promotes malignant transformation of mammary carcinoma.[16] These findings provide evidence for the carcinogenicity potential of CNT exposure.

So far, most reports of CNT-induced carcinogenesis focused only on chronic exposure but focused very limited on the state after chronic exposure. Previous evidence proved that the effects of postchronic exposure to toxic chemicals are different from acute/chronic exposure.[17,18] For instance, postchronic cadmium-exposed human lung cells exhibited greater intrinsic DNA damage, which is highly prone to malignant transformation.[19] In our previous study, we found that postchronic exposure to cigarette smoke increases aberrant DNA methylation and oncogene expression of human lung

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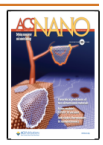

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Steroids Enable Mesenchymal Stromal Cells to Promote CD8$^+$ T Cell Proliferation Via VEGF-C

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Mesenchymal stromal cells (MSCs) function as a formidable regulator of inflammation and tissue homeostasis and expanded MSCs are shown to be effective in treating various inflammatory diseases. Their therapeutic effects require the existence of certain inflammatory cytokines. However, in the absence of sufficient proinflammatory stimuli or in the presence of anti-inflammatory medications, MSCs are animated to promote immune responses and unable to alleviate inflammatory disorders. In this study, it is demonstrated that steroid co-administration interferes the efficacy of MSCs in treating acute graft-versus-host disease (aGvHD). Molecular analysis reveals that vascular endothelial growth factor C (VEGF-C) is highly induced in MSCs by steroids and TNFα and VEGF-C in turn promotes CD8$^+$ T cell response. This immune promoting effect is abolished by blockade or specific genetic ablation of VEGFR3 in CD8$^+$ T cells. Additionally, administration of VEGF-C alone exacerbates aGvHD progression through eliciting more vigorous CD8$^+$ T cell activation and proliferation. Further studies demonstrate that VEGF-C augments the PI3K/AKT signaling process and the expression of downstream genes, such as Cyclin D1. Thus, the data demonstrate that steroids can reverse the immunosuppressive effect of MSCs via promoting VEGF-C-augmented CD8$^+$ T cell response and provide novel information for designing efficacious MSC-based therapies.

1. Introduction

The cardinal traits of mesenchymal stromal cells (MSCs) during tissue repair and regeneration are their concerted actions of immunoregulation, production of multiple growth factors, and multiple differentiation potential under certain conditions.[1] The discovery of the prominent immunosuppressive properties of MSCs in vitro raises the possibility for their application in the treatment of autoimmune diseases.[2] Indeed, the first case report that exogenously administered MSCs could successfully alleviate refractory acute graft-versus-host disease (aGvHD) leading to extensive investigations on the applications of MSCs in various autoimmune diseases.[3] Many studies have demonstrated that the therapeutic effects of MSCs on autoimmune diseases variably rely on their high expression of immunosuppressive factors, including indoleamine 2,3-dioxygenase (IDO),[4] inducible nitric oxide synthase (iNOS),[5] transforming growth factor-β(TGF-β),[6] insulin like growth factor 2,[7] hepatic growth

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Emerging targeted drug delivery strategies toward ovarian cancer

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ABSTRACT

Ovarian cancer is a high-mortality malignancy in women. The contemporary clinical chemotherapy with classic cytotoxic drugs, targeted molecular inhibitors would mostly fail when ovarian cancer cells become drug-resistant or metastasize through the body or when patients bare no more toleration because of strong adverse effects. The past decade has spotted varying targeted delivery systems including antibody-drug conjugates (ADCs), peptide/folate/aptamer-drug conjugates, polymer-drug conjugates, ligand-functionalized nanomedicines, and dual-targeted nanomedicines that upgrade ovarian cancer chemo- and molecular therapy effectively in preclinical/clinical settings via endowing therapeutic agents selectivity and bypassing drug resistance as well as lessening systemic toxicity. The targeted delivery approaches further provide means to potentiate emergent treatment modalities such as molecular therapy, gene therapy, protein therapy, photodynamic therapy, dual-targeting therapy and combination therapy for ovarian cancer. This review highlights up-to-date development of targeted drug delivery strategies toward advanced, metastatic, relapsed, and drug resistant ovarian cancers.

Abbreviations: OC, ovarian cancer; EOC, epithelial ovarian cancer; HGSOC, high-grade serous cancer; LGSOC, low-grade serous cancer; ADC, antibody-drug conjugates; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; DAR, drug-to-antibody ratio; IMGN853, mirvetuximab soravtansine; FR, folate receptor; FRα, folate receptor α; sulfo-SPDB, N-succinimidyl 4-(2-pyridyldithio)-2-sulfobutanoate; CDX, cell-derived xenograft; PDX, patient-derived xenograft; CMC, chemical manufacturing control; Q3W, every three weeks; ORR, objective response rate; NaPi2b, sodium phosphate transporter; MMAE, monomethyl auristatin E; MCVC-PAB, maleimidocaproylvaline-citrulline-p-aminobenzyloxycarbonyl; LIFA, lifastuzumab vedotin; AF-HPA, antimitotic auristatin F-hydroxypropylamide; MTD, maximum-tolerated dose; CA125, cancer antigen 125; CD166, cluster determinant 166; CD44, cluster determinant 44; Pt, platinum; PTX, paclitaxel; GSH, glutathione; HER1, human epidermal growth factor receptor 1; HER2, human epidermal growth factor receptor 2; FDA, Food and Drug Administration; PARP, poly ADP-ribose polymerase; PLK1, polo-like kinase 1; NGs, nanogels; TAMs, tumor-associated macrophages; TICs, tumor-initiating cells; CR, complete response; Val-Ala-PAB, valyl-alanyl-*para*-aminobenzyloxy; NucA, nucleolin aptamer; PDCs, polymer-drug conjugates; HA, hyaluronic acid; GEM, gemcitabine; ROS, reactive oxygen species; CBTA, cyclobutane-1,2,3,4-tetracarboxylic dianhydride; L-BSO, $_{L}$-buthionine sulfoximine; NCe-FA, folate-conjugated nanoceria; TLR4, toll-like receptor 4; EGFR, epithelial growth factor receptor; EPI-HCl, epirubicin hydrochloride; Cy5, cyanine5; MNs, micellar nanoparticles; CR, complete response**; FAK, focal adhesion kinase; HA-MSN, HA-functionalized mesoporous silica nanoparticles; LHRH, luteinizing hormone-releasing hormone; Gro-α, growth-regulated oncogene α; shRNA, short hairpin RNA; GrB, granzyme B; CC, cytochrome C; Tf, transferrin; R8, octaarginine

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Research Article

Task-Specific Tailored Cationic Polymeric Network with High Base-Resistance for Unprecedented $^{99}TcO_4^-$ Cleanup from Alkaline Nuclear Waste

Jie Li,[†] Baoyu Li,[†] Nannan Shen, Lixi Chen, Qi Guo, Long Chen, Linwei He, Xing Dai, Zhifang Chai, and Shuao Wang*

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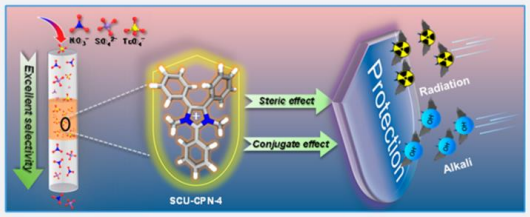
ABSTRACT: Direct removal of $^{99}TcO_4^-$ from alkaline nuclear waste is desirable because of the nuclear waste management and environmental protection relevant to nuclear energy but is yet to be achieved given that combined features of decent base-resistance and high uptake selectivity toward anions with low charge density have not been integrated into a single anion-exchange material. Herein, we proposed a strategy overcoming these challenges by rationally modifying the imidazolium unit of a cationic polymeric network (SCU-CPN-4) with bulky alkyl groups avoiding its ring-opening reaction induced by OH^- because of the steric hindrance effect. This significantly improves not only the base-resistance but also the affinity toward TcO_4^- as a result of enhanced hydrophobicity, compared to other existing anion-exchange materials. More importantly, SCU-CPN-4 exhibits record high uptake selectivity, fast sorption kinetics, sufficient robustness, and promising reusability for removing $^{99}TcO_4^-$ from the simulated high-level waste stream at the U.S. Savannah River Site, a typical alkaline nuclear waste, in both batch experiment and dynamic column separation test for the first time.



INTRODUCTION

The advanced nuclear fuel cycle has been considered a critical requirement for the sustainable development of nuclear energy. To date, PUREX (plutonium uranium reduction extraction) process is the most used technology that has been employed for used fuel reprocessing in commercial plants. However, it still suffers from some drawbacks, for example, the flammability of the organic solvents, the occurrence of radiation-induced solvent degradation, high construction costs, and production of considerable amounts of radioactive wastes.[1,2] Therefore, new reprocessing approaches that enable the separation of fission products from actinides in a more environment-friendly and cost-effective manner should be further investigated. A new conceptual process (carbonate extraction, CARBEX) that aims to reprocess used nuclear fuel using high-alkaline carbonate media with oxidizing agents (i.e., H_2O_2) is considered as an alternative way of PUREX in nuclear fuel management.[3−5] Additionally, unlike the acidic stream in PUREX process, the alkaline nature of CARBEX process makes it a good choice for the management of alkaline high-level radioactive waste (HLW). On the other hand, it has been estimated that ~18 000 m^3 of alkaline HLW are stored in Mayak Production Association[1] and millions of gallons of alkaline HLW are stored in Hanford Site, Washington State, and Savannah River Site (SRS), South Carolina, U.S.A.[6] most of which are leftover by the cold war and are still stored in underground tanks awaiting pretreatment and safe disposal.[7,8] A crucial challenge to conquer is how to efficiently separate fission products under highly alkaline conditions.

^{99}Tc mainly presents as a soluble pertechnetate anion ($^{99}TcO_4^-$) in aerobic conditions because of its noncomplexing nature and low charge density.[7,8] This makes the depth removal of $^{99}TcO_4^-$ difficult by the precipitation method. In addition, $^{99}TcO_4^-$ can easily migrate into the environment via groundwater during long-term storage.[9−11] Moreover, the volatile nature of Tc(VII) complexes brings higher risk of leakage during waste vitrification. In fact, Tc-99 has been leaked to the subsurface environment of several HLW storage sites, resulting in serious contamination of underground water,[11] seawater,[12,13] and rivers.[14,15] Thus, it is highly desirable to seek an effective strategy for $^{99}TcO_4^-$ removal from highly alkaline conditions. However, this task still represents a challenge given the harsh conditions of strong

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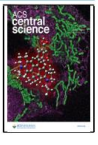

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Article

UCN@C_s(6)-C_{82}: An Encapsulated Triangular UCN Cluster with Ambiguous U Oxidation State [U(III) versus U(I)]

Qingyu Meng,[‖] Laura Abella,[‖] Wei Yang,[‖] Yang-Rong Yao, Xinye Liu, Jiaxin Zhuang, Xiaomeng Li, Luis Echegoyen, Jochen Autschbach,* and Ning Chen*

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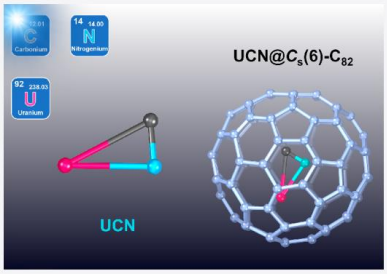
ABSTRACT: Understanding the chemical behavior of actinide elements is essential for the effective management and use of actinide materials. In this study, we report an unprecedented η^2 (side-on) coordination of U by a cyanide in a UCN cluster, which was stabilized inside a C_{82} fullerene cage. UCN@C_s(6)-C_{82} was successfully synthesized and fully characterized by mass spectrometry, single crystal X-ray crystallography, cyclic voltammetry, spectroscopy, and theoretical calculations. The bonding analysis demonstrates significant donation bonding between CN^- and uranium, and covalent interactions between uranium and the carbon cage. These effects correlate with an observed elongated cyanide C−N bond, resulting in a rare case where the oxidation state of uranium shows ambiguity between U(III) and U(I). The discovery of this unprecedented triangular configuration of the uranium cyanide cluster provides a new insight in coordination chemistry and highlights the large variety of bonding situations that uranium can have.



INTRODUCTION

The study of actinide clusters and gas-phase molecules provided important fundamental knowledge of the bonding behavior of actinides.[1−3] However, while actinide gas-phase molecules and clusters were widely investigated by combined spectroscopic and theoretical methods, the systematic characterization of their bonding motifs is still extremely challenging as these species are generally not stable under ambient conditions and can hardly be obtained on a macroscopic scale. Interestingly, our recent discovery of a novel endohedral fullerene family, actinide clusterfullerenes, shows that fullerene cages can be utilized as effective nanocontainers to stabilize and study rare and reactive actinide clusters, which contain unique actinide metal−ligand bonding motifs.[4−6] For example, the first reported actinide clusterfullerene, U_2C@I_h(7)-C_{80} contained a bent U═C═U cluster with two axial U═C double bonds, a bonding structure never observed in molecular compounds.[6] A study of U_2C_2@I_h(7)-C_{80} showed that it was the first molecule featuring a bonding motif with two U centers bridged by a C≡C unit.[4] These results showed that usual actinide bonding motifs can be stabilized and obtained in macroscopic quantities as endohedral clusters inside fullerene cages. Thus, the continuing exploration of novel actinide clusterfullerenes not only expands the research area of fullerene chemistry but also, more importantly, deepens our understanding of additional bonding motifs that actinides can exhibit.

CN^- is one of the most common ligands in coordination chemistry. Due to its strong coordination ability, it can stabilize various oxidation states of different metals and adopt different bonding patterns, thus providing a rich variety of compounds with different structures and physicochemical properties.[7] Therefore, the study of uranium cyanide complexes is essential for a comprehensive understanding of the 5f and 6d orbital participation in actinide−ligand multiple bonds. To date, several uranium complexes with CN^- ligands have been reported, including CN^- ligand bridging,[8−10] carbon bonding to the uranium center (UCN),[8,11−14] and nitrogen bonding to the uranium center (UNC).[13] All of the uranium cyanide complexes reported so far adopt these two coordination modes and show a near-linear configuration.

Fullerene cages were also found to be capable of stabilizing metal−cyanide clusters. Monometallic cyanide clusterfullerene (CYCF), YCN@C_s(6)-C_{82}, was first reported by Yang and coworkers in 2013.[15] So far, a series of lanthanide based CYCFs have been synthesized, isolated, and characterized, including MCN@C_{2v}(19138)-C_{76} (M = Y, Tb, and Lu),[16,17] YCN@C_s(6)-C_{82},[15] MCN@C_{84} (M = Y, Tb, Dy),[18] and MCN@C_{82}

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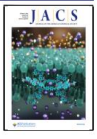

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Fluorescent Probes | Very Important Paper

Activatable Polymeric Nanoprobe for Near-Infrared Fluorescence and Photoacoustic Imaging of T Lymphocytes

Yan Zhang[+], Shasha He[+], Wan Chen, Yinghua Liu, Xuefei Zhang, Qingqing Miao,* and Kanyi Pu**

Abstract: *Development of real-time non-invasive imaging probes to assess infiltration and activation of cytotoxic T cells (CTLs) is critical to predict the efficacy of cancer immunotherapy, which however remains challenging. Reported here is an activatable semiconducting polymer nanoprobe (SPNP) for near-infrared fluorescence (NIRF) and photoacoustic (PA) imaging of a biomarker (granzyme B) associated with activation of CTLs. SPNP comprises a semiconducting polymer (SP) conjugated with a granzyme B cleavable and dye-labeled peptide as the side chain, both of which emit NIRF and PA signals. After systemic administration, SPNP passively targets the tumor and in situ reacts with granzyme B to release the dye-labeled peptide, leading to decreased NIRF and PA signals from the dye but unchanged signals from the polymer. Such ratiometric NIRF and PA signals of SPNP correlate well with the expression level of granzyme B and intratumoral population of CTLs. Thus, this study not only presents the first PA probes for in vivo imaging of immune activation but also provides a molecular design strategy that can be generalized for molecular imaging of other immune-related biomarkers.*

Introduction

Cancer immunotherapy that harnesses the host immune system to eliminate malignant cancer cells represents a promising clinical approach to treat various cancers.[1] Increasing evidences have revealed that the success of anti-cancer immunity strongly correlates with the presence of tumor-infiltrating T lymphocytes due to the pivotal role of T lymphocytes in antitumor immunity.[2] Thus, evaluation of the presence and activation of T lymphocytes is critical for monitoring cancer immunotherapeutic efficacy and predicting the cancer treatment outcome, which involves the biopsies assessment and anatomical measurement in clinical settings. While the invasive biopsies are often evaluated by post-therapeutic time scales and may poorly correlate with the clinic pathology; the imaging modalities including computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET), offer non-invasively diagnostic abilities.[3] However, these imaging modalities generally lack molecular sensitivity or specificity, which necessitates the development of alternative approaches to enable early and accurate assessment of the immune responses associated with T lymphocytes.

Molecular optical imaging enables early visualization and detection of subtle molecular abnormalities with high sensitivity and specificity.[4] Although fluorescence probes have been extensively exploited for imaging of cancer biomarkers, only few examples were reported for in vivo imaging of T lymphocytes, which include dye-iron oxide nanoparticles, and hemi-cyanine macromolecular reporter.[5] Moreover, fluorescence probes often encounter the tissue of shallow tissue penetration depth due to high photon absorption and scattering.[6] In contrast, photoacoustic (PA) imaging that integrates near-infrared (NIR) excitation with thermal-ultrasonic detection provides deeper tissue penetration (up to 12 cm) relative to fluorescence imaging.[7] Activatable PA imaging probes with biomarker-triggered signals offer measurable and quantifiable real-time information on pathological status at the molecular level.[8] Among many PA agents including gold nanoparticles,[9] two-dimensional materials,[10] carbon-based nanomaterials,[11] porphysomes,[7a,12] dye-doped nanoparticles,[13] semiconducting polymer nanoparticles (SPN) are structurally versatile for construction of activatable PA imaging probes.[14] Till now, activatable PA probes have been used for in vivo imaging of a variety of biomarkers and biologically metabolites, including aberrant pH,[15] reactive oxygen species (ROS),[14a,16] metal ions,[17] enzyme biomarker.[18] However, to the best of our knowledge, there are currently no activatable PA probes capable of real-time in vivo monitoring of T lymphocytes.

Herein, we report a semiconducting polymer nanoprobe (SPNP) that changes its NIR fluorescence (NIRF) and PA signals to detect granzyme B for real-time in vivo imaging of immune activation in the course of cancer therapy. Granzy-

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Theranostic Agents

Aggregation of Gold Nanoparticles Triggered by Hydrogen Peroxide-Initiated Chemiluminescence for Activated Tumor Theranostics

*Qiulian Mao, Jing Fang, Anna Wang, Yuqi Zhang, Chaoxiang Cui, Shuyue Ye, Yan Zhao, Yali Feng, Jiachen Li, and Haibin Shi**

Abstract: *Developing endogenous photo-activated theranostic platforms to overcome the limitation of low tissue-penetration from external light sources is highly significant for cancer diagnosis and treatment. We report a H_2O_2-initiated chemiluminescence (CL)-triggered nanoparticle aggregation strategy to activate theranostic functions of gold nanoparticles (AuNPs) for effective tumor imaging and therapy. Two types of AuNPs (tAuNP & mAuNP) were designed and fabricated by conjugating 2,5-diphenyltetrazole and methacrylic acid onto the surface of AuNPs, respectively. Luminol was adsorbed onto the mAuNPs to afford self-illuminating mAuNP/Lu NPs that could produce strong CL by reaction with H_2O_2 in the tumor microenvironment, which triggers significant aggregation of AuNPs resulting in enhanced accumulation and retention of AuNPs for activated photoacoustic imaging and photothermal therapy of tumors. We thus believe that this approach may offer a promising tool for effective tumor treatment.*

Introduction

With the rapid development of nanotechnology, nanomaterials have been widely recognized to have a great potential as nanomedicine for cancer diagnosis and treatment due to their adjustable size, large surface area, and passive targeting capability.[1] Nevertheless, the potential toxicity, difficult metabolism, low diagnostic and therapeutic efficacy are the major concerns that severely hinder the wide biomedical applications of nanomaterials in living system. Hence, it is highly demanded and urgent to develop an intelligent and efficient theranostic nanoplatform for precise cancer diagnosis and treatment.

Gold nanoparticles (AuNPs), as one type of noble metal nanomaterials, have received great attention as promising theranostic agents for disease treatment owing to excellent biocompatibility, ease of surface modification, and unique optical property.[2] One particularly important feature is the localized surface plasmon resonance (LSPR) in near-infrared (NIR) region, which plays a crucial role in photoacoustic imaging (PAI) and photothermal therapy (PTT) applications.[3] To date, AuNPs have been well demonstrated to be outstanding photoacoustic and photothermal agents for cancer imaging and therapy because of the unique physicochemical property, strong NIR absorption, and high optical-thermal conversion efficacy.[4] Among them, the optical property of AuNPs are intimately related to their size, morphology, and surface decoration.[5] The spherical solid AuNPs with small size are actually more suitable for in vivo tumor theranostic applications owing to the longer blood circulation time, shorter biological half-life, and deeper tissue penetration.[6] Unfortunately, they are easily excreted by body leading to low tumor accumulation, which in consequence causes poor diagnostic and therapeutic efficacy in living system. However, large gold nanoparticles (>50 nm) normally exhibit strong NIR absorption that is essentially key factor for PAI and PTT applications, but they can be readily entrapped by reticuloendothelial system (RES) leading to unsatisfactory theranostic outcomes.[7] To address above contradiction, great efforts have been recently devoted to manipulate the aggregation of small AuNPs by utilizing external stimuli,[8] such as thiol-containing molecules,[9] acidic extracellular pH,[10] disease-associated enzymes,[11] and DNA, etc,[12] which is capable of not only maximizing the accumulation and retention of AuNPs within tumors, but also shifting the surface plasmon resonance to NIR region for PAI and PTT applications.

Although significant improvements have been achieved thus far, the complex biological microenvironment tends to pose uncontrollable particle aggregation leading to serious side effect to organisms. Light has recently been documented to be a promising stimulus to locally trigger the aggregation of nanoparticles for various biological applications owing to its simple operation, low cost, and spatiotemporal controllability.[13] We have previously developed a type of photo-crosslinkable AuNPs, and for the first time achieved light-induced aggregation of small AuNPs in vivo, as a consequence realizing the activated PAI and PTT of tumors in living mice (Scheme 1 a).[14] Nevertheless, the broad application of this approach in vivo is still impeded by its shallow tissue penetration of 405 nm laser as well as low crosslinking efficiency. Therefore, it is highly significant to develop new advanced strategies for specifically and effectively manipulating the aggregation of AuNPs within tumors for enhanced PAI and PTT in vivo.

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In Vivo Uranium Sequestration using a Nanoscale Metal–Organic Framework

*Xiaomei Wang[+], Lei Chen[+], Zhuanling Bai[+], Duo Zhang, Jingwen Guan, Yijing Zhang, Cen Shi, and Juan Diwu**

Abstract: *An agent for actinide sequestration with fast uranium uptake kinetics and efficient in vivo uranium removal using a nanoscale metal–organic framework (nano-MOF) is proposed. UiO-66 nanoparticles post-synthetically functionalized with carboxyl groups, UiO-66-$(COOH)_4$-180, exhibit the fastest uranium uptake kinetics reported with more than 65% of uranyl in fetal bovine serum (FBS) removed within 5 min. Moreover, the in vivo bio-distribution studies show that the material partially accumulates in kidneys and femurs where uranium mainly deposits facilitating the in vivo sequestration of uranium. The results of the in vivo uranium decorporation assays with mice show that UiO-66-$(COOH)_4$-180 could successfully reduce the amounts of uranyl deposited in kidneys and femurs by up to 55.4% and 36.5%, respectively, and is significantly more efficient than the commercial actinide decorporation agent, $ZnNa_3$-DTPA.*

In the past several decades, advances in the nuclear energy industry, both for civilian and military purposes, has left a lasting legacy on our planet in accumulating uranium waste and contamination and concentrated stockpiles of depleted uranium. This buildup is a significant threat to public health in the event of waste leakage, nuclear incident, or terrorist attacks.[1–3] If uranium is introduced into the human body after exposure, it quickly deposits in kidneys and bones in the form of the hexavalent uranyl ion (UO_2^{2+}) following a short retention time in blood. The combined chemotoxicity and radiotoxicity of uranium can lead to irreversible kidney damage, urinary system disease, DNA damage, and disruption of biomolecules.[4–7] To date, chelation therapy is considered the most effective treatment for uranium decorporation and removal from the body.

Over the years, a series of decorporation agents have been extensively studied for in vivo uranyl chelation aiming at reducing the uranium content of the whole body.[8–13] 5LIO-(Me-3,2-HOPO) and 3,4,3-LI-1,2-HOPO have been regarded as the optimal ligands for clinical applications. However, both HOPO ligands show limited effect in reducing the amount of uranium in bones.[14,15] Our recent work reported a new uranium chelator, 5LIO-1-Cm-3,2-HOPO, that could significantly remove uranium from bones.[15c] Using sodium bicarbonate to decorporate uranium is also recommended, but its application is restricted due to its disturbance of the normal acid-base balance in the body.[16–19] The DTPA ligand is the only authorized chelating agent to treat the internal contamination of actinides, but the performance of DTPA for uranium decorporation is limited in both kidneys and bones. An effect that is likely ascribed to its poor uranium-specific binding affinity. For instance, the stability constant $\log\beta_{110}$ (13.78) of DTPA with uranyl ions is smaller than values of DTPA with essential divalent metal ions at physiological pH (i.e. Zn^{II} ($\log\beta_{110}$, 18.0), Co^{II} ($\log\beta_{110}$, 17.9), Cu^{II} ($\log\beta_{110}$, 20.3), and Ni^{II} ($\log\beta_{110}$, 18.5)).[20] Therefore, DTPA type decorporation agents are commonly used in the form of $CaNa_3$-DTPA or $ZnNa_3$-DTPA to avoid hypocalcemia or even death due to Zn^{II} or Ca^{II} depletion.[21,22] This issue is complicated further by the competitive binding of uranyl by molecular chelators with siderophores that also significantly affects the binding kinetics and removal efficacy of uranium.

The challenge to reduce in vivo uranium content without causing Zn^{II} or Ca^{II} depletion has perplexed most chelating agents currently which fail to out compete thermodynamically stable uranyl complexes that can be formed either with biomolecules in kidneys or with the inorganic phosphate ligand in bones for uranyl. In sharp contrast, functionalized metal–organic framework (MOF) materials have shown high adsorption selectivity, ultrafast sorption kinetics, and extremely high depletion ratio for uranium in the environment.[23–25] This is due to its advantages of large surface area, tunable structural topology, adjustable pore size, biocompatibility, and facile and efficient functionalization. Thus far, most MOFs used for environmental remediation purposes are in the microscale regime, whereas nanoscale MOFs (nano-MOFs) can be expected to exhibit an elevation in guest uptake kinetics making their biological applications more viable.[26–29] Furthermore, nano-MOFs have been studied extensively as effective detoxicants. For instance, Horcajada et al. proposed that a biocompatible and stable metal-organic framework (MOF, MIL-127) can be used as an oral detoxifying adsorbent agent to reduce the salicylate gastrointestinal absorption in the digestive system.[30] Farha et al. has recently reported the efficient removal of uremic toxins using Zr-based MOFs in human serum albumin (HSA).[31] Herein, we utilize nanoscale MOFs for the first time as uranium sequestration agents to rapidly trap uranyl and significantly reduce the whole body uranium content in vivo.

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十、获奖情况

序号	奖励编号	奖励名称	奖励类型	获奖等级	获奖人员（固定人员）
1	2020-J-253-2-04-R04	缺血性心脏病细胞治疗关键技术创新及临床转化	国家科技进步奖	二等奖	胡士军
2	2020-031-R02	肿瘤多模态诊疗一体化探针相关基础研究	高等学校科学研究优秀成果奖	一等奖	高明远、李桢、汪勇、史海斌、曾剑峰
3	2020-1-33-R1	血小板调控机制及其相关血栓与出血疾病诊断治疗应用研究	江苏省科技进步奖	一等奖	戴克胜、周泉生、阮长耿
4	2020GFJBJ3006-R01	认知功能辐射损伤机制和防治的创新技术 研究	国防科学技术进步奖	三等奖	田野
5		中国核设施营运单位操纵人员心理测评系统的研发	中国核学会核科技成果奖	无	刘玉龙
6	2018-3-140-R5	放射性皮肤损伤的基础与救治新技术的研究	苏州市医学会预防医学科技奖	二等奖	曹建平、张琦、朱巍、焦旸、杨红英
7	2018-216	智能辐射检测系统与辐射损伤防治新技术	中国核能行业协会科学技术奖	三等奖	曹建平
8	2019-236	辐射仪器青年科学家奖(Radiation Instrumentation Early Career Award)	辐射仪器青年科学家奖(Radiation Instrumentation Early Career Award)	无	何亦辉

十一、内部协作课题

序号	项目编号	申请人	职称	项目名称	资助经费(万元)	起止时间
1	GZN1202101	吴德沛	教授	肠道菌群在骨髓型放射病救治中的应用及临床转化研究	150	2021.06-2023.12

十二、科研创新课题

序号	项目编号	项目名称	负责人	资助金额（万元）	资助年度
1	GZC00101	心脏类器官在 X 射线辐照下的生物效应及分子机制探索	胡士军	100	2021.1.1-2022.12.31
2	GZC00102	肿瘤靶向 SPECT 可视化纳米硼药的制备及其在硼中子俘获治疗中的应用研究	赵利	30	2021.1.1-2022.12.31
3	GZC00201	靶向放射超敏蛋白 Beclin 的肿瘤放疗增敏与放射防护救护“单靶双效”应用新范式探索研究	王建荣	100	2021.06.01-2023.05.30
4	GZC00202	细胞背包的设计及在放射免疫治疗中的应用	张乐帅	50	2021.06.01-2022.05.30
5	GZC00301	肠道固有层细胞 Caspase-2 分子决定肠型放射病公鼠死亡的机制与应对策略研究	陈　秋	30	2021.12.01-2022.11.30
6	GZC00302	基于个体辐射敏感性及其昼夜节律依赖性的空间辐射防护新策略研究	周光明	50	2021.12.01-2022.11.30

十三、开放课题

序号	项目编号	负责人	工作单位	课题名称	金额（万）	执行时间
1	GZK1202101	周菊英	苏州大学附属第一医院	免疫细胞的代谢重编程在宫颈癌放疗抵抗中的作用及机制研究	5	2021.06-2022.12
2	GZK1202102	吴永友	苏州大学附属第二医院	胃癌靶向性 NIR-II 纳米探针的构建及其在胃癌精准诊疗中的研究	5	2021.06-2022.12
3	GZK1202103	肖灿	苏州大学附属第一医院	放射性口腔黏膜炎损伤蛋白代谢机制的研究	5	2021.06-2022.12
4	GZK1202104	江波	首都医科大学附属北京天坛医院	用于评估胶质瘤烷化剂耐药的 MRI/PET 双模态探针构建及活体成像研究	5	2021.06-2022.12
5	GZK1202105	李明	苏州大学附属第一医院	基于肠道菌群-宿主代谢物组学分析探索放射性肾损伤的生物标记物及机制的研究	5	2021.06-2022.12
6	GZK1202106	朱维培	苏州大学附属第二医院	LINC00460/miR-361-3p/Gli1 通路与宫颈癌细胞辐射敏感性相关性研究	5	2021.06-2022.12
7	GZK1202107	李芳	苏州大学	人羊水干细胞源外泌体通过 hsa-circTHBS1/mmu-miR-140-3p/CXCR4 对电离辐射后毛发再生的作用机制	5	2021.06-2022.12
8	GZK1202108	祁琳	苏州大学附属第二医院	低剂量辐射引发中性粒细胞诱捕网在复发性流产发病中的作用及机制研究	5	2021.06-2022.12
9	GZK1202109	朱静	常熟市第二人民医院	低氘水对恶性肿瘤患者免疫功能的影响	5	2021.06-2022.12

序号	项目编号	负责人	工作单位	课题名称	金额（万）	执行时间
10	GZK1202110	陈杰	苏州市立医院	细菌介导的蛋白酶运输纳米系统用于肿瘤 放射治疗研究	5	2021.06-2022.12
11	GZK1202111	侯君	复旦大学附属中山医院	一种促进核沾染创面愈合的可吸收水凝胶 PCECA plus 的研制和功能研究	5	2021.06-2022.12
12	GZK1202112	张于娟	苏州大学	SPECT-NIR II 智能响应性双模态贯序成像探针研究	5	2021.06-2022.12
13	GZK1202113	秦建忠	苏州大学附属第二医院	低剂量 X 线联合可注射纳米金水凝胶对骨感染的治疗及组学机制研究	5	2021.06-2022.12
14	GZK1202114	潘建斌	南京大学	环境中痕量铀的高灵敏检测装置研制	5	2021.06-2022.12
15	GZK1202115	卞华慧	苏州大学附属第二医院	CCIN 基因突变在铀中毒致生殖毒性中的作用机制研究	5	2021.06-2022.12
16	GZK1202116	朱业锦	南京中医药大学	新型黄酮类化合物 GL-V9 对放射性肠损伤防护作用及机制的研究	5	2021.06-2022.12
17	GZK1202117	曾凯	东华理工大学	铀酰化合物电喷雾萃取质谱快速鉴别方法及应用	3	2021.06-2022.12
18	GZK1202118	廖剑平	南宁师范大学	放射性视网膜病变图像分析方法研究	3	2021.06-2022.12
19	GZK1202119	范志海	苏州大学附属第二医院	基于射线响应性丝素水凝胶的促血管化骨生成因子可视化递送与骨再生机制研究	3	2021.06-2022.12
20	GZK1202120	张丽柯	南阳市第一人民医院	藏红花酸对放射性肺损伤免疫功能的影响及机制研究	3	2021.06-2022.12

序号	项目编号	负责人	工作单位	课题名称	金额（万）	执行时间
21	GZK1202121	徐志红	苏州思萃同位素技术研究所有限公司	含氚废水净化技术的研发	3	2021.06-2022.12
22	GZK1202122	吴琼	苏州大学附属第一医院	基于类器官体外 3D 培养模型的急性胃肠型辐射损伤救治药物体外筛选	3	2021.06-2022.12
23	GZK1202123	郭凌川	苏州大学附属第一医院	CST1 通过 TRIM21 促进结直肠癌肝转移的分子机制	3	2021.06-2022.12
24	GZK1202124	陈磊	苏州市立医院	海藻酸-碘-131/左旋咪唑介入放疗联合免 疫治疗的应用基础研究	3	2021.06-2022.12
25	GZK1202125	邢伟	常州市第一人民医院	基于超小纳米影像探针的肾脏缺血再灌注 损伤的诊疗一体化研究	3	2021.06-2022.12
26	GZK1202126	秦磊	苏州大学附属第一 医院	靶向纳米探针用于肝癌多模态诊疗和抑制转移的研究	3	2021.06-2022.12
27	GZK1202127	邓胜明	苏州大学附属第一医院	肿瘤微环境调控协同的放射性诊疗一体化纳米药物的研发	3	2021.06-2022.12
28	GZK1202128	张鹏	苏州大学附属第二医院	3-乙酰基-11-酮基-β-乳香酸（ AKBA）对放射性脑脊髓病的相关研究	3	2021.06-2022.12
29	GZK1202129	王益民	苏州大学附属第三医院	Tspan9 促进骨肉瘤发生发展的作用机制 及放疗增敏相关性研究	3	2021.06-2022.12
30	GZK1202130	余奇	上海美中嘉和肿瘤门诊部	不同线束（光子、碳离子）辐射对患者免疫功能的影响及其机制研究	3	2021.06-2022.12
31	GZK1202131	李珉	苏州大学附属第一医院	FAP 对卵巢癌的作用及放疗敏感性影响的研究	3	2021.06-2022.12

序号	项目编号	负责人	工作单位	课题名称	金额（万）	执行时间
32	GZK1202132	王小艳	长治医学院	基于肿瘤微环境刺激响应型放射性探针的胃癌成像及声动力治疗研究	3	2021.06-2022.12
33	GZK1202133	江波	苏州大学附属第二医院	低剂量 X-ray 照射通过影响泛素连接酶 MDM2 降解 GAP43 的功能促进周围神经损伤修复的分子机理研究	自筹	2021.06-2022.12
34	GZK1202134	段善州	苏州大学附属第二医院	新型纳米载体新型纳米载体共载氧气与 ADAR1-siRNA 增强非小细非小细胞肺癌放疗与免疫治疗敏感性敏感性的作用机制 研究	自筹	2021.06-2022.12
35	GZK1202135	古小松	苏州大学附属第二医院	Mimecan 对冠脉微循环障碍患者动脉硬化的调节作用及机制	自筹	2021.06-2022.12
36	GZK1202136	蔡武	苏州大学附属第二医院	超小纳米氧化铁 CE-MRA 在急性缺血性脑卒中静脉溶栓后血管再通中的应用基础研究	自筹	2021.06-2022.12
37	GZK1202137	杨欢	苏州大学附属第二医院	外泌体介导的 RP3-340B19.3/STAU1/IκBζ/NF-κB 信号通路调控三阴性 乳腺癌放疗敏感性的临床及机制研究	自筹	2021.06-2022.12
38	GZK1202138	汪东兴	苏州大学附属第二医院	癫痫患者左乙拉西坦单药治疗疗效与 PET 影像和肠道菌群的相关性研究	自筹	2021.06-2022.12
39	GZK1202139	陈炜博	苏州大学附属第二医院	环状 RNA 调控直肠癌放射敏感性机制研究	自筹	2021.06-2022.12

序号	项目编号	负责人	工作单位	课题名称	金额（万）	执行时间
40	GZK1202140	郭亮生	苏州大学附属第二医院	基于多模态多功能探针的宫颈癌诊疗一体化研究	自筹	2021.06-2022.12
41	GZK1202141	黄江	苏州大学附属第二医院	视网膜血管内皮细胞源性外泌体介导的 miRNA 在放射性视网膜病变中的作用机制	自筹	2021.06-2022.12

十四、体制机制和平台建设

重点实验室实行管理委员会领导下的主任负责制，学术委员会对实验室发展战略和重大决策提供咨询和指导。下设综合办公室，负责实验室日常事务管理；按照研究方向设立研究团队，进行项目的组织与实施；建设仪器开放共享平台，对内对外开放共享；通过实验室资助，已购置或自研 16 台大型仪器设备，设备总金额五千余万元。

序号	设备型号	设备名称	产地国	购置时间	设备价格(万元)	国重室出资(万元)
1	ASAP2460	多站拓展式全自动快速比表面与孔隙度分析仪	美国	2018.01	60.1	60.1
2	Talos F200S G2	高分辨场发射透射电镜	美国	2018.12	794.38	794.38
3	E500-10/12	电子自旋（顺磁）共振波谱仪	德国	2018.12	297.78	297.78
4	D8VENTURE	X 射线单晶衍射仪	德国	2018.12	259	259
5	非标定制	空间零磁环境模拟设备	中国	2019.01	186.78	186.78
6	Invivo2 1000	低氧工作站	英国	2019.03	182.94	182.94
7	自研	辐射敏感器官剂量测量体模	中国	2019.06	430	430
8	CPL-300	全波长圆偏振光谱联用仪	日本	2019.08	298.34	240
9	FV3000	激光共聚焦显微镜	日本	2019.09	192.88	154.3
10	Fluidigm Hyperion Imaging System	组织质谱成像系统	加拿大	2019.11	779.9	479.9
11	TS10K	高性能计算集群	中国	2019.11	307.76	240
12	SPL-SC-Pro-7	双波段眼科 OCT 成像系统	中国	2019.12	144	116
13	**AX**	**高分辨多光谱亚细胞激光辐照仪**	**日本**	**2021.01**	**239.5**	**192**
14	**HDX-MS**	**氢-氘交换质谱**	**英国**	**2021.01**	**360**	**288**
15	**VIVO Intravital Imaging System**	**微循环活体成像显微系统**	**美国**	**2021.03**	**372.62**	**372.62**
16	**DDLH2.0/30-500**	**低能电子加速器**	**中国**	**2021.07**	**555**	**555**
合计					**5460.98**	**4848.80**

十五、2021 大事记

2021 年 1 月 29 日，教育部党组成员、副部长翁铁慧莅临放射医学与辐射防护国家重点实验室调研考察

2021 年 3 月 16 日下午，苏州市政协主席、党组书记周伟强、市政协秘书长金建立一行调研考察苏大放射医学与辐射防护国家重点实验室并拜访柴柴之芳院士

2021 年 4 月 14 日上午，中国共产党中央军事委员会装备发展部王世恩处长、刘登参谋来国重室调研

2021 年 4 月 20 日，全国人大常委会副委员长、中国红十字会会长陈竺一行来到放射医学与辐射防护国家重点实验室，听取了国重室副主任时玉舫教授的汇报

2021 年 4 月 29 日，上海市教卫工作党委书记沈炜、上海市教委副主任毛丽娟、上海理工大学书记吴坚勇、上海大学校长刘昌胜一行来苏州大学放射医学与辐射防护国家重点实验室参观调研

2021 年 5 月 28 日下午，原中国人民解放军总医院（301 医院）院长、解放军军医进修学院院长、中央保健委员会委员朱士俊少将一行参观国重室

2021 年 6 月 10 日，江苏省人力资源和社会保障厅党组成员、副厅长朱从明一行莅临放射医学与辐射防护国家重点实验室参观调研

2021 年 6 月 15 日，江苏高校放射医学协同创新中心（以下简称“协同中心”）第三建设期发展规划专家咨询论证会召开

2021 年 6 月 18 日，广西壮族自治区妇女联合会副主席、党组副书记、一级巡视员陈映红，百色市人民政府副市长彭斌，右江民族医学院党委书记邓砚一行调研国重室

2021 年 7 月 16 日下午，国家发展改革委社会司副司长孙志诚、国家发改委社会发展司卫生健康处处长刘丹等一行莅临调研放射医学与辐射防护国家重点实验室

2021 年 10 月 18 日，江苏高校放射医学协同创新中心 2021 年推进会在青岛召开

2021 年 10 月 26 日——29 日，省财政厅监督检查局蔡根任组长的检查组一行对国重室省科技创新财政扶持政策执行情况开展为期三天的调研检查

十六、科普活动

放射医学与辐射防护国家重点实验室作为放射医学领域唯一的国家重点实验室，目前为江苏省和苏州市科普教育基地，拥有院士领衔的科普团队、丰富的科普设施条件和强大的管理运行团队。2020 年以来，各级领导高度重视国重室发展及科普工作情况，苏州市政协主席周伟强、江苏省委书记娄勤俭、国防科工局吴艳华副局长及中国科协科普部钱岩副部长先后参观考察国重室和科普展，国重室科普团队参加全国科普教育基地（江苏）调研座谈，广泛开展与各级科普教育基地交流合作，为科普基地具体工作的落实指明方向。

2021 年，在庆祝建党百年诞辰之际，国重室全面贯彻落实《全民科学素质行动计划纲要》精神，在“全国科普日”等重要节点，围绕“与核同行”主题，开展了一系列科普活动，如：“建党百年创伟业，大国底气从核来”两弹一星精神及核技术应用展、《对撞》“赛先生说”苏州科学文化讲坛、实验室开放日及科技夏令营、“核你一起，医学解密”科普作品大赛等，累计参与人数达 96 万余人。

两弹一星精神及核技术应用展

科普共建基地签约仪式

《对撞》“赛先生说”

实验室开放日

实验室科技夏令营

“核你一起，医学解密”科普作品大赛

国重室在本年度获 2021 年度长三角优秀科级志愿服务组织；2021 年全国科技活动周暨第 33 届江苏省科普宣传周优秀组织单位；2021 年“魅力之光”杯全国核科普讲解大赛优秀组织单位。国重室主办的“以核济世护健康”—全科技创新周暨实验室开放日活动获“典赞·科普苏州”十大科普活动；《辐射与健康》和《放射性核素小侦探》科普系列丛书分别获江苏省和苏州市科普项目立项资助。原创作品获全国高校学生课外“核+X”大赛等多项国家、省、市级荣誉。

十七、存在问题

1、根据实验室建设规划，实验场所应集中整体布局。实验室空间紧张，906楼迟迟无法改造，已经严重影响放药平台建设。从长远发展来看，建议学校考虑给重点实验室单独建楼，不仅有利于实验室发展，更是加强放射性管理的必需。

2、重点实验室科研成果原创性和成果转化有待加强。部分选题的科学性不强；实验室各中心发展不平衡；成果转化应按照国家和学校的有关规定进行，加大转化力度。

3、高水平人才培养和引进需要进一步加强。高水平人才对国重实验室的发展至关重要，人才引进永远在路上，要充分利用好国重实验室相对独立的人事权。

4、研究生素质有待提高。建议增加苏州大学本科生推免攻读硕士研究生的比例，增加硕博连读的人数。要求学生做到“五有”：有思想，有品味，有爱心，有担当，有奉献。

5、实验室重器欠缺。中能粒子加速器进展迟缓，将丧失我们在放射医学的优势，后果不堪设想，实验室及苏州大学的优势将不复存在。

6、新冠疫情对国内和国际学术交流影响严重。