

**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**



**2022**

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**苏州大学**

**Soochow University**

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# 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。

2022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。实验现有成员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、俄罗斯工程院外籍院士1人、国际宇航科学院院士2人、杰青7人、优青8人。2022年度阮长耿院士荣获江苏省基础研究重大贡献奖，讲座教授Tom K. Hei获得江苏省医学会授予国际科学技术合作奖，第五娟教授荣获亚洲辐射研究协会青年科学家奖，张正彪教授牵头完成的“高分子结构设计与精准合成”项目获得中国化工学会基础研究成果奖一等奖，曹建平教授牵头完成的“放射性皮肤损伤救治新技术的研究”项目获得辐射防护学会科技进步奖二等奖，陈新建获得中国产学研合作促进会产学研创新成果奖优秀奖。国重实验室与中国疾控中心放射医学与健康研究所合作主办的英文期刊《Radiation Medicine and

Protection》4 月成为中国科学引文数据库来源期刊，11 月入选中国科技期刊卓越行动计划选育高水平办刊人才子项目。

在科研方面，2022 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 49 项，总金额 1.6 亿余元。值得指出的是，胡士军、张正彪和王旻凹教授分别牵头获得了科技部重点研发计划资助，王旻凹教授获国防科工局核能开发项目以及基金委重大仪器研制项目、李培山和曾剑锋教授获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 252 篇，其中影响因子大于 10 的 91 篇，SCI 引用逾万次。获得授权发明专利 85 项，其中外国发明专利 7 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。新增合作企业及单位包括苏州博瑞生物医药公司、宁波昊祥新材料科技有限公司、通瑞生物医药（上海）有限公司、苏州思萃同位素技术研究有限公司、苏州吾丛孵化器管理有限公司、右江民族医学院医学检验学院及影像学院。与波黑巴尼亚卢卡大学医学院签署贫铀弹污染防治的战略合作协议。

2022 年国重室获批全国科普教育基地、全国核科普教育基地及苏州市科学家精神教育基地。实验室举办了“核你一起，医学解密”科普创意大赛（3-10 月）、“强国有我、核你一起”大学生志愿宣讲团（6-8 月）、“创新强核、科学报国”科普大家谈讲座活动（8-10 月）、第十届“魅力之光”杯全国核科普夏令营（8 月）、“核星起航”专家科普进课堂（5-12 月）等系列科普活动。累计线上+线下参加人员达 5110 万人次。获全国“核+X”大赛一等奖 1 项；全国核科普知识竞赛一等奖 1 项、讲解员大赛获二等奖、三等奖各 1 项，核学会先进个人 3 人获；“典赞·科普苏州”年度科普人物 1 项等各类科普荣誉 20 余项。

实验室有 75 人次被邀请在国际国内学术会议上作各类学术报告；共有 16 人次被邀请来实验室作学术报告。另外，实验室成功举办了第二届分子精准合成与碳循环化学国际研究生创新论坛（2022. 10. 14），中能多粒子超导医学研究加速器”主加速器建设方案评审会（2022. 07. 09），第四届泛太湖血栓与止血国际学术研讨会（2022. 11. 04）和 2022 年放射医学与生物分析前沿交叉学术研讨（2022. 12. 03）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、俄罗斯工程院外籍院士 1 人、国际宇航科学院院士 2 人、杰青 7 人、优青 8 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	王旻凹	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



序号	姓名	性别	出生年月	专业	技术职务
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 楨	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、优青
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、高层次人才
35	武 艺	男	196503	血栓与血管生物学	特聘教授

序号	姓名	性别	出生年月	专业	技术职务
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

序号	姓名	性别	出生年月	专业	技术职务
58	邓超	男	197511	化学	教授
59	刘志勇	男	198101	放射化学	教授
60	焦旻	女	197711	放射医学	教授
61	曾剑峰	男	198706	化学	教授、优青
62	董宁征	女	197001	临床医学	研究员
63	王艳龙	男	198604	化学	特聘教授
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	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

序号	姓名	性别	出生年月	专业	技术职务
80	刘汉洲	男	198505	化学	副教授
<b>技术人员</b>					
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	高级实验师
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	高级实验师
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	高级实验师
94	闫思齐	女	198905	核物理	实验师
<b>管理人员</b>					
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	助理研究员

序号	姓名	性别	出生年月	专业	技术职务
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
1	柴之芳	中国核学会	常务理事
2	柴之芳	英国皇家化学会	会士
3	柴之芳	科技部仪器评估专家组	组长
4	柴之芳	中国科学院咨询委员会	委员
5	曹建平	中国毒理学会	常委
6	曹建平	中国毒理学会放射毒理专业委员会	副主任委员
7	曹建平	国家核和辐射突发事件卫生应急队伍	领导小组成员
8	曹建平	中华医学会放射医学与防护学分会	常务委员
9	曹建平	中华预防医学会放射卫生专业委员会	常务委员
10	曹建平	中国卫生监督协会放射卫生专业委员会	常务委员
11	曹建平	中国核学会	理事委员
12	高明远	中国同位素与辐射防护行业协会	副理事长
13	高明远	意大利 CIMTEC 学术会议之“先进生物材料和纳米技术的医学应用”系列学术会议	国际顾问委员
14	高明远	中国医学科学院医学影像研究中心学术委员会	委员
15	高明远	中美纳米医学与纳米生物技术学会	Board of Directors
16	高明远	中国研究型医院学会肿瘤影像诊断学专业委员会	常委
19	王爻凹	中国环境科学学会环境化学分会	委员
21	王爻凹	核能材料产业发展联盟	第一届理事会理事

序号	人员	学术组织名称	职务
22	王爻凹	中国核学会核化工分会	第九届理事会理事
23	王爻凹	中国化学会第三十届理事会分子筛专业	委员会委员
24	王爻凹	中国化学会第三十届理事会晶体化学专业	委员会委员
25	周光明	国际空间研究委员会 COSPAR F2 组	主席
26	路建美	中国化工学会	会士
27	路建美	中国化学学会	会士
28	刘玉龙	中国应急管理学会核应急管理工作委员会	核应急智库专家
29	时玉舫	EU-MS2 (European MSC Consortia)	顾问
30	韩悦	中国中西医结合学会血液学专业委员会	副主任委员
31	田野	中国毒理学会特种医学毒理专业委员会	副主任委员
32	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
33	周光明	中国环境诱变剂学会辐射与健康专业委员会	副主任委员
34	田野	中国辐射防护学会放射治疗分会	副理事长
35	周光明	中国核学会核应急医学分会	副理事长
36	周光明	中国生物物理学会辐射与环境生物物理学分会	副理事长
37	陈华兵	中国医药生物技术协会造影技术分会	常务委员
38	陈华兵	中国抗癌协会纳米肿瘤学专业委员会	常务委员
39	韩悦	中国老年医学会血液学分会	常务委员
40	胡士军	中国生物工程学会干细胞工程技术分会	常务委员
41	涂彧	中国计量协会医学计量专业委员会	常务委员

序号	人员	学术组织名称	职务
42	周光明	中国毒理学会特种医学毒理专业委员会	常务委员
43	刘芬菊	中国核医学辐射研究与技术分会	常务理事
44	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

## 2、重要学术期刊任职

序号	姓名	学术期刊名称	职务
1	柴之芳	Radiochimca Acta	共同主编
2	柴之芳	Radiation Medicine and Protection	名誉主编
3	曹建平	Radiation Medicine and Protection	主编
4	时玉舫	Cell Death & Disease	主编
5	时玉舫	Oncogene	副主编
6	时玉舫	Cell Regeneration	副主编
7	时玉舫	Stem Cell Research & Therapy	副主编
8	时玉舫	Cell& Bioscience	副主编
9	钟志远	Journal of Controlled Release	副主编
10	邵常顺	Frontiers in Oncology	副主编
11	周光明	Life Sciences in Space Research	副主编
12	武 艺	Thrombosis Journal	副主编
13	陈新建	IEEE Transactions on Medical Imaging	副主编
14	陈新建	IEEE Journal of Translational Engineering in Health and Medicine	副主编
15	李瑞宾	NanoImpact	副主编



序号	姓名	学术期刊名称	职务
16	史海斌	Frontiers in Oncology	副主编
17	周光明	Journal of Radiation Research	副主编
18	周光明	British Journal of Radiology/Open	副主编
19	史海斌	Frontiers in Bioengineering and Biotechnology	客座副主编
20	刘芬菊	辐射研究与辐射工艺学报	副主编

### 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、FLASH 治疗机制

近年来，放疗联合肿瘤免疫治疗在临床取得了革命性突破，但伴随的正常组织毒副反应限制了联合治疗的普及，已然成为放射医学领域亟待解决的重大科学问题。团队经过研究发现，相较于常规剂量率 X 射线，平均剂量率超 100 Gy/s 的 FLASH X 线照射可以缓解免疫检查点 PD-L1 基因敲除小鼠的肠道损伤，并显著改善受照小鼠的存活率。尽管相同剂量的 FLASH 光子与常规剂量率 X 射线照射造成的肠上皮基因组 DNA 损伤基本相同，但 FLASH 照射诱导的胞浆 DNA 片段数量低于常规剂量率照射，由此诱导了更低的 cGAS-STING 信号与更轻微的肠道炎性毒副反应。

基于上述研究，团队开创性地提出了全新的“DNA 完整性”假说，以解释 FLASH 照射的保护效应。该假说认为“瞬时”照射期间 DNA 分子的相对完整性是 FLASH 照射缓解正常组织炎性损伤的重要生物学基础，即在常规剂量率照射长达数百秒的持续时间内，DNA 不断遭到损伤、完整性逐步遭受破坏，从而产生了大量 DNA 碎片；而 FLASH 照射的持续时间仅为 0.1s，在此期间 DNA 的完整性得以保留，从而减少了 DNA 碎片的产生与免疫副反应的发生。

与经典的“氧消耗”假说侧重强调 FLASH 照射的瞬时剂量率不同，“DNA 完整性”假说更为强调剂量沉积的时间与平均剂量率。该理论有助于以全新的视角更为全面地审视 FLASH 保护效应的分子机理，并促进 FLASH 照射向临床的转化与应用，促进放疗联合免疫治疗的推广与普及。相关成果以“FLASH X-ray spares intestinal crypts from pyroptosis initiated by cGAS-STING activation upon radioimmunotherapy”为题，发表于 PNAS 杂志（2022, 119(43): e2208506119）。

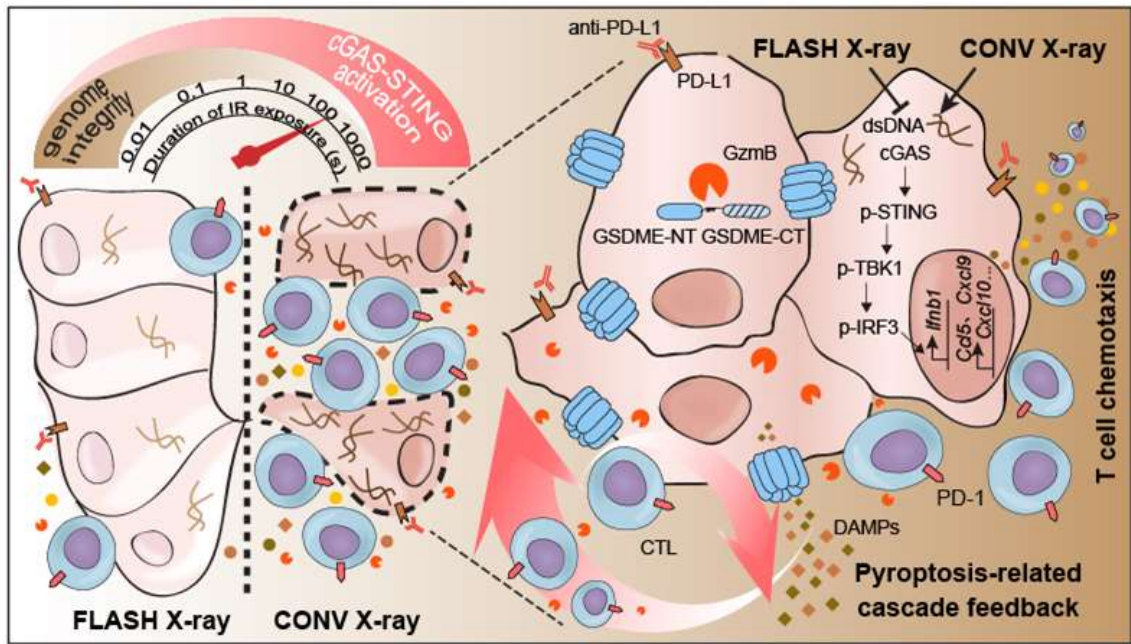


图 1.1 FLASH 光子照射与“DNA 完整性”假说

## 2、铁死亡与放射性肠损伤

小肠粘膜对电离辐射 (Ionizing radiation, IR) 高度敏感, 全身照射 (如事故性照射时发生) 以及腹盆腔肿瘤放疗等都可引起小肠组织结构和功能的损伤。尽管目前放射性肠损伤的发病机制及辐射防护药物研究已取得了一定进展, 但对于其发病机制的认识仍然不足, 这也是缺乏有效防治手段的主要原因。铁死亡是近年新发现的一种铁依赖性的、以细胞内活性氧堆积为特征的非凋亡形式的细胞死亡, 铁代谢在其中扮演着十分重要的作用。小肠作为机体中吸收膳食铁的唯一部位以及铁的暂时性储存器官之一, 在铁代谢过程中扮演着重要角色。然而, 以往关于放射性肠损伤发病机制的研究多集中在电离辐射诱导的 DNA 损伤特别是 DNA 双链断裂损伤以及由此诱导的细胞凋亡方面, 电离辐射损伤后小肠是否发生铁死亡, 肠组织内的铁乃至膳食中的铁在其中是否以及如何发挥作用, 均未被阐明。

本研究揭示了放射性肠损伤中的铁过载和细胞铁死亡现象, 机制研究表明电离辐射促进了介导铁蛋白自噬的货物受体——核受体共激活因子 4 (NCOA4) 的表达, NCOA4 随后介导了胞浆铁蛋白的自噬降解。铁蛋白的降解进一步释放了大量的游离铁, 并进而激活了位于线粒体膜上的线粒体铁转运蛋白 2 (Mfrn2)。胞质游离铁通过 Mfrn2 转运到线粒体并导致线粒体中铁过载和过量 ROS 的产生, 最终触

发肠上皮细胞脂质过氧化和铁死亡(图 1)。使用铁螯合剂去铁胺 (DFO) 或缺铁饮食干预可显著减少铁过载和铁死亡的发生, 减轻小肠黏膜损伤, 从而提高致死剂量全腹照射小鼠的存活率, 为防治放射性肠损伤提供了新思路和新靶点。相关成果以 “NCOA4-mediated ferritinophagy is involved in ionizing radiation-induced ferroptosis of intestinal epithelial cells” 为题发表在《Redox Biology》上(2022, DOI: 10.1016/j.redox.2022.102413)。

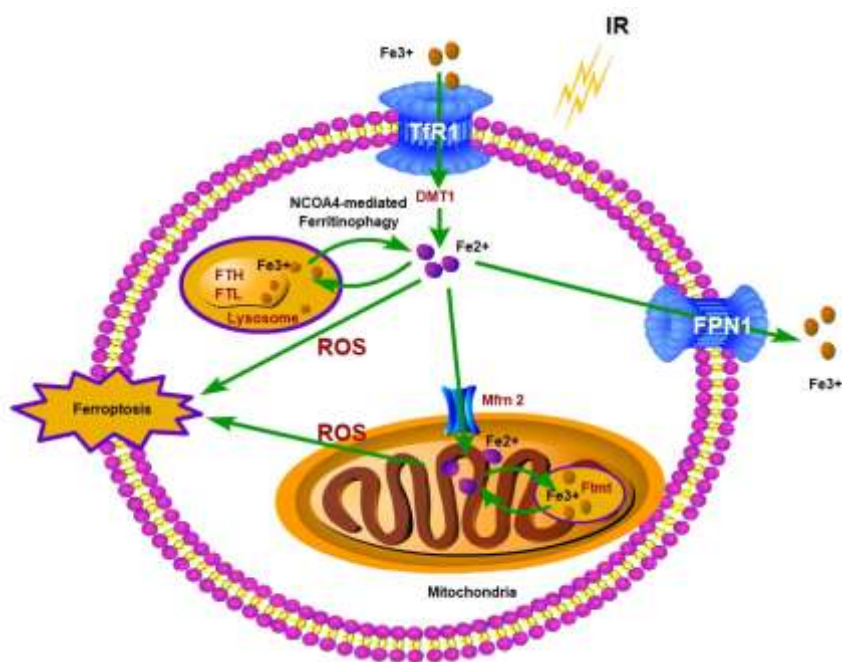


图 1.2 IR 导致肠上皮细胞铁蛋白自噬和铁死亡的机制示意图

### 3、电离辐射调控肿瘤组织力学微环境

细胞通过力学感受器接受外界物理力学信号, 并由细胞骨架系统产生相对应的细胞内部物理力学系统和信号传递系统。细胞力学系统失调会导致包括肿瘤在内的多种疾病。在前期的研究中我们发现电离辐射诱导的 lncRNA CRYBG3 能够调节生物力学传导通路的核心—F-actin 的解聚/聚合, 进而影响生物力学传导通路的效应分子 YAP/TAZ 的活性来调控肿瘤细胞的增殖与侵袭转移。本论文采用肿瘤细胞和小鼠移植瘤、转移瘤模型实验揭示了 lncRNA CRYBG3 调控 YAP/TAZ 转录活性的分子机制以及 lncRNA CRYBG3 沉默后的生物学效应, 并且通过 lncRNA CRYBG3 将电离辐射与生物力学传导通路结合起来, 为探寻癌症的起源以及肿瘤临床治疗提供全新的视野。

该工作发现长链非编码 RNA CRYBG3 能够调控肌动蛋白细胞骨架的组装，促进 LATS1/2 磷酸化，导致 YAP/TAZ 的转录活性受限，从而调节肿瘤的增殖和侵袭转移。该文章创新性的将辐射生物效应与当前研究的前沿领域-生物力学传导结合起来。为辐射治癌的有效性提供新的理论依据，并可能为肿瘤的临床治疗提供新的靶点。相关成果以” Ionizing radiation-induced long noncoding RNA CRYBG3 regulates YAP/TAZ through mechanotransduction”为题发表在《Cell Death & Disease》杂志（2022, 13(3)：209）

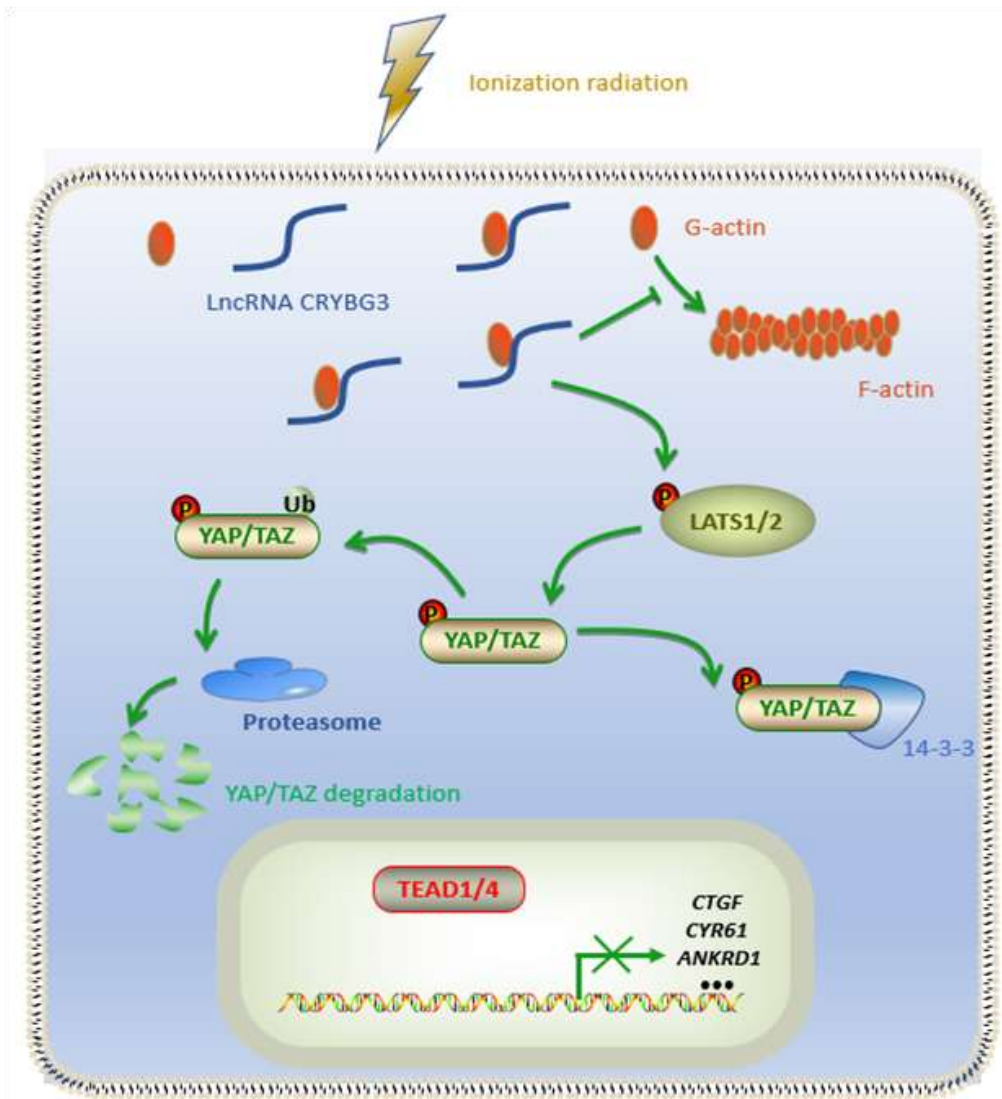


图 1.3 电离辐射调控肿瘤组织力学微环境

## （二）先进放射诊断和治疗

### 1、长余辉发光分子影像

余辉发光是指在光激发停止后，材料仍能持续发光的现象。不同于荧光成像这种传统的光学成像方式，余辉成像不依赖于实时的光激发，只需要光预先照射材料，因而将光照射过程与信号收集过程分离开来，避免了组织自发荧光造成的背景信号的干扰，成像的信噪比更高。因此，余辉成像在生物医学成像应用中更具优势。

在前期工作中，苗庆庆教授首次建立了基于有机聚合物纳米材料的“分子余辉发光成像”新方法，构建了近红外分子余辉强发光体系并开展了活体成像分析应用，实现了高灵敏（比近红外荧光高 80 倍）、高穿透深度（4 cm）的余辉发光成像（*Nat. Biotechnol.* 2017, 35, 1102-1110）。在上述研究基础上，本研究旨在发展更多具有优异性能的新型有机余辉发光材料，并深入探究余辉发光机制，实现高灵敏的体内成像应用。研究发现，有机小分子二氢卟吩具有余辉发光的性质，通过筛选系列二氢卟吩衍生物，并研究了余辉发光性能及构效关系。与之前报道的基于聚合物余辉发光材料相比，该体系具有长半衰期（1.5 小时）、余辉主体结构发射近红外余辉发光、生物相容性好等优势。此外，本研究通过彻底的结构表征与理论计算相结合，揭示了二氢卟吩分子余辉发光的分子机制。最后开展了余辉成像手术导航的实验并成功地用于小鼠腹腔微小肿瘤（3 mm<sup>3</sup>）的切除，证实了余辉发光具有极高的成像信噪比和灵敏度，在生物医学成像方面具有极大的应用前景。相关成果以“Near-Infrared Afterglow Luminescence of Chlorin Nanoparticles for Ultrasensitive In Vivo Imaging”为题发表在 *Journal of the American Chemical Society* 杂志上（2022, 144, 6719 - 6726）

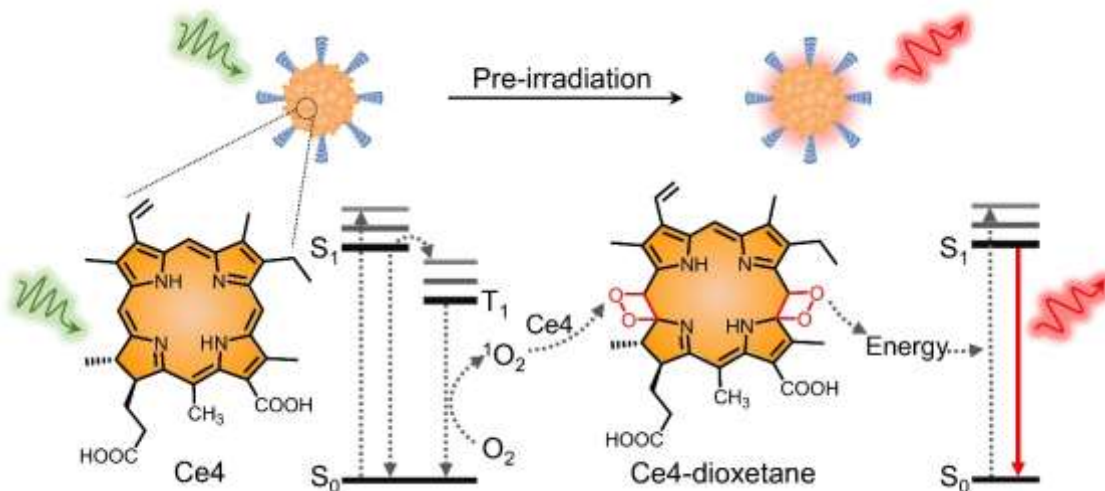


图 2.1 二氢卟吩 e4 的余辉发光过程示意图

## 2、超小纳米颗粒增强小胶质细胞自噬水平治疗帕金森病

帕金森病是第二常见的神经退行性疾病，目前仍无法治愈，其特征是多巴胺能神经元的进行性丢失和以纤维状  $\alpha$ -突触核蛋白为主要蛋白成分的神经元内包含体（称为路易小体）的积聚。小胶质细胞作为神经系统重要的先天性免疫细胞，增强小胶质细胞的自噬水平有利于防止帕金森病中路易小体的形成。据报道，小胶质细胞膜上高表达的热敏性 TRPV1 阳离子通道能够介导钙离子转运而增强其自噬水平。然而，如何可控开启和按需激活小胶质细胞膜上的 TRPV1 通道面临巨大挑战。构建按需激活 TRPV1 通道的纳米颗粒对提高小胶质细胞清除  $\alpha$ -突触核蛋白聚集体的能力和帕金森病的治疗效果具有重要意义。

在前期工作之中，分子影像与核医学研究中心团队构建了“富含空位”、具有优异光热转化性能的超小纳米颗粒，并将其成功用于肿瘤的光声成像、光热治疗、光动力治疗、化学动力治疗等 (Adv. Mater. 2016, 28, 8927 - 8936; Adv. Mater. 2016, 28, 5072 - 5079; ACS Nano, 2017, 11, 5633-5645; ACS Nano, 2019, 13, 1342-1353; Adv. Funct. Mater. 2020, 30, 1906128; Adv. Funct. Mater. 2022, 32, 2108971)。“富含空位”的超小 Cu<sub>2-x</sub>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，在聚焦超声辅助下可以高效穿越血脑屏障，是治疗脑疾病的理想载体 (Nano Lett, 2018, 18, 4985-4992)。研究团队将超小 Cu<sub>2-x</sub>Se 纳米颗粒整合负载槲皮素，发现所得纳米颗粒具有多种酶活性，能有效抑制小胶质细



细胞的过度激活，并将其极化为具有神经保护作用的 M2 表型，缓解脑部氧化应激和改善炎症环境，显著提高帕金森病小鼠的运动和记忆能力 (J. Am. Chem. Soc. 2020, 142, 21730–21742)。

在上述基础之上，研究团队首先在超小  $\text{Cu}_2\text{-xSe}$  纳米颗粒表面耦联 TRPV1 抗体，利用所得纳米颗粒的靶向性和光热转化性能可控按需地开启小胶质细胞表面的 TRPV1 通道，通过 ATG5 和  $\text{Ca}^{2+}/\text{CaMKK2}/\text{AMPK}/\text{mTOR}$  信号通路增强小胶质细胞的自噬水平，从而揭示其吞噬和降解  $\alpha$ -突触核蛋白的机理。然后，通过聚焦超声打开帕金森小鼠的血脑屏障，将超小纳米颗粒高效递送至脑部，通过 NIR II 激光光照增强自噬而有效地清除  $\alpha$ -突触核蛋白，从而改善帕金森小鼠的运动和记忆能力。该研究表明光控膜离子通道在神经退行性疾病治疗中有着巨大的潜力。相关成果以“Controlled Activation of TRPV1 Channels on Microglia to Boost Their Autophagy for Clearance of Alpha-Synuclein and Enhance Therapy of Parkinson’s Disease”为题发表在 Adv. Mater. 杂志上 (2022, 0. 1002/adma. 202108435)。

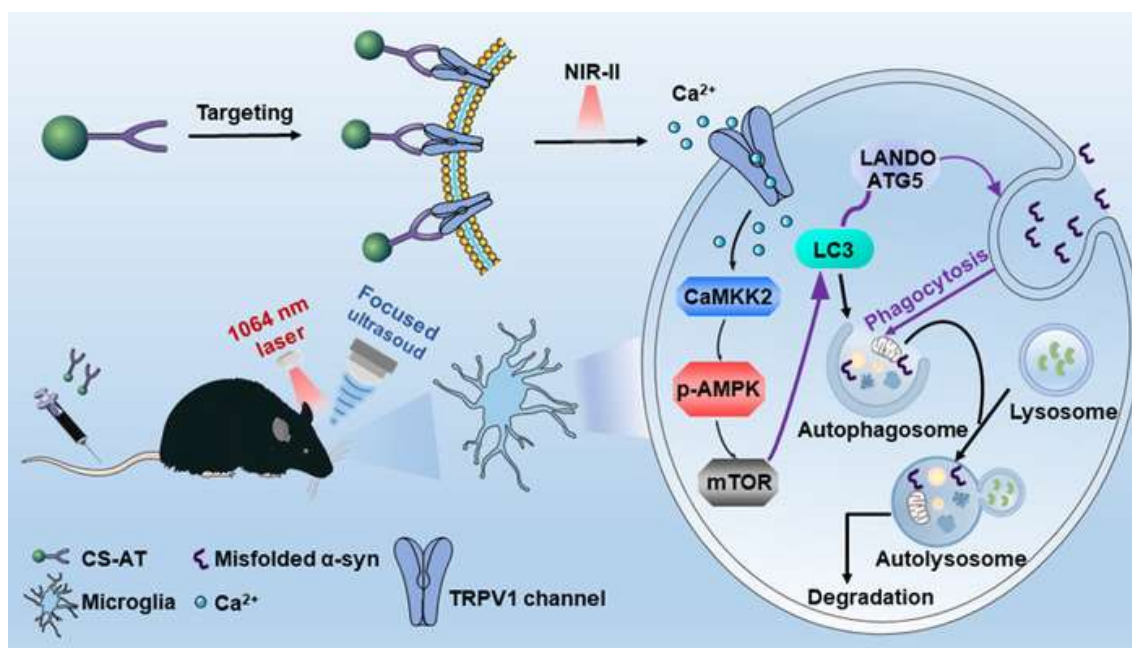


图 2.2 增强小胶质细胞自噬水平促进其吞噬和降解  $\alpha$ -突触核蛋白的示意图

### 3、基于代谢稳态调节纳米药物的肿瘤放射免疫治疗

细胞代谢的灵活变化满足了肿瘤组织内环境稳态和生长的需求。恶性肿瘤细胞响应各种细胞外源性和内源性的信号来获得代谢适应性，其代谢特性和偏好会

发生一定变化。即使在同一个病人或实验模型中，原发肿瘤和转移肿瘤也有不同的代谢特征，导致针对单一代谢途径的治疗疗效不佳。

肿瘤微环境（TME）中肿瘤细胞和肿瘤相关巨噬细胞（TAMs）的特殊代谢特征，一直是肿瘤治疗的难点，本研究设计的代谢稳态调节纳米药物能够同时靶向肿瘤细胞和肿瘤相关巨噬细胞的糖酵解和线粒体能量代谢途径，联合放射治疗，驱动免疫治疗。本研究采用聚乙二醇包被的脂质体作为甘露糖和盐酸左旋咪唑的靶向递送系统（DDS），同时抑制糖酵解和线粒体能量代谢，改善放疗诱导 M2 型巨噬细胞极化的免疫抑制微环境，增强放疗产生的免疫原性死亡，激活  $\text{IFN-}\gamma$  +  $\text{CD8}^+$  T 细胞和 granzyme B+  $\text{CD8}^+$  T 细胞，发挥抗肿瘤免疫效应。

总之，我们提供了一种针对肿瘤细胞和免疫抑制性细胞特殊代谢特征的新治疗策略，通过靶向递送调节细胞代谢的药物，充分发挥放射治疗介导的免疫治疗。相关成果以“Metabolic homeostasis-regulated nanoparticles for antibody-independent cancer radio-immunotherapy”为题在 *Advanced Materials* 上发表（2022, doi.org/10.1002/adma.202207343）。

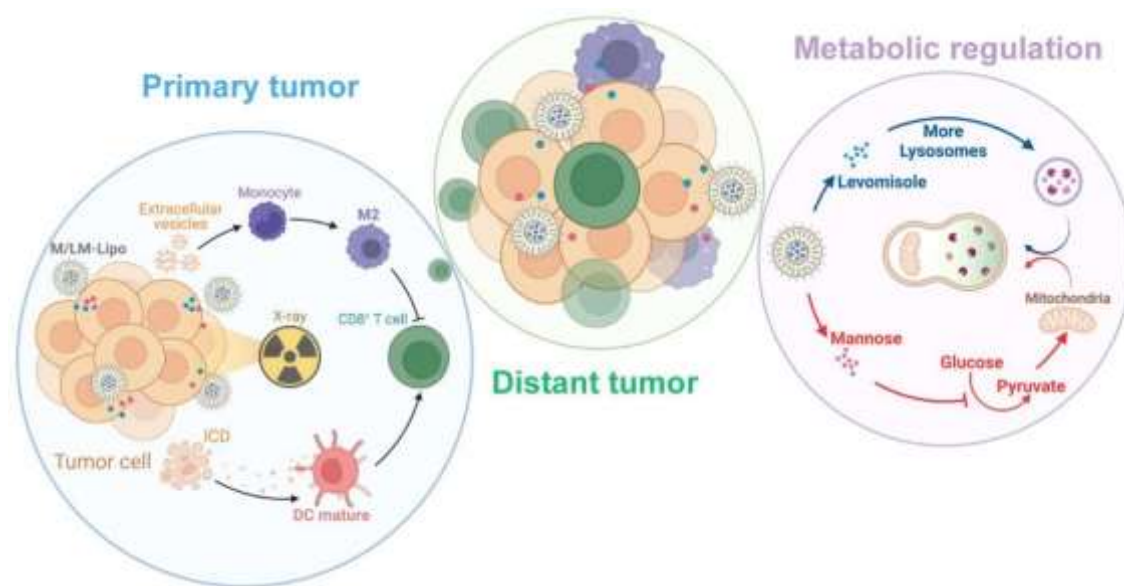


图 2.3 纳米药物的肿瘤放射免疫治疗。

### （三）辐射防护

#### 1、氡污染控制

氡( $\text{Rn}$ )是一种无色、无臭、无味普遍存在的放射性惰性气体，其同位素( $^{219}\text{Rn}$ 、

$^{220}\text{Rn}$  和占主导的  $^{222}\text{Rn}$ ) 及子体是人类所受天然辐射的主要来源之一。尽管  $\text{Rn}$  在空气中的浓度极低 ( $< 8.0 \times 10^{-15} \text{ mol/m}^3$ ), 但  $\text{Rn}$  可通过呼吸道吸入, 饮食等途径进入人体, 其衰变产生的  $\alpha$  粒子对人体呼吸系统产生放射性随机性效应可辐照诱发肺癌, 导致  $\text{Rn}$  成为肺癌诱因的主要元凶之一。 $\text{Rn}$  及其衰变子体于 2012 年被国际癌症研究机构 (IARC) 认定为人类致癌物 (I 组), 据数据统计在我国国家发生的肺癌病例中, 12%-16% 由氡气引发, 其中 4% 的肺癌死亡病例由氡导致 (Environmental Health Perspectives, 2018, 126, 057009)。世卫组织国际氡项目建议室内氡浓度的参考水平为  $100 \text{ Bq/m}^3$ , 以最大限度地减少室内氡暴露对健康的危害。同时,  $\text{Rn}$  的放射性本底是中微子研究等前沿物理实验中的主要干扰背景之一, 因此实验场所必须严格控制  $\text{Rn}$  的浓度水平 ( $< 1 \text{ mBq/m}^3$ )。遗憾的是, 目前广泛应用的除  $\text{Rn}$  技术主要是通风和物理阻隔, 都很难实现对  $\text{Rn}$  的深度去除, 而且能耗相对较大, 因此开发高效和节能的除  $\text{Rn}$  方法迫在眉睫。然而由于  $\text{Rn}$  的化学惰性与吸附剂之间只存在弱的范德华 (vdW) 相互作用, 以及相对于空气中主要气体组分 (如:  $\text{H}_2\text{O}$ ,  $\text{N}_2$ ,  $\text{CO}_2$  等) 的浓度, 氡的浓度极低 ( $< 1.8 \times 10^{-14} \text{ bar}$ ,  $< 106 \text{ Bq/m}^3$ ), 因此, 设计合成在环境条件下深入去除  $\text{Rn}$  的吸附材料仍然是领域的一大挑战。

研究团队在实验上通过原位配体取代法合成出和  $\text{Im-1}$  中  $\text{Im}/\text{bIm}$  的比例最为接近的改性 ZIF-7 材料—ZIF-7- $\text{Im}$ , 并通过  $^1\text{H NMR}$ 、PXRD、FT-IR 以及  $\text{Xe}$  与空气中主要组分气体吸附等测试表征证实了  $\text{Im}$  的成功取代以及结构内孔道的成功改性。 $\text{Rn}$  穿透实验结果表明原始 ZIF-7 对  $\text{Rn}$  基本没有捕获能力, 这与理论计算的高动力学能垒结果相吻合; 而 ZIF-7- $\text{Im}$  则展现出优异的  $\text{Rn}$  吸附能力。在相同条件下报道的所有  $\text{Rn}$  吸附剂中, ZIF-7- $\text{Im}$  展示了创纪录的  $\text{Rn}$  吸附容量 ( $Q = 24.1 \text{ Bq/g}$ ) 和  $8.6 \text{ L/g}$  的  $K_d$  值, 这几乎是目前性能最好的商业 AC 材料 ( $Q = 14.1 \text{ Bq/g}$ ,  $K_d = 5.2 \text{ L/g}$ ) 的两倍。相关成果以 “Thermodynamics-Kinetics-Balanced Metal-Organic Framework for In-Depth Radon Removal under Ambient Conditions” 为题发表于 Journal of the American Chemical Society 上 (2022, 144, 30, 13634 - 13642)。

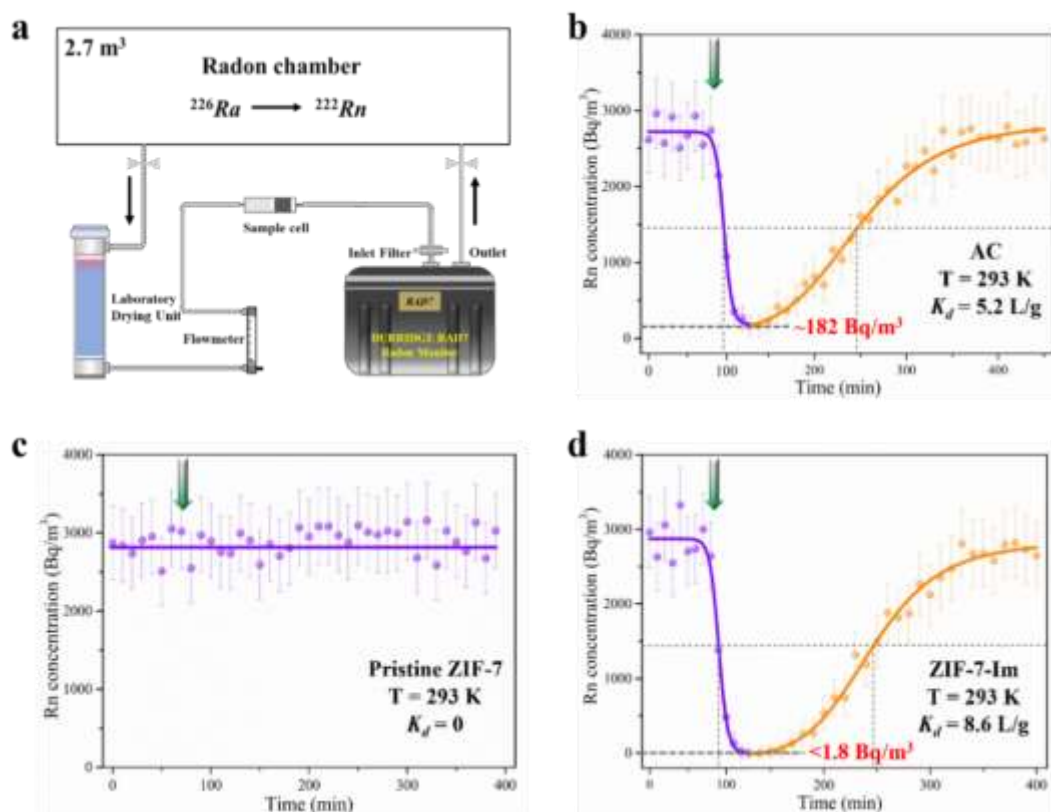


图 3.1 Rn 穿透实验的示意图模型及椰壳活性炭、原始 ZIF-7 以及 ZIF-7-Im 三种材料的 Rn 穿透实验结果

## 2、半导体金属有机框架辐射探测

金属有机框架材料（MOFs）是一类具有高孔隙率、高比表面积且具有极高设计性的框架类固体材料。其是通过金属离子与有机物配体通过配位键连接形成具有无限延展性的配位聚合物。由于金属离子种类丰富、有机配体涉及多样、拓扑学结构复杂，MOFs 材料的结构变化丰富、设计性极强。其在气体分离、污染物去除、催化等领域的潜力被越来越多的科研人发掘出来，使得 MOFs 材料成为具有广阔市场前景的一种新兴材料。在光电领域，MOFs 材料长久以来被大家认为是一种绝缘体。近些年来，随着科研工作者们对于 MOFs 材料认识的深入，半导体 MOFs 材料开始进入人们视野，其潜在的丰富设计性给半导体领域带来了无限可能，科研工作者利用 MOFs 材料在电催化、化学传感器、储能装置、场效应晶体管等领域均取得一定突破。过去两年时间里，苏州大学放射医学与辐射防护国家重点实验室王芑凹教授和王亚星副教授在国际上率先将半导体 MOFs 材料应用于辐射探

测领域,取得了系列重要成果(J. Am. Chem. Soc. 2019, 141, 8030–8034; Angew. Chem. Int. Ed. 2020, 59, 11856 – 11860; J. Am. Chem. Soc. 2020, 142, 16218 –16222)。然而,利用 MOFs 材料的本征结构优势来提升高能射线探测性能的策略还未被提出。近期该团队又发现,利用 MOFs 自身特有的多孔性,将预先筛选的客体分子引入 MOFs 材料的孔道内,可以实现强主客体相互作用,改变材料原有的 HOMO/LUMO 轨道排布。并且给原有的禁带中引入中间能带,进而改变激子行为,最终实现优化光电性能的目的。

在本工作中,作者揭示了半导体 MOFs 中的激子行为可以通过框架-客体的相互作用来调控,而这一理念通常在传统的无机或有机半导体中无法实现。通过在铽基多孔半导体 MOF (TbTATAB) 丰富的孔隙中引入缺电子分子 RhB<sup>+</sup> (引入客体分子后化合物称为 RhB<sup>+</sup>@TbTATAB), 作者观察到了从框架到客体显著的能量转移,这与激子种类从 Wannier-Mott 激子到 Frenkel 激子的转换有关。相关成果已发表于 Journal of the American Chemical Society (2022, 144, 5, 2189–2196)。

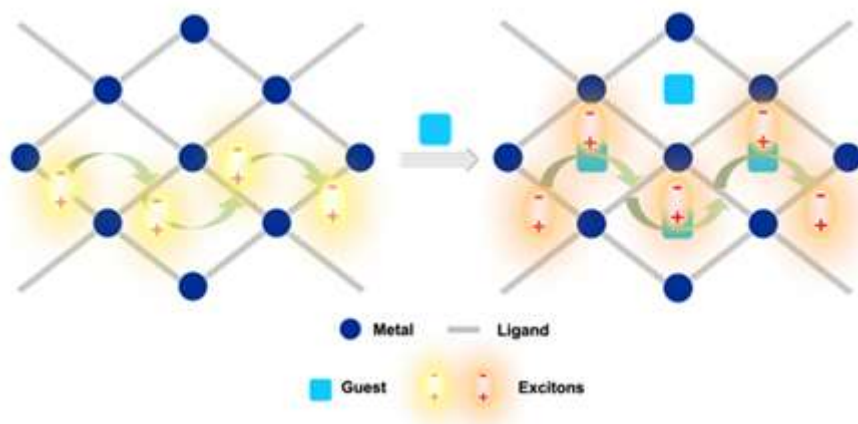


图 3.2 TbTATAB 和 RhB<sup>+</sup>@TbTATAB 激子类型转变的示意图。

### 3、功能化的金属有机框架 (MOFs) 用于内污染铀促排

闪烁体可以将 X 射线光子的能量转化为可见光信号,闪烁体是 X 射线探测器的核心部分,它在医学成像、安全检查和工业应用中发挥着至关重要的作用。X 射线探测器是通过将多个闪烁体与光电探测器阵列耦合来制造的。由于闪烁体的辐射发光信号在产生后呈各向同性传播,在相邻的闪烁体像素之间经常存在光学串扰,导致空间分辨率和成像质量的下降。为实现高效成像,使用过程中需加大辐照剂量,不可避免加重了辐射风险。因此,如何控制闪烁体的辐射荧光传播方

向，有望从根本上提升 X 射线成像质量。研究团队近年来一直致力于新型辐射探测材料研究，前期开发了一系列新型闪烁体和半导体探测材料(Angew. Chem. Int. Ed. 2018, 57, 7883; J. Am. Chem. Soc., 2019, 141, 8030; Angew. Chem. Int. Ed., 2020, 59, 11856)。在本工作中，研究团队从闪烁体发光特性和结构关系角度出发，提出了发展具有手性结构的新型闪烁体思路。从化学结构角度来看，传统闪烁体绝大多数为中心对称结构，其辐射发光呈各向同性传播。本工作通过分子设计合成了手性钙钛矿闪烁体，由于手性结构的极化特征，利用手性闪烁体首次实现了闪烁光传播方向控制。研究团队开发的厘米尺寸的闪烁体可以进一步被组装成为极化闪烁体阵列，通过对比成像研究证明极化闪烁体阵列能够明显减弱辐射成像中的光串扰问题，提升了边界成像效果。本工作为精确控制闪烁光传播方向提供了新的思路，为进一步发展高效闪烁体，以小的辐照剂量获得高品质 X 射线成像效果提供了参考。相关成果以“Circularly Polarized Radioluminescence from Chiral Perovskite Scintillators for Improved X-ray Imaging” 为题发表于 Angewandte Chemie-International Edition 上。(2022, 61, e202208440)

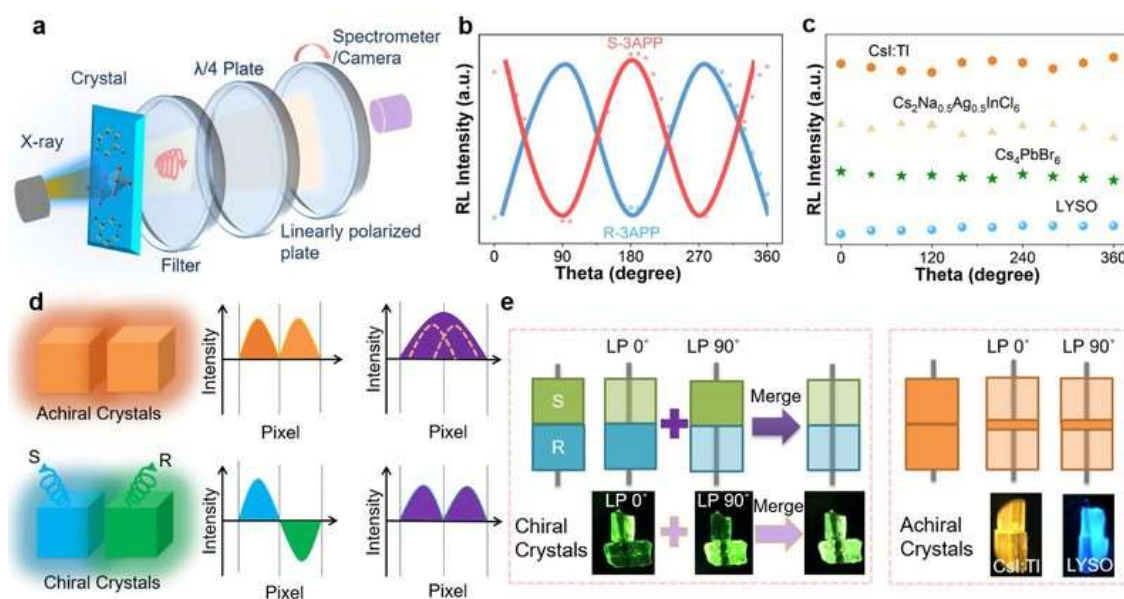


图 3.3 实验室搭建的手性辐射测试装置；b. 新型闪烁体的偏振辐射荧光特征；  
c. 传统闪烁体的辐射荧光特征；d. 手性闪烁体用于减少光串扰概念示意图；  
e. 不同结构闪烁体成像的边界效应比较。

## 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	<b>280.25</b>
4	国家重点研发计划	特定环境条件下干细胞对组织器官发育和功能重塑的调控	2022YFA1104300	胡士军	2796
5	国家重点研发计划	聚乳酸的规模化制备及关键单体丙交酯的一步法产业示范	2022YFB3704900	张正彪	2200
6	基金委重大仪器研制项目	面向高放射性锶系元素化学研究的台式 X 射线吸收谱仪研制	22227809	王爻凹	845.92
7	国家重点研发计划	T-ALL 免疫微环境图谱刻画及细胞免疫治疗策略的优化	2022YFC2502703	杨 林	360
8	国家重点研发计划国际合作项目	新型填料材料研究及其在含氙废水精馏处理技术中的应用	2022YFE0105302	王爻凹	300
9	国家重点研发计划子课题	完善消化肿瘤 HFRT 的放射防护与损伤控制体系	2022YFC2503702	曹建平	300
10	国家自然科学基金重点项目	钙钛矿半导体探测器中信息载流子的传输及收集机理研究	U2267211	何亦辉	280
11	国家自然科学基金重点项目	核工业职业照射致晶状体损伤先进评估模型构建及机制研究	U2267220	刘玉龙	280
12	国家自然科学基金重点项目	多功能囊泡纳米疫苗用于高效肿瘤免疫治疗	52233007	钟志远	269
13	国家自然科学基金重点项目	骨髓微环境促炎巨噬细胞介导巨核前体细胞过甲基化在移植后巨核系重建不良中的机制研究	82230005	韩 悦	261
14	国家自然科学基金重点项目	血小板 GPIb $\alpha$ 对肿瘤血行转移的调控作用及其机制研究	82230003	戴克胜	261
15	国家自然科学基金重点项目	氙与气载放射性智能化监控及其联合暴露致肺损伤筛查关键技术研究	2022YFC2503204	涂 彧	250

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
16	国家自然科学基金海外优青项目	纳米探针的传感以及活体成像	XXXX	崔家斌	200
17	国家自然科学基金优青项目	纳米分子影像探针及活体成像	82222033	曾剑峰	200
18	国家自然科学基金优青项目	脂质代谢与炎症反应调节	32222025	李培山	200
19	国家重点研发计划子课题	XXXX	XXXX	钟志远	200
20	国家自然科学基金专项项目	胸主动脉夹层发生发展机制和预警干预策略研究(联合申请B)	82241202	胡士军	200
21	国家自然科学基金重点项目参与	航天极端环境下机体不同组织器官间的交互调控作用研究	82192882	胡文涛	78
22	国家自然科学基金面上项目	氧化物介质表面氢键微环境中低能电子贴附还原二氧化碳技术及机理研究	U2267224	盛道鹏	70
23	国家重点研发计划子课题参与	T-ALL 动态演变规律及靶向细胞死亡相关治疗策略的研究	2022YFC2502702	徐鹏(学术骨干)	60
24	国家重点研发计划子课题参与	细胞功能和免疫环境调控的超敏仿生材料	2022YFB3804603	邓超	60
25	国家自然科学基金面上项目	新型辐射光致发光剂量计材料的研制及机理研究	22276132	刘汉洲	54
26	国家自然科学基金面上项目	高灵敏、高特异性分子余辉发光探针用于肿瘤早期诊断的研究	22274107	苗庆庆	54
27	国家自然科学基金面上项目	RPRM 调控电离辐射旁效应信号的作用和分子机制	32271279	杨红英	54
28	国家自然科学基金面上项目	电化学高效脱盐-核素分离深度净化高盐低放废液研究	22276129	华道本	54
29	国家自然科学基金面上项目	电离辐射致酿酒酵母基因组突变的频谱分析与特征提取	82273583	俞家华	50
30	国家自然科学基金青年项目	LNC CRYBG3 靶向 eEF1A1/TRAP1 调控碳离子辐射诱导的肺癌干细胞线粒体损伤	12205215	吴安庆	30
31	省部级项目	二氧化碳的辐射催化转化应用基础研究	BK20220026	王爻凹	300



序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
32	省部级项目	辐射诱导的个性化细胞外囊泡纳米疫苗的开发与应用	BK20190044	杨 凯	200
33	省部级项目	基于 STING 激动剂的新型纳米佐剂研究	BE2022724	陈华兵	100
34	省部级项目	构建电离辐射响应的三维结构色水凝胶剂量计	BK20221359	胡 亮	10
35	市厅级项目	用于捕获核电站尾气中 Kr、Xe 的多孔材料的筛选与验证	22KJA150006	王艳龙	30
36	市厅级项目	超小纳米探针修复受损脑膜淋巴管增强脑胶质瘤免疫治疗	22KJA310004	李 楨	30
37	市厅级项目	奥沙利铂白蛋白纳米粒的研究与开发	ZXL2022508	陈华兵	100
38	市厅级项目	天然高分子水凝胶载体构建及其在肿瘤微环境多重调控与放射免疫治疗中的应用	ZXL2022484	杨光保	50
39	市厅级项目	新型磁共振造影剂的设计以及临床转化	ZXL2022515	崔家斌	50
40	市厅级项目	用于核医学成像的钙钛矿半导体探测基元研究	苏财教〔2022〕63号	何亦辉	38.75
41	企业合作项目	体外制造人血小板技术	H220406	王建荣	300
42	企业合作项目	中放废液形态分析及吸附材料研制服务合同	/	王旻凹	221.6
43	企业合作项目	放射性药物的合作开发	H220203	许玉杰	150
44	企业合作项目	大型污染金属设备样品放化分析技术服务采购合同	/	第五娟	147
45	企业合作项目	紫外固化丙烯酸树脂材料开发研究项目	H220271	张正彪	144.2
46	企业合作项目	面向放疗的高分子水凝胶颗粒的可控制备	/	胡亮	105
47	企业合作项目	水同位素精馏节能系统研发	/	王旻凹	100
48	企业合作项目	新型 PSMA 靶向放射性诊疗药物的临床前研究	/	钟志远	70
49	企业合作项目	化合物在 CDX 模型鼠的体内分布研究	/	刘志勇	20
合计					16353.72

## 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	第二届分子精准合成与碳循环化学国际研究生创新论坛	全球性	承办	2022-10-14	600	苏州市
2	第一届精准高分子化学与功能材料国际研讨会	全球性	主办	2022-11-03	70, 线上最高18万人参与	苏州市
3	中能多粒子超导医学研究加速器”主加速器建设方案评审会	全国性	主办	2022-07-09	28	苏州市
4	首届放射医学专业建设与人才培养研讨会	全国性	主办	2022-08-26	120	苏州市
5	2022年国家级继续教育项目《核和辐射损伤医学应急演练与临床处理》培训班及中国核学会核应急医学分会学术交流研讨会	全国性	主办	2022-11-08	50	苏州市
6	苏州血液免疫与移植出凝血论坛	全国性	主办	2022-09-02	80	苏州市
7	中华医学会第十七次全国血液学学术会议	全国性	承办	2022-09-22	2000	上海市
8	FLASH放疗技术研发中心成立仪式暨学术研讨会	区域性	主办	2022-01-09	50	苏州市
9	“中能多粒子超导医学研究加速器”终端评审会	区域性	主办	2022-06-04	30	苏州市
10	第四届泛太湖血栓与止血国际学术研讨会	区域性	主办	2022-11-04	150	苏州市
11	2022年放射医学与生物分析前沿交叉学术研讨	区域性	主办	2022-12-03	400	苏州市

## 2、专家来访

序号	时间	报告人	主题	单位
1	2022-08-21	栾天罡	微萃取与质谱联用在环境分析中的应用	广东工业大学
2	2022-08-14	刘震	基于仿生分子识别的生命分析及生物医学应用	南京大学
3	2022-09-19	Han Zuilhof	Advanced click chemistry for nanocontrol: from surfaces to single polymer studies	Wageningen University
4	2022-09-21	宋继彬	活体比率成像与分子测量	北京化工大学
5	2022-09-09	唐晓英	未来智慧医学	北京理工大学
6	2022-08-15	陈雨	材料医学	上海大学
7	2022-08-15	王艳丽	创新纳米制剂构建及其临床应用	海南医学院
8	2022-11-3	张海元	纳米材料的能级电子结构调控及其生物医学应用	中国科学院长春应用化学研究所
9	2022-01-12	夏帆	界面匹配的生命分子检测	中国地质大学
10	2022-07-14	田阳	神经分子识别与脑成像分析	华东师范大学
11	2022-08-10	王树	有机共轭分子光学探针与生物应用	中科院化学所
12	2022-07-08	宇兴江	胶质瘤干细胞与肿瘤微环境	华中科技大学
13	2022-08-18	柴人杰	通过基因治疗促进内耳干细胞再生功能性毛细胞的研究	东南大学
14	2022-08-23	于晓波	蛋白组学分子芯片与精准医疗	国家蛋白质科学中心-北京(凤凰中心)
15	2022-10-08	陈赛娟	江苏省成人白血病大数据研究探讨	上海交通大学附属瑞金医院
16	2022-10-08	王广基	前沿科技支撑肿瘤精准医学发展	中国药科大学

### 3、参加会议

序号	会议名称	举办地点	参加人员	会议类型
1	国家重点实验室第一届学术委员会 第四次会议暨学术交流会	苏州市	周光明	全国性
2	中国粒子治疗设施设计与建设圆桌 论坛	线上	周光明	全国性
3	第十一届全国环境化学大会	哈尔滨市	李瑞宾	全国性
4	香山科学会议-第 730 次学术讨论会	北京市	何亦辉	全国性
5	第十一届全国环境化学大会	哈尔滨市	马付银	全国性
6	FRPT2022 (FLASH 全球性年会)	西班牙 巴塞罗那	张昊文	全球性
7	第十一届全国环境化学大会	哈尔滨市	杨再兴	全国性
8	第十一届全国环境化学会议	哈尔滨市	孟烜宇	全国性
9	中国辐射防护 2022 年学术年会	青岛	王晓梅	全国性
10	第十一届全国环境化学大会	哈尔滨	王晓梅	全国性
11	2021 第十五届中国医院院长年会 “干细胞临床研究与转化”专场	上海市	时玉舫	全国性
12	NIH immunology seminar	线上	时玉舫	全球性
13	中华医学会生殖医学分会年会	上海市	时玉舫	全国性
14	The anti-viral immune response to COVID-19 Webinar	线上	时玉舫	全球性
15	第二届肿瘤基础及转化研究广济 前沿论坛	线上	时玉舫	全国性
16	the 28th Annual Meeting of ISCT, International Society for Cell & Gene Therapy	线上	时玉舫	全球性
17	中华医学会第十五次全国生殖医学 学术会议	线上	时玉舫	全国性
18	第十六届钱江国际心血管病会议	线上	时玉舫	全国性
19	苏州医学会肿瘤学分会年会	苏州市	时玉舫	全国性

序号	会议名称	举办地点	参加人员	会议类型
20	第十一届全国环境化学大会	黑龙江省 哈尔滨市	谌 宁	全国性
21	团簇构造、功能及多级演化”重大研 究计划年度学术交流会	福建省厦 门市	谌宁	全国性
22	2022 年环境友好材料国际会议	四川省绵 阳市	谌宁	全国性
23	International Symposium of Healthcare Biotechnology	杭州	陈华兵	全球性
24	第 11 届环境化学会议	哈尔滨	杨再兴	全国性

## 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	ZL201810072546.6	三维视网膜 oct 图像的血管检测和配准方法、设备及应用	2022-06-24	中国	陈新建
2	ZL202110140542.9	一种基于循环自适应多目标加权网络的糖尿病视网膜病变区域自动分割方法	2022-06-17	中国	陈新建
3	ZL202011236869.8	一种使用 OCT 信号进行眼底屈光补偿判定与成像优化的方法	2022-11-08	中国	陈新建
4	ZL201910942993.7	一种上下文金字塔融合网络及图像分割方法	2022-04-12	中国	陈新建
5	ZL2020 1 1083642.4	用于放射性核素沾染去污的组合物及其制备方法与应用	2022-03-22	中国	崔凤梅
6	ZL 2018 1 0825480.3	一种内膜为正电的聚酯肽囊泡及其制备方法与应用	2022-02-25	中国	邓 超 钟志远
7	ZL 2018 1 0826941.9	一种内膜为负电的聚酯肽囊泡及其制备方法与应用	2022-02-25	中国	邓 超 钟志远
8	ZL 2019 1 0819116.0	透明质酸-g-聚酪氨酸-硫辛酸共聚物，聚多肽纳米粒及其制备方法与应用	2022-04-15		邓 超 钟志远
9	ZL 2022 1 0025998.5	一种近红外纳米光敏剂及其制备方法和应用	2022-10-18	中国	郭正清
10	ZL 2020 1 0149420.1	一种二氢卟吩纳米光敏剂及其制备方法和应用	2022-02-15	中国	郭正清
11	ZL 2018 1 1302450.0	纳米光敏剂及其制备方法和应用	2022-02-01	中国	郭正清
12	ZL201911380170.6	一种高拉伸、强粘附的光热水凝胶及其制备方法以及应用	2022-08-09	中国	胡 亮

序号	专利号	专利名称	授权公告日	国家	完成人 (固定人员)
13	ZL201910584833.X	基于共轭微孔聚合物的复合催化剂及其制备和应用	2022-03-01	中国	华道本
14	ZL202111204945.1	双疏型含铂催化剂材料、其制备方法及应用	2022-05-31	中国	华道本
15	ZL202110458910.4	一种活性氧响应性藏红花素纳米颗粒及其制备方法和应用	2022-10-11	中国	华道本
16	ZL 2019 1 1078064.2	一种二维纳米材料作为脱氢酶的应用	2022-02-15	中国	李瑞宾
17	ZL 202111032630.3	一种磁共振造影剂及其制备和应用	2022-08-09	中国	李 楨
18	ZL 201910256608.3	基于黑磷的近红外二区荧光纳米探针及其制备和应用	2022-03-01	中国	李 楨
19	US11224866B2	Tricobalt tetraoxide dodecahedron / carbon nitride nanosheet composite and application thereof in exhaust gas	2022.01.18	美国	路建美
20	US11325110B2	Magnetic Fe <sub>2</sub> O <sub>3</sub> nanospheres with PNH surface modification and application hereof in water treatment	2022.05.10	美国	路建美
21	US11325115B2	Visible-light response hybrid aerogel and preparation method and application thereof in waste gas processing	2022.05.10	美国	路建美
22	US11345616B2	A heterojunction composite material consist of one-dimensional In <sub>2</sub> O <sub>3</sub> hollow nanotube and two-dimensional ZnFe <sub>2</sub> O <sub>4</sub> nanosheets, its preparation method and application in water pollutant removal	2022.05.31	美国	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)
23	US11389789B2	Visible-light responsive titanium dioxide nanowire/metal organic skeleton/carbon nanofiber membrane and preparation method and application thereof	2022.07.19	美国	路建美
24	US11401651B2	Carbon cloth material coated with iodine-doped bismuthyl carbonate, preparation method thereof, and application in oil-water separation	2022.08.02	美国	路建美
25	US11439990B2	Titanium carbide nanosheet/layered indium sulfide heterojunction and application thereof in degrading and removing water pollutants	2022.09.13	美国	路建美
26	202011128871.3	一种金属配位卟啉基共轭聚合物及其制备方法及其在光催化降解水体有机污染物方面的应用	2022.02.25	中国	路建美
27	201910936647.8	负载金纳米粒子的中空介孔碳纳米球复合材料及其制备方法与在持续处理 CO 中的应用	2022.04.15	中国	路建美
28	202010901547.4	氧化钨纳米棒/碳化钛量子点/硫化铟纳米片 Z 型异质结复合材料及其制备方法与应用	2022.04.15	中国	路建美
29	202010815127.4	钒掺杂钛酸锶纳米纤维材料、制备方法及其在压电催化去除水体污染物中的应用	2022.04.15	中国	路建美
30	202011476754.6	利用三元 NiO 纳米片@双金属 CeCuOx 微片核壳结构复合材料低温热处理甲苯的方法	2022.04.15	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)
31	202011476774.3	三元 NiO 纳米片@双金属 CeCuOx 微片核壳结构复合材料及其制备与应用	2022.04.15	中国	路建美
32	201910539497.7	表面修饰 PNH 的磁性 Fe2O3 纳米小球及其在水处理中的应用	2022.04.15	中国	路建美
33	202011449881.7	基于多孔聚合物修饰的金属碳纳米管复合膜分离含染料废水的方法	2022.04.15	中国	路建美
34	201910436704.6	良柔性三明治型 PN 结电存储器件	2022.04.15	中国	路建美
35	201811362521.6	基于单宁酸和铁(III)配位化合物的电存储材料及其制备方法与电存储器件	2022.05.13	中国	路建美
36	202011166337.1	Cs3Bi2Br9@TiO3 钙钛矿异质结在光催化降解 MBT 中的应用	2022.05.17	中国	路建美
37	202011160061.6	一种负载铂的花状铁钼复合材料及其制备方法与在低温热催化处理甲苯中的应用	2022.06.03	中国	路建美
38	201911144604.2	一种基于钙钛矿 Cs2PdBr6 的湿敏传感器及其制备方法和用途	2022.06.07	中国	路建美
39	202011128872.8	三维/二维 Ni-Co 双金属氧化物/g-C3N4 纳米复合材料及其制备方法与应用	2022.06.07	中国	路建美
40	202110130294.X	高分子凝胶用单体及高分子凝胶与制备方法	2022.06.21	中国	路建美
41	202110127768.5	多孔交联材料及其制备方法与应用	2022.06.21	中国	路建美
42	201810864928.2	半导体电存储材料及其制备方法与由其制备的柔性电存储器件及制备方法	2022.06.21	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)
43	202011105376.0	基于钙钛矿 Cs <sub>2</sub> PdBr <sub>6</sub> 纳米中空球的一氧化碳传感器及其制备方法和用途	2022.07.19	中国	路建美
44	202011105313.5	可用于低浓度二氧化氮的克酮酸菁聚合物传感器及其制备方法	2022.07.19	中国	路建美
45	201910969750.2	负载在氮掺杂碳空心球上的硫化镉锌及其制备方法与在废水处理中的应用	2022.07.19	中国	路建美
46	201910996313.X	负载铂和钌双金属的氧化锆纳米管复合材料及其制备方法与在低温热催化处理甲苯中的应用	2022.07.19	中国	路建美
47	201710405712.5	一种可见光催化降解有机污染物的反蛋白石材料及其制备方法	2022.08.12	中国	路建美
48	202011408116.0	一种基于银棱锥状纳米颗粒表面增强拉曼基底及其制备方法	2022.08.16	中国	路建美
49	202010394408.7	基于片状柔性碳布的 Co <sub>3</sub> O <sub>4</sub> 纳米结构微生物复合材料及其制备方法与应用	2022.08.16	中国	路建美
50	202011380639.9	Fe/Fe <sub>3</sub> C 嵌入 N 掺杂碳复合材料及其制备方法与其在微生物燃料电池中的应用	2022.08.16	中国	路建美
51	201910960100.1	铈掺杂钛酸锶反蛋白石材料的制备方法与其在压电协同光催化去除水体中有机污染物的应用	2022.09.09	中国	路建美
52	201910995581.X	一种二维 I 掺杂 BiOIO <sub>3</sub> /g-C <sub>3</sub> N <sub>4</sub> 复合催化剂及其制备方法与应用	2022.10.14	中国	路建美
53	ZL201910450839.8	纳米磷光探针及其用途	2022-07-05	中国	葛翠翠

序号	专利号	专利名称	授权公告日	国家	完成人 (固定人员)
54	ZL 202210134630.2	一种余辉发光纳米材料及其制备方法与应用	2022-11-07	中国	苗庆庆
55	ZL 2020 1 0081216.0	一种可激活光学分子探针及其制备方法与应用	2022-02-15	中国	苗庆庆
56	ZL202110745393.9	辐照加固的无人机机载一体化辐射探测系统	2022-07-26	中国	屈卫卫
57	ZL202110742470.5	无人机机载一体化辐射探测系统	2022-10-18	中国	屈卫卫
58	ZL202011324287.5	一种基于碲锌镉的空间带电粒子望远镜	2022-07-12	中国	屈卫卫 周光明
59	ZL202011348473.2	眼晶状体剂量测量装置及方法	2022-10-04	中国	屈卫卫 周光明
60	ZL202011348454.x	空间辐射探测装置及方法	2022-12-16	中国	屈卫卫 周光明
61	ZL202010313574.X	高稳定性近红外二区纳米荧光探针及其制备方法和应用	2022-03-15	中国	史海斌
62	ZL202011263517.1	红光介导的核酸锚定型荧光探针及其制备方法和应用	2022-04-15	中国	史海斌
63	ZL 2021 1 0895665.3	水溶性 Cu <sub>2</sub> -XS 纳米颗粒及其制备方法和应用	2022-11-15	中国	汪 勇 张乐帅 王杨云
64	ZL 202010459763.8	巴弗洛霉素 A1 在体外诱导白血病细胞逆编程成为造血干祖细胞的应用	2022-04-06	中国	王建荣
65	ZL 201910596322.X	放射超敏蛋白 Beclin1 作为机体核辐射保护的靶点	2022-11	中国	王建荣
66	ZL 2020 1 1528323.X	选择性快速去除强碱性溶液中 Sr <sup>2+</sup> 的金属有机框架材料及其制备和应用	2022-05-17	中国	王爻凹
67	ZL201910674455.4	MOF 纳米粒子在制备放射性核素促排剂中的应用	2022.09.28	中国	王爻凹 第五娟
68	ZL201910028279.7	吡咯烷酮类化合物的应用	2022.05.31	中国	王爻凹 第五娟

序号	专利号	专利名称	授权公告日	国家	完成人 (固定人员)
69	ZL202010803689.7	一种 <sup>177</sup> Lu 标记的金纳米团簇及其制备方法和应用	2022-10-25	中国	杨 凯
70	ZL 2020 1 0810464.4	抑制剂、抑制剂组合物、药物及其应用	2022-05-17	中国	杨 林
71	ZL 2019 1 0652242. 1	基纳米材料在制备缓解或者治疗 HD 药物中的应用	2022-04-15	中国	杨再兴
72	ZL 2019 1 0780522.0	还原响应的靶向聚乙二醇-聚碳酸酯美登素前药胶束的制备方法	2022-08-16	中国	钟志远
73	ZL 2019 1 0172613.8	还原敏感可逆交联的具有不对称膜结构的聚合物囊泡及其在制备治疗肝癌药物中的应用	2022-02-25	中国	钟志远
74	ZL 2020 1 0167801.2	基于交联生物可降解聚合物囊泡的抗肿瘤纳米佐剂及其制备方法与应用	2022-04-26	中国	钟志远
75	ZL 2020 1 0576347.6	载小分子药物的碳酸酯聚合物囊泡及其应用	2022-08-12	中国	钟志远
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78	ZL 2021 1 0631563.0	基于转发器的无人机抗核辐射性能综合评测方法和系统	2022-05-31	中国	周光明
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80	ZL 2021 1 0341847.6	LINC00084 在制备乏氧肿瘤放疗辅助药物中的作用	2022-03-29	中国	周光明 胡文涛
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83	ZL 2021 1 0631568.3	无人机视频采集模块 抗核辐射性能评测方法 和系统	2022-07-12	中国	周光明 聂 晶
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85	ZL 2021 1 1056235.9	一种镧标记的纳米载体 在制备治疗神经内分泌 肿瘤药物中的应用	2022-03-29	中国	朱 然

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3	Poly(amino ester)s as an emerging synthetic biodegradable polymer platform: Recent developments and future trends	Progress in Polymer Science	Xin Wang*, Zhengbiao Zhang*, Nikos Hadjichristidis*	2023, 136, 101634
4	Precise recognition of palladium through interlaminar chelation in a covalent organic framework	Chem	Yaoyao Bai, Long Chen, Linwei He, Baoyu Li, Lixi Chen, Fuqi Wu, Lanhua Chen, Mingxing Zhang, Zhiyong Liu, Zhifang Chai, and Shuao Wang*	2022, 8, 1442-1459
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6	Reciprocal regulation of mesenchymal stem cells and immune responses.	Cell Stem Cell	Ying Wang, Jiankai Fang, Benming Liu, Yufang Shi*.	2022, 29(11): 1515-1530.
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77	Light-Triggered Hypoxia-Responsive Nanoscale Metal-Organic Frameworks for Highly Efficient Antitumor Treatment	Advanced Optical Materials	Guangbao Yang, Anivind Kaur Bindra, Soo Zeng Fiona Phua, Jiawei Liu, Hongwei Wu, Dongdong Wang, Cheng Qian, Guofeng Liu, and Yanli Zhao	2022, 2201043
78	Macrophage-Targeted Hydroxychloroquine Nanotherapeutics for Rheumatoid Arthritis Therapy	ACS applied materials & interfaces	Hanghang Fang, Yongjie Sha, Liang Yang, Jingjing Jiang, Lichen Yin, Jiaying Li, Bin Li, Bert Klumperman, Fenghua Meng, Zhiyuan Zhong	2022, 14(7), 8824–8837
79	Anchoring Group-Mediated Radiolabeling of Inorganic Nanoparticles—A Universal Method for Constructing Nuclear Medicine Imaging Nanoprobes	ACS Applied Materials & Interfaces	Jianxian Ge, Lei Chen, Baoxing Huang, Yun Gao, Dandan Zhou, Yi Zhou, Can Chen, Ling Wen, Qing Li, Jiangfeng Zeng*, Zhiyuan Zhong, Mingyuan Gao*	2022, 14, 7, 8838–8846
80	The Non-Monotonic Relationship between the Oxidation State of Graphene-based Materials and its Cell Membrane Damage Effects	ACS Applied Materials & Interface	Xiuhua Yin#, Shitong Zhang#, Ling Wen#, Juan Su, Jian Huang, Guangxin Duan*, Zaixing Yang*	2022, DOI: 10.1021/acsmi.2c03520
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83	Two-Dimensional Imprinting Strategy to Create Specific Nanotrap for Selective Uranium Adsorption with Ultrahigh Capacity.	ACS Applied Materials & Interfaces	Xu Meiyun, Zhou Lei, Zhang Linjuan, Zhang Shitong, Chen Fulong, Zhou Ruhong, Daoben Hua	2022, 14 (7), 9408–9417
84	Acidity-Activated Charge Conversion of <sup>177</sup> Lu-Labeled Nanoagent for the Enhanced Photodynamic Radionuclide Therapy of Cancer	ACS Applied Materials & Interface	Yuan Zhang#, Guanglin Wang#, Qing Li*, Yue Jiang, Wan Chen, Min Zhao, Gaolin Liang, Qingqing Miao*	2022, 14, 3, 3875–3884
85	Reducing Chemo-/Radioresistance to Boost the Therapeutic Efficacy against Temozolomide-Resistant Glioblastoma	ACS Applied Materials & Interface	Baofeng Yun, Zhengpeng Gu, Zheng Liu, Yaobao Han, Qiao Sun, Zhen Li	2022, 14(34), 38617–38630
86	Crystal Facet-Modulated WO <sub>3</sub> Nanoplate Photoanode for Photoelectrochemical Glyoxal Semi-oxidation into Glyoxylic Acid	ACS Applied Materials & Interfaces	Zhefei Zhao, Mengnan Qu, Mengkai Zhu, Hongmei Shi, Xingyu Luo, Tianyang Guo, Qiao Sun, Lianzhou Wang, Huajun Zheng	2022, DOI: 10.1021/acsa mi.2c14442
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96	Disrupted mitochondrial homeostasis coupled with mitotic arrest generates antineoplastic oxidative stress.	Oncogene	Xiaohe Hao, Wenqing Bu, Guosheng Lv, Limei Xu, Dong Hou, Jing Wang, Xiaojie Liu, Tingting Yang, Xiyu Zhang, Qiao Liu, Yaoqin Gong, Changshun Shao*.	2022, 41(3), 27-443
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102	Decorporation of uranyl in kidneys using an engineered nanocomposite	Environmental Science: Nano	Cen Shi, <sup>‡</sup> Xiaomei Wang, <sup>‡</sup> Qiwen Sun, Lei Chen, Jingwen Guan, Linwei He, Yijing Zhang, Yujie Xu, Jianping Cao, Zhifang Chai, Shuao Wang and Juan Diwu*	2022, 9, 2704–2712
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105	Surface Microstructure Modulation Strategy to Design an Amphiphobic Platinum Nanocatalyst for Efficient Catalytic Oxidation of Hydrogen Isotopes	ACS Sustainable Chemistry & Engineering	Xu Meiyun, Chen Fulong, Zhou Lei, Xu Zhihong; He Qingling, Daoben Hua	2022, 10 (21), 7180
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110	Effective low dose Anlotinib induces long-term tumor vascular normalization and improves anti-PD-1 therapy	Frontiers in Immunology	Fan P, Qiang H, Liu Z, Zhao Q, Wang Y, Liu T, Wang X, Chu T, Huang Y*, Xu W*, Qin S*	2022, DOI: 10.3389/fimmu.2022.937924
111	Requirements for human cardiomyocytes	Cell Prolif	Yu M, Lei W, Cao J, Wang L, Ma A, Zhao ZA, Yang HT, Shen Z, Lan F, Cao F, Liang P, Pei X, Xiang AP, Yu J, Zhang Y, Zhang Y, Li Q, Zhou J, Wei J, Peng Y, Zhu H, Liang L, Cao N, Fu B, Hao J, Zhao T, Hu S	2022, 55(4): e13150
112	Upregulation of HIF-1 $\alpha$ contributes to complement activation in transplantation-associated thrombotic microangiopathy	British journal of haematology	Jiaqian Qi, Tingting Pan, Tao You, Yaqiong Tang, Tiantian Chu, Jia Chen, Yi Fan, Shuhong Hu, Fei Yang, Changgeng Ruan, Depei Wu*, Yue Han*	2022, 199(4), 603-615
113	Recurrent mutations in multiple components of the SWI/SNF complex in myelodysplastic syndromes and acute myeloid leukaemia	British Journal Of Haematology	Hong Yao, Li Huo, Nana Ping, Hong Liu, Hongzhi Li, Zixuan Ding, Hongjie Shen, Jundan Xie, Qiaocheng Qiu, Liang Ma, Airui Jiang, Qian Wang, Depei Wu, Xiaofei Yang, Yaohua Song, Suning Chen	2022, 196(2), 441-444

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118	A dual-response drug delivery system with X-ray and ROS to boost the anti-tumor efficiency of TPZ via enhancement of tumor hypoxia levels	Nanoscale	Panli Han, Lianxue Zhang, Yaqi Fu, Youyu Fu, Jianxiang Huang, Jinlin He, Peihong Ni, Taimoor Khan, Yang Jiao, Zaixing Yang, Ruhong Zhou	2023, 15, 237-247
119	Retinoic acid inhibits the angiogenesis of human embryonic stem cell-derived endothelial cells by activating FBP1-mediated gluconeogenesis	Stem Cell Res Ther	Yang Z, Yu M, Li X, Tu Y, Wang C, Lei W, Song M, Wang Y, Huang Y, Ding F, Hao K, Han X, Ni X, Qu L, Shen Z, Hu S	2022, 13(1), 239
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122	In Vivo Quantitative Assessment of Radiation Dose Based on Rati-ometric Photoacoustic Imaging of Tumor Apoptosis.	Analytical Chemistry	Jing Fang, Yan Zhao, Anna Wang, Yuqi Zhang, Chaoxiang Cui, Shuyue Ye, Qiulian Mao, Yali Feng, Jiachen Li, Chenjie Xu, and Haibin Shi*	2022, 94, 5149-5158
123	Millimeter-Scale Semiconductive Metal-Organic Framework Single Crystal for X-ray Imaging	Cell Reports Physical Science	Liwei Cheng†, Chengyu Liang†, Baoyu Li†, Haoming Qin, Pinhong Mi, Bin Chen, Yizhou Yan, Jian Xie, Xing Dai, Chao Zhang, Yanlong Wang, Yaxing Wang*, Shuao Wang	2022, 3, 101004
124	A spider hanging inside a carbon cage: off-center shift and pyramidalization of Sc <sub>3</sub> N clusters inside C <sub>84</sub> and C <sub>86</sub> fullerene cages	Inorganic Chemistry Frontiers	Ze Fu, Min Guo, Yang-Rong Yao, Qingyu Meng, Yingjing Yan, Qin Wang, Yi shen, Ning Chen	2022, 9, 4913-4920
125	Black Phosphorus Quantum Dots Enhance the Radiosensitivity of Human Renal Cell Carcinoma Cells through Inhibition of DNA-PKcs Kinase	Cells	Yue Lang, Xin Tian, Hai-Yue Dong, Xiang-Xiang Zhang, Lan Yu, Ming Li, Meng-Meng Gu, Dexuan Gao, Zeng-Fu Shang	2022, 11(10), 1651
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130	Fabrication of injectable hydrogels from an anticancer peptide for local therapeutic delivery and synergistic photothermal-chemotherapy	Journal of Materials Chemistry B	Na Liu, Shunjie Wu, Xin Tian, Xinming Li	2022, 10, 5165-5173
131	Supramolecular assemblies of histidine-containing peptides with switchable hydrolase and peroxidase activities through Cu(II) binding and co-assembling	Journal of Materials Chemistry B	Yue Zhang, Xin Tian, Xinming Li	2022, 10, 3716-3722
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156	Downregulation of exosomal MHC-I promotes glioma cells escaping from systemic immunosurveillance	Nanomedicine	Sun T, Li Y, Wu J, Cao Y, Yang Y, He Y, Huang W, Liu B, Yang W	2022; 46: 102605.
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159	Strategies to improve the therapeutic effect of pluripotent stem cell-derived cardiomyocytes on myocardial infarction	Front Bioeng Biotechnol	Xiao Y, Chen Y, Shao C, Wang Y, Hu S, Lei W	2022, 10, 973496
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162	The role of crm-1 in ionizing radiation-induced nervous system dysfunction in <i>Caenorhabditis elegans</i>	Neural Regeneration Research	Hui-Qiang Long, Jin Gao, 3, Shu-Qing He, Jian-Fang Han, Yu Tu, Na Chen	2022, doi.org/10.4103/
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164	The development of molecular and nano actinide decorporation agents	Chinese Chemical Letters	Xiaomei Wang, Cen Shi, Jingwen Guan, Yemeng Chen, Yigong Xu, Juan Diwu, Shuao Wang	2022, 33, 3395–3404
165	Efficient separation between trivalent americium and lanthanides enabled by a phenanthroline-based polymeric organic framework	Chinese Chemical Letters	Afshin Khayambashi, Long Chen, Xue Dong, Kai Li, Zhipeng Wang, Linwei He, Suresh Annam, Lixi Chen, Yaxing Wang, Matthew V. Sheridan, Chao Xu, Shuao Wang	2022, 33, 3429–3434
166	Improving in vivo Uranyl Removal Efficacy of a Nano-Metal Organic Framework by Interior Functionalization with 3-Hydroxy-2-pyridinone	Chinese Chemical Letters	Mengping Chen, Lang Lang, Lei Chen, Xiaomei Wang, Cen Shi, Qiwen Sun, Yigong Xu, Juan Diwu, Shuao Wang	2022, 40, 2054–2060
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168	Reactive oxygen species-responsive nanodrug of natural crocin-i with prolonged circulation for effective radioprotection	Colloids and Surfaces B-Biointerfaces	Wang Lu, Cao Yua, Zhang Xiaoyi, Liu Chang, Yin Jia, Kuang Liangju, He Weiei, Hua Daoben	2022, 213, 112441

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170	Plasma Metabolomics Identifies the Dysregulated Metabolic Profile of Primary Immune Thrombocytopenia (ITP) Based on GC-MS	Frontiers in pharmacology	Ziyan Zhang, Xiaojin Wu, Meng Zhou, Jiaqian Qi, Rui Zhang, Xueqian Li, Chang Wang, Changgeng Ruan and Yue Han*	2022, 13, 845275
171	An automated approach for predicting glioma grade and survival of LGG patients using CNN and radiomics	Frontiers in oncology	Chenan Xu, Yuanyuan Peng, Weifang Zhu, Zhongyue Chen, Jianrui Li, Wenhao Tan, Zhiqiang Zhang* and Xinjian Chen*	2022, 12, 969907
172	Up-Regulation of TRIM32 Associated With the Poor Prognosis of Acute Myeloid Leukemia by Integrated Bioinformatics Analysis With External Validation	Frontiers in oncology	Xiaoyan Xu, Jiaqian Qi, Jingyi Yang, Tingting Pan, Haohao Han, Meng Yang and Yue Han*	2022, 12, 848395
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174	Epigallocatechin-3-Gallate (EGCG) Modulates the Composition of the Gut Microbiota to Protect Against Radiation-Induced Intestinal Injury in Mice	Frontiers in oncology	Cai S, Xie LW, Xu JY, Zhou H, Yang C, Tang LF, Tian Y, Li M	2022, 12, 848107
175	Effects of PEG Chain Length on Relaxometric Properties of Iron Oxide Nanoparticles-Based MRI Contrast Agent	Nanomaterials	Jianxian Ge, Cang Li, Ning Wang, Ruru Zhang, Mohammad Javad Afshari, Can Chen, Dandan Kou, Dandan Zhou, Ling Wen*, Jianfeng Zeng,* and Mingyuan Gao	2022, 12(15), 2673

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178	Charge transport and photoconductivity in a hybrid uranium (IV) halide perovskite	Inorganic Chemistry	Fuwan Zhai, Baoyu Li, Liangwei Yang, Xing Dai, Chengyu Liang, Chuanqin Xia, Zhifang Chai, Yaxing Wang, and Shuao Wang	2022, 61, 13256-13260
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181	Turn-up Luminescent Sensing of Ultraviolet Radiation by Lanthanide Metal-Organic Frameworks	Inorganic Chemistry	Sida Zhang,▽ Lixi Chen,▽ Jian Xie,▽ Yugang Zhang, Feng Huang, Xia Wang, Kai Li, Fuwan Zhai, Qian Yang, Lanhua Chen, Yaxing Wang, Xing Dai, Zhifang Chai, and Shuao Wang	2022, 61, 4561-4565
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202	Recent Advances in Hydrogel-Based Sensors Responding to Recent Advances in Hydrogel-Based Sensors Responding to Ionizing Radiation	Gels	Ping Zhang , Li Jiang , Hong Chen and Liang Hu	2022, 8, 238
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205	Effective mitigation of gadolinium deposition using the bidentate hydroxypyridinone ligand Me-3,2-HOPO	Dalton Transactions	Qiwen Sun,‡ Xiaomei Wang,‡ Cen Shi,‡ Jingwen Guan, Lanhua Chen, Yumin Wang, Shuao Wang and Juan Diwu*	2022, 51, 13055–13060

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214	Effect of 3,3'-diselenodipropionic Acid on Dextran Sodium Sulfate-Induced Ulcerative Colitis in Mice.	Biological Trace Element Research	Jia-Yang Zheng, Jia-Ying Xu, Lin Zhang, Zhang-Min Wang, Xue-Bin Yin, Li-Qiang Qin	2022, DOI10.1007/s12011-022-03491-1
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243	Progress in solid state and coordination chemistry of actinides in China	Radiochimica Acta	Kai Li, Wei Liu, Hailong Zhang, Liwei Cheng, Yugang Zhang, Yaxing Wang*, Ning Chen*, Congqing Zhu*, Zhifang Chai and Shuao Wang*	2022, 11, doi.org/10.1515/ract-2022-0024
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246	Nanobody-based anti-CD22-chimeric antigen receptor T cell immunotherapy exhibits improved remission against B-cell acute lymphoblastic leukemia	Transplant Immunology	Tingting Zhang, Tian Wang, Fengtao You, Zixuan Li, Dan Chen, Kailu Zhang, Shuaiyu Tian, Binjie Sheng, Hai Wu, Licui Jiang, Renyuxue Ma, Gangli An, Huimin Meng, Lin Yang*	2022, 71, 101538
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250	N-Acetylcysteine as Prophylactic Therapy for Transplantation-Associated Thrombotic Microangiopathy: A Randomized, Placebo-Controlled Trial	Transplantation and cellular therapy	Tingting Pan, Jiaqian Qi, Yaqiong Tang, Yifang Yao, Jia Chen, Hong Wang, Jingyi Yang, Xiaoyan Xu 1, Qin Shi, Yuejun Liu, Xuefeng He, Feng Chen, Xiao Ma, Xiaohui Hu, Xiaojin Wu, Depei Wu*, Yue Han*	2022, 28(11), 764
251	N-Acetyl-L-Cysteine Potentially Inhibits Complement Activation in Transplantation-Associated Thrombotic Microangiopathy	Transplantation and cellular therapy	Jiaqian Qi, Shuhong Hu, Xuefeng He, Tingting Pan, Liping Yang, Rui Zhang, Yaqiong Tang, Depei Wu*, Yue Han*	2022, 28(4), 216
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RESEARCH ARTICLE

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## Controlled Activation of TRPV1 Channels on Microglia to Boost Their Autophagy for Clearance of Alpha-Synuclein and Enhance Therapy of Parkinson's Disease

Jiaxin Yuan, Hanghang Liu, Hao Zhang, Tingting Wang, Qing Zheng, and Zhen Li\*

Parkinson's disease (PD) is characterized with accumulation of Lewy bodies with a major component of fibrillar alpha-synuclein ( $\alpha$ -syn). Herein, boosting PD therapeutic efficacy by enhancing the autophagy of microglia to phagocytose and degrade  $\alpha$ -syn via controlled opening of their surface TRPV1 channels with rationally designed photothermal nanoagent is reported. The Cu<sub>2</sub>-Se-anti-TRPV1 nanoparticles (CS-AT NPs) are fabricated to target the microglia and open their surface TRPV1 channels under the second near infrared (NIR-II) laser irradiation to cause influx of Ca<sup>2+</sup> to activate ATG5 and Ca<sup>2+</sup>/CaMKK2/AMPK/mTOR signaling pathway, which promote phagocytosis and degradation of  $\alpha$ -syn. The CS-AT NPs are efficiently delivered by focused ultrasound into striatum of PD mice with high expression of TRPV1 receptors. The athletic ability of PD mice treated by CS-AT NPs and NIR-II irradiation is significantly improved due to the phagocytotic clearance of  $\alpha$ -syn by microglia with enhanced autophagy. The enzyme tyrosine hydroxylase, ionized calcium binding adapter protein 1, glial fibrillary acidic protein, and pSer129- $\alpha$ -syn (p- $\alpha$ -syn) of treated PD mice are almost recovered to the normal levels of healthy mice. This study provides insights into the activation of microglial autophagy by targeting surface ion channels to improve the treatment of PD and other neurodegenerative diseases.

$\alpha$ -syn can spread through the adjacent neurons in anatomically connected brain regions, and serve as seeds to induce the aggregation and deposition of  $\alpha$ -syn monomers,<sup>[1-5]</sup> which could increase oxidative stress, depolarize mitochondria, disturb protein clearance, and alter the cytoskeleton, leading to neuronal damage and the progression of PD.<sup>[6]</sup> The accumulation of  $\alpha$ -syn in the midbrain plays a key role in the pathogenesis of PD,<sup>[7]</sup> and how to eliminate  $\alpha$ -syn aggregates is crucial for the success of treatment.

In the brain, microglia as an important type of innate immune cells play vital roles in supporting brain development, monitoring the neuronal activity, regulating learning and memory capabilities, and act as local phagocytes and damage sensors in the brain parenchyma.<sup>[8-9]</sup> They can phagocytose and degrade misfolded and aggregated proteins (such as  $\alpha$ -syn) to prevent the formation of LBs.<sup>[10,11]</sup> Recent studies suggest that microglia ingested and degraded neuron-released  $\alpha$ -syn aggregates through selective autophagy,

which was mediated by Toll-like receptor (TLR) 2, TLR4-NF- $\kappa$ B, and LC3-associated endocytosis (LANDO).<sup>[12-14]</sup> Further studies show that the production of inflammatory factors and neurodegeneration would proceed unchecked in the absence of LANDO.<sup>[15,16]</sup> There are many ways to activate the autophagy of microglia, including use of rapamycin as an autophagy inducer,<sup>[17]</sup> capsaicin (CAP) as an agonist of transient receptor potential vanilloid subtype 1 (TRPV1),<sup>[18]</sup> and P2 $\times$ 7 receptors (P2 $\times$ 7Rs) as the members of the family of ionotropic ATP-gated receptors,<sup>[19]</sup> of which targeting their surface rich TRPV1 receptors is the most promising approach.<sup>[20]</sup>

TRPV1 receptors are temperature-sensitive cationic channels,<sup>[21,22]</sup> which have been demonstrated to be an effective target for the treatment of neurodegenerative diseases by using CAP as stimuli.<sup>[23,24]</sup> However, the direct use of CAP as TRPV1 agonist in clinical practice is limited by its toxic side effects.<sup>[25]</sup> In particular, the uncontrollable continuous stimulation by CAP can cause the influx of excessive calcium ions (Ca<sup>2+</sup>) into microglia to damage mitochondria and even cause apoptosis, it is crucial to control the influx of Ca<sup>2+</sup> under stimulation.<sup>[26]</sup> In addition, it is very difficult to modulate TRPV1 signal transduction by using CAP due to the lack of its targeting capability, and

### 1. Introduction

Parkinson's disease (PD) as the second most common neurodegenerative diseases remains incurable. It is characterized by progressive loss of dopaminergic neurons, and accumulation of intraneuronal inclusions, which are well-known as Lewy bodies (LBs) with fibrillar alpha-synuclein ( $\alpha$ -syn) aggregates as a major protein component.<sup>[1,2]</sup> It has been widely believed that  $\alpha$ -syn can be varied in the early stage of PD and pathological

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# Metabolic Homeostasis-Regulated Nanoparticles for Antibody-Independent Cancer Radio-Immunotherapy

Wenhao Shen, Teng Liu, Pei Pei, Junmei Li, Sai Yang, Yanxiang Zhang, Hailin Zhou, Lin Hu, and Kai Yang\*

The special metabolic traits of cancer cells and tumor-associated macrophages (TAMs) in the tumor microenvironment (TME) are promising targets for developing novel cancer therapy strategies, especially the glycolysis and mitochondrial energy metabolism. However, therapies targeting a singular metabolic pathway are always counteracted by the metabolic reprogramming of cancer, resulting in unsatisfactory therapeutic effect. Herein, this work employs poly(ethylene glycol)-coated (PEGylated) liposomes as the drug delivery system for both mannose and levamisole hydrochloride to simultaneously inhibit glycolysis and restrain mitochondrial energy metabolism and thus inhibit tumor growth. In combination with radiotherapy, the liposomes can not only modulate the immunosuppressive TME by cellular metabolism regulation to achieve potent therapeutic effect for local tumors, but also suppress the M2 macrophage proliferation triggered by X-ray irradiation and thus enhance the immune response to inhibit metastatic lesions. In brief, this work provides a new therapeutic strategy targeting the special metabolic traits of cancer cells and immunosuppressive TAMs to enhance the abscopal effect of radiotherapy for cancer.

## 1. Introduction

Glycolysis in cytoplasm and energy metabolism in mitochondria provide the main energy/biosynthetic precursors for eukaryotes.<sup>[1]</sup> In the tumor microenvironment (TME), it is generally acknowledged that cancer cells consume and transform much glucose into lactate and pyruvate through Warburg metabolism in the cytoplasm.<sup>[2]</sup> The Warburg effect has also been observed in other rapidly proliferating cells, such as tumor-associated macrophages (TAMs) with immunosuppressive functions.<sup>[3]</sup> The accumulated lactic acid in TME could lead to the polarization toward M2 macrophages, further promoting tumor

metastasis and treatment resistance.<sup>[4]</sup> Moreover, upon the increased bioenergetic and biosynthetic demand as well as the elevated oxidative stress during tumor growth, cancer cells would autonomously reprogram their metabolism pathways.<sup>[5]</sup> Thereafter, the lactate and pyruvate generated from Warburg metabolism and glutamine would flow into mitochondria and participate in the tricarboxylic acid (TCA) cycle, which provide key metabolites for macromolecule synthesis and produce oncometabolites to maintain the cancer phenotype to support tumor anabolism.<sup>[6]</sup> Accordingly, glycolysis and mitochondrial metabolism are promising targets to develop novel cancer therapy strategies.

Radiotherapy is a widely applied cancer treatment modality. Despite some reports on radiotherapy-mediated immunogenic cell death (ICD) to stimulate immune response, the abscopal effect is rare in clinical cancer treatment.<sup>[7]</sup> Recently, studies

have shown that damage-related molecular patterns (DAMPs) and lncRNA in tumor-derived exosomes (TEX) released during ICD would increase the polarization of M2 macrophages via HIF1 $\alpha$ /GLUT-1 pathway, providing immunosuppressive TME supporting the proliferation, invasion and metastasis of cancer cells.<sup>[8]</sup> These results provide a possible explanation for the limited immune response and scarce abscopal effect after radiotherapy.<sup>[9]</sup> In this regard, interfering the TEX-induced polarization of M2 macrophages to reprogram the immunosuppressive TME would improve the antitumor activity and may augment the immune response to achieve sufficient abscopal effect.

Mannose is a monosaccharide molecule which has been reported to impair tumor growth and enhance chemotherapy by influencing glucose metabolism and inducing PD-L1 degradation in TME.<sup>[10]</sup> Levamisole hydrochloride is an immune stimulator which has been applied in the treatment for cancer and steroid-sensitive idiopathic nephrotic syndrome.<sup>[11]</sup> However, the unsatisfactory tumor accumulation of these water-soluble molecules and stress-responsive cancer metabolic reprogramming would impair the therapies targeting a singular metabolic pathway. In this work, we have developed a liposome which has been approved for the cancer treatment by the U.S. Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMEA) as the DDS to load both of mannose and levamisole

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## Article

## Precise recognition of palladium through interlaminar chelation in a covalent organic framework

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## SUMMARY

Palladium isotopes as fission products in used nuclear fuel represent precious alternative resources besides its natural reserves and therefore have a high extraction value. The practical use of currently proposed solvent extraction is challenging, originating from the limited stability and separation selectivity of the extractants under harsh reprocessing conditions. Herein, we present an interlayer synergistic binding strategy, a metal-recognition manner deviating from chelation within a single ligand molecule in solvent extraction, for selective palladium chelation in a covalent organic framework. The experimental, structural, and theoretical analyses corroborate that the enol-to-keto tautomerization leads to selective synergistic chelation of Pd<sup>2+</sup> instead of other undesired metal ions, where two oxygen donors from adjacent layers and two free nitrate ions work together in a planar tetracoordination model. Fast adsorption kinetics, high adsorption capacity, and one-round enrichment of Pd<sup>2+</sup> from the simulated high-level nuclear waste solution are unprecedentedly achieved in the dynamic breakthrough experiment.

## INTRODUCTION

As one of the light platinum group metals (PGMs), palladium (Pd) plays a vital role in automotive industries to convert noxious emissions to harmless products, electronic sectors to produce circuit boards, and fine chemicals to manufacture vitamins, antibiotics, and others.<sup>1</sup> However, the abundance of Pd in the Earth's crust is extremely low, at only 0.1–3 ng g<sup>-1</sup>.<sup>2</sup> The conventional refining process from minerals requires numerous recycling and intermediate steps, giving rise to tedious and labor-intensive operations.<sup>3</sup> Considering the low abundance of Pd combined with the complex refining process, extraction of Pd<sup>2+</sup> from used nuclear fuel (UNF) is regarded as a promising alternative approach to obtain a large amount of Pd.<sup>4</sup> It was predicted that the accumulated Pd<sup>2+</sup> in UNF will increase up to 1,000 tons by 2030, making up to 11% of total proven recoverable palladium reserves.<sup>5</sup> Solvent extraction is the commonly accepted method for the selective uptake of Pd<sup>2+</sup> from UNF.<sup>6</sup> However, extractants have a high propensity to decompose in extreme conditions of high acidity, strong radioactivity, and elevated temperature. In addition, the chemical composition of UNF is extremely complicated since more than 40 elements and 1,500 nuclides are present in fresh UNF due to the nuclear fission of <sup>235</sup>U.<sup>7</sup> The coexisting metal ions, especially Ni, Cd, and Ag with similar chemical properties to Pd, notably decrease the solvent extraction efficiency. It is therefore a daunting challenge to achieve high separation capability, considering the integration of sufficient stability, selectivity, capacity, and solubility within one extractant.

## The bigger picture

Separation of palladium isotopes from used nuclear fuel is of high significance but faces notable challenges, due to the harsh fuel reprocessing condition with combined high acidity, strong radiation, and vast interfering ions. Compared with the proposed solvent extraction method, where the extractants suffer from limited stability and efficiency, covalent organic frameworks are shown as a new generation of solid extractant not only because of their elevated stability in acids and resistance to radiations but also because they exhibit a distinct interlayer synergistic binding mode, markedly deviating from chelation within a single ligand molecule, with notably enhanced selectivity for Pd extraction. This leads to previously unachieved one-round enrichment and purification of Pd from the simulated high-level nuclear waste solution. This strategy, in general, opens a new avenue to remedy various types of pollutants and to extract many strategic resources in complex conditions.



## Thermodynamics-Kinetics-Balanced Metal–Organic Framework for In-Depth Radon Removal under Ambient Conditions

Xia Wang,<sup>#</sup> Fuyin Ma,<sup>#</sup> Shengtang Liu,<sup>#</sup> Lixi Chen,<sup>#</sup> Shunshun Xiong, Xing Dai, Bo Tai, Linwei He, Mengjia Yuan, Pinhong Mi, Shicheng Gong, Guodong Li, Yi Tao, Jun Wan, Long Chen, Xuhui Sun, Quan Tang, Linfeng He, Zaixing Yang,<sup>\*</sup> Zhifang Chai, and Shuao Wang<sup>†</sup>

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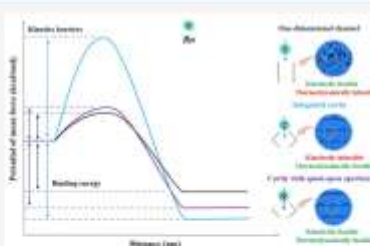
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**ABSTRACT:** Radon (Rn), a ubiquitous radioactive noble gas, is the main source of natural radiation to human and one of the major culprits for lung cancer. Reducing ambient Rn concentration by porous materials is considered as the most feasible and energy-saving option to lower this risk, but the in-depth Rn removal under ambient conditions remains an unresolved challenge, mainly due to the weak van der Waals (vdW) interaction between inert Rn and adsorbents and the extremely low partial pressure ( $<1.8 \times 10^{-14}$  bar,  $<10^9$  Bq/m<sup>3</sup>) of Rn in air. Adsorbents having either favorable adsorption thermodynamics or feasible diffusion kinetics perform poorly in in-depth Rn removal. Herein, we report the discovery of a metal–organic framework (ZIF-7-1m) for efficient Rn capture guided by computational screening and modeling. The size-matched pores in ZIF-7-1m abide by the thermodynamically favorable principle and the exquisitely engineered quasi-open apertures allow for feasible kinetics with little sacrifice of sorption thermodynamics. The as-prepared material can reduce the Rn concentration from hazardous levels to that below the detection limit of the Rn detector under ambient conditions, with an improvement of at least two orders of amplitude on the removal depth compared to the currently best-performing and only commercialized material activated charcoal.



### INTRODUCTION

As a common component of air, radon (Rn) is a radioactive noble gas and constitutes the largest single fraction (~40%) of the natural radiation to the public.<sup>1</sup> Generally, Rn radioisotopes (<sup>219</sup>Rn, <sup>220</sup>Rn, and, dominantly, <sup>222</sup>Rn) arise from the decay of <sup>235</sup>U, <sup>232</sup>Th, and <sup>238</sup>U, which widely exist in soils, rocks, and even building materials.<sup>2</sup> Although at an ultralow concentration in air, Rn, if inhaled, may induce stochastic effects in the body and is recognized as one of the leading contributors to lung cancer,<sup>3</sup> causing 3% deaths of all cancer mortality in 66 countries.<sup>4</sup> This effect is chronic and dose-related; thus, it is encouraged to control the irradiation of Rn to a level as low as reasonably achievable,<sup>5</sup> especially in the poorly ventilated places where Rn tends to accumulate. Meanwhile, Rn is the main interference in ultrasensitive gas rare-event physics experiments because its decay can produce unwanted background events analogous to genuine signals,<sup>6</sup> necessitating a strict control of the Rn level ( $<1$  mBq/m<sup>3</sup>,  $<1.8 \times 10^{-23}$  bar). Unfortunately, the currently applied techniques, mainly ventilation and physical blocking, for Rn reduction are inefficient for its in-depth removal and are energy-consuming, posing the need for developing more efficient and energy-saving approaches.

Adsorption by porous materials is considered as a promising method that can be universally applied to capture Rn with little

energy input. As a chemically inert gas, Rn can only weakly interact with adsorbents through the van der Waals (vdW) force. Besides, the ultralow Rn concentration in air<sup>7,8</sup> makes its in-depth removal under ambient conditions an unresolved challenge because of the much higher concentrations of competing gases (N<sub>2</sub>, O<sub>2</sub>, H<sub>2</sub>O etc. with at least 12 orders of magnitude in excess) in air. In this case, the level of Rn removal depth (i.e., the solid/gas phase distribution ratio of Rn) for a certain sorbent material with large excess of suitable active sites is dependent on how strong the material can interact with Rn. Such active sites, from a logical principle from the thermodynamics viewpoint, should process pores with shape and size matched with the Rn atom in order to maximize the vdW interaction. However, most adsorbents explored to date fail to follow this thermodynamics principle and suffer from low removal efficiency under ambient conditions.<sup>9,10</sup> The currently best-performing and only commercialized Rn adsorbent is coconut activated charcoal (AC). Possessing a wide pore size distribution, AC, on one hand, offers macro- and meso-pores for fast gas diffusion kinetics but, on the other hand, possesses only a very small fraction of micropores that serve as the

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## In Vivo Uranium Decorporation by a Tailor-Made Hexadentate Ligand

Bin Chen,<sup>#</sup> Sheng Hong,<sup>#</sup> Xing Dai,<sup>#</sup> Ximeng Li, Qi Huang, Tingfeng Sun, Dehan Cao, Hailong Zhang, Zhifang Chai, Juan Diwu,<sup>\*</sup> and Shuao Wang<sup>#</sup>

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**ABSTRACT:** The sequestration of uranium, particularly from the deposited bones, has been an incomplete task in chelation therapy for actinide decorporation. Part of the reason is that all previous decorporation ligands are not delicately designed to meet the coordination requirement of uranyl cations. Herein, guided by DFT calculation, we elaborately design a hexadentate ligand (TAM-2LI-MAM<sub>2</sub>), whose preorganized planar oxo-donor configuration perfectly matches the typical coordination geometry of the uranyl cation. This leads to an ultrahigh binding affinity to uranyl supported by an *in vitro* desorption experiment of uranyl phosphate. Administration of this ligand by prompt intraperitoneal injection demonstrates its uranyl removal efficiencies from the kidneys and bones are up to 95.4% and 81.2%, respectively, which notably exceeds all the tested chelating agents as well as the clinical drug ZnNa<sub>2</sub>-DTPA, setting a new record in uranyl decorporation efficacy.

Uranium, which is a strategic resource used as nuclear fuel, with strong chemical toxicity and long-term radioactivity, gradually deposits in the kidneys and bones once it enters the body.<sup>1</sup> The fact that uranium is identified as a bone volume seeker and that the bone-accumulated percentage of uranium content relative to the whole body load is up to 75% during chronic exposure<sup>2</sup> renders bone decorporation an intractable problem in contrast to the quick and relatively simple excretion of uranium from the kidneys. At present, the most efficient treatment to address this is chelation therapy,<sup>3</sup> the decorporation efficiency of which depends heavily on the binding affinities of chelation ligands toward uranyl cations.

Under physiological conditions, the dominant existing form of uranium, i.e., UO<sub>2</sub><sup>2+</sup> (U(VI)), presents a linear geometry with two oxygen atoms in axial positions, which compels coordination (four to six) that merely occurs in the equatorial plane perpendicular to the O=U=O axis.<sup>4</sup> Recently reported results of *in vivo* U(VI) decorporation assays demonstrate that extensively studied hydroxypyridinone (HOPO)-based chelating agents as well as currently approved drugs—the diethylenetriamine pentaacetate trisodium calcium/zinc salts (CaNa<sub>2</sub>-DTPA/ZnNa<sub>2</sub>-DTPA)—all suffer from the poor removal efficiency of U(VI) from deposited bone, probably attributable to the following reasons: (a) bidentate chelating agents tend to bind U(VI) in the stoichiometry of 2:1 or even 3:1, thereby their efficiency is hampered by the limited local concentration of sequestration agents in the deposited tissues; (b) tetradentate ligands, represented as 5LI0-Me-3,2-HOPO,<sup>5</sup> could chelate uranyl with four oxygen donors from two HOPO units, yet are inadequate to surpass the binding affinities of hydroxyapatite (HAP) as the major constituent of the skeleton; (c) the nonplanar hexadentate ligands as well as the ligands with higher denticity,<sup>6</sup> such as TREN-HOPO, 3,4,3-LI-HOPO, and ZnNa<sub>2</sub>-DTPA, are unable to display distinct advantages despite their multiply available donor

atoms, owing to the mismatched coordination geometry with uranyl cations. From the perspective of coordination chemistry, planar hexadentate chelators can fully satisfy the equatorial coordination sites of uranyl, thereby resulting in higher binding affinities;<sup>7</sup> however, not a single *in vivo* decorporation study has ever been performed up to now. Herein, a pioneering theoretical simulation is performed, demonstrating the superiority of the planar hexadentate ligand in the strong binding of U(VI), and the ligand synthesized accordingly achieves a breakthrough in uranium decorporation efficiency.

Such a targeted hexadentate ligand could be composed of three bidentate chelating moieties via a suitable linkage, wherein specific 2LI linkers (two methylene units) with limited flexibility can specially match the coordination requirement of uranyl cations and simultaneously restrict the binding of transition metal ions holding an octahedral coordination geometry,<sup>7a-d</sup> thus reducing the depletion of biologically related trace elements during U(VI) excretion. Among the available bidentate chelating moieties, catechol presents a powerful binding affinity toward uranyl cations but has a certain biotoxicity. Moreover, maltol, which is commonly used as a food additive, features low cost, ready availability, low biotoxicity, and high aqueous solubility. It has a comparable chelating ability to HOPOs, yet is less studied.<sup>8</sup> For these reasons, the hexadentate ligand TAM-2LI-MAM<sub>2</sub> consisting of the forceful 2,3-dihydroxyterephthalamide (TAM) and maltol-

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## Thermodynamics-Kinetics-Balanced Metal–Organic Framework for In-Depth Radon Removal under Ambient Conditions

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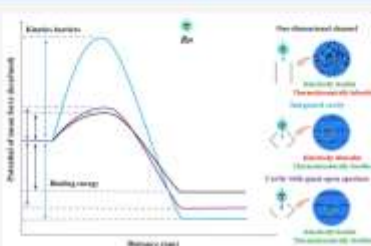
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### INTRODUCTION

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## Alkaline Phosphatase-Controllable and Red Light-Activated RNA Modification Approach for Precise Tumor Suppression

Jing Fang, Yali Feng, Yuqi Zhang, Anna Wang, Jiachen Li, Chaoxiang Cui, Yirui Guo, Jinfeng Zhu, Zhengzhong Lv, Zhongsheng Zhao, Chenjie Xu, and Haibin Shi\*

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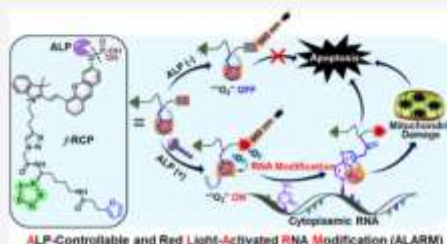
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**ABSTRACT:** RNA interference (RNAi) has proved to be a promising modality for disease treatment. However, the promise of conventional RNA therapeutics for clinical application is severely impeded by low delivery efficiency and susceptibility of RNAs to serum RNases. Therefore, developing advanced RNAi technology is an increasing demand for achieving precise medicine. Herein, for the first time, we propose an alkaline phosphatase (ALP)-controllable and red light-activated RNA modification (ALARM) approach for anti-tumor therapeutic application. An ALP-responsive NIR fluorogenic probe *f*-RCP consisting of a tumor-targeting cyclic RGD peptide, an ALP-activated photosensitizer CyOP, and an <sup>1</sup>O<sub>2</sub>-susceptible furan module for RNA modification was rationally designed and synthesized. Studies have demonstrated that *f*-RCP can specifically target to liver carcinoma HepG2 cells and spontaneously emit activated NIR/photoacoustic signals upon cleavage by the ALP enzyme, allowing for sensitive detection of ALP-positive tumors. More notably, we surprisingly found that the capability of *f*-RCP producing singlet oxygen (<sup>1</sup>O<sub>2</sub>) under red light irradiation could be simultaneously unlocked, which can ignite the covalent cyclization reaction between furan and nucleobases of intracellular RNA molecules, leading to significant mitochondrial damage and severe apoptosis of tumor cells, in consequence realizing efficient tumor suppression. Most importantly, the potential therapeutic mechanism was first explored on the transcriptomic level. This delicate ALARM strategy may open up new insights into cancer gene therapy.



### INTRODUCTION

The treatment of malignant tumor still faces huge challenges and bottlenecks such as tumor heterogeneity, drug resistance, and systemic toxicity.<sup>1–3</sup> Among the conventional therapeutic modalities, gene therapy as an emerging technique to regulate the expression of targeted gene holds immense potential for treating various human diseases including cancer.<sup>4–14</sup> Over the past decades, considerable efforts have been devoted to developing gene silencing techniques.<sup>15–21</sup> However, the low delivery efficiency, potential systemic toxicity, and high cost of gene therapeutics greatly hinder their extensive applications in clinical practices.<sup>22–26</sup> Therefore, it is highly urgent to explore advanced gene interference techniques for improving the therapeutic efficacy of tumors while minimizing its side effects for normal tissues and/or organs.

Ribonucleic acid (RNA) as a vital component of the Central Dogma has been well recognized for its roles in transcription and translation.<sup>27–30</sup> RNA interference (RNAi) technology has proved to be a promising modality for cancer and other disease treatments by silencing the target gene expression. Thus far, two types of RNAi therapeutic strategies have been developed to silence the RNA molecules that are associated with certain

diseases by utilizing antisense oligonucleotides<sup>31–34</sup> and small molecules.<sup>35,36–38</sup> However, their promise for clinical application is greatly impeded by low delivery efficiency, susceptibility of RNA to serum RNases, poor gene silencing activity due to noncovalent interaction,<sup>39–41</sup> and potential systemic toxicity.<sup>42–44</sup> Numerous studies have recently demonstrated that the covalent modification of RNA strands can disturb the function of targeted RNA, leading to dysregulated expression of downstream proteins that may impact various cellular processes,<sup>45–49</sup> which has been considered to be a promising approach for gene silencing. Op de Beeck and Madder have previously reported a photo-induced cross-linking method to study the intermolecular interaction of DNA–DNA and protein–DNA through the <sup>1</sup>O<sub>2</sub>-initiated cycloaddition reaction between furan and

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## Near-Infrared Afterglow Luminescence of Chlorin Nanoparticles for Ultrasensitive *In Vivo* Imaging

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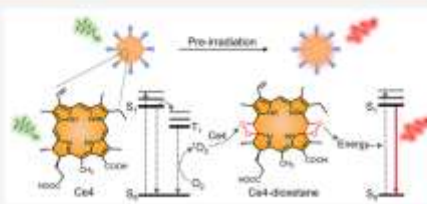
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**ABSTRACT:** Afterglow imaging holds great potential for ultrasensitive biomedical imaging. As it detects photons after the cessation of real-time light excitation, autofluorescence can therefore be effectively eliminated. However, afterglow imaging is still in its infant stage due to the lack of afterglow agents with satisfactory lifetime, biocompatibility, and high luminescence brightness, particularly afterglow in the near-infrared region for *in vivo* applications. To address these issues, this study for the first time reports chlorin nanoparticles (Ch-NPs) emitting afterglow luminescence peaking at 680 nm with a half-life of up to 1.5 h, which is almost 1 order of magnitude longer than those of other reported organic afterglow probes. In-depth experimental and theoretical studies revealed that the brightness of the afterglow luminescence is strongly correlated with the singlet oxygen ( $^1O_2$ ) capacity and the oxidizability of the chlorins. Benefiting from the ultralong half-life and the minimized imaging background, small metastatic tumor foci of 3 mm<sup>3</sup> were successfully resected under the guidance of the afterglow luminescence generated upon a single shot of activation prior to the injection, which was impossible for conventional near-infrared fluorescence imaging due to tissue autofluorescence.



### INTRODUCTION

Optical imaging that capitalizes on the detection of photons to decipher molecular and biological processes offers powerful tools for biology and medicine.<sup>1–3</sup> However, as a commonly used optical imaging technique, fluorescence imaging requires real-time light excitation that induces tissue autofluorescence and consequently results in a compromised signal-to-noise ratio (SNR) and a reduced tissue detection depth, unfavorable for imaging sensitivity and specificity.<sup>4,5</sup> Hence, self-luminescence imaging approaches including chemiluminescence, bioluminescence, and afterglow luminescence that require no real-time light excitation have attracted increasing enthusiasm in recent years to circumvent tissue autofluorescence.<sup>6–11</sup> However, chemiluminescence and bioluminescence imaging rely on reactive species- and enzyme-initiated redox reactions to trigger luminescence, respectively.<sup>12,13</sup> Their imaging signals are easily perturbed by internal stimuli such as the enzymatic or redox microenvironment and the availability of the substrate.<sup>14,15</sup> In comparison with fluorescence, the afterglow luminescence only requires preillumination of afterglow agents; in comparison with chemiluminescence and bioluminescence, the afterglow luminescence requires no particular chemical mediator or exogenous enzyme, which highlights the advantages of the latter approach for biomedical applications.<sup>16,17</sup>

Nevertheless, afterglow luminescence imaging does need afterglow luminescent agents comprising inorganic or organic active materials that have been used for tumor imaging,<sup>18–23</sup> lymph node mapping,<sup>22,26</sup> imaging of drug-induced hepatotoxicity,<sup>19</sup> monitoring of drug release,<sup>27</sup> specific detection of cancer exosomes,<sup>28</sup> imaging of blood vessels,<sup>29</sup> predicting anticancer efficiency,<sup>30</sup> and imaging-guided therapy.<sup>31–33</sup> In comparison with the inorganic luminescence materials, better biosafety profile and easier afterglow luminescence tunability are expected from the organic counterparts.<sup>34,35</sup> To date, there are only a few organic afterglow systems reported based on either semiconducting polymers or small molecular systems comprising multiple ingredients.<sup>3,3,26,30,36</sup> However, due to the short wavelength and the relatively low intensity of the afterglow luminescence, efforts including implemental amplification, cascade red-shifted strategies, and optimization of the molecular structure through complex organic synthesis are being made.<sup>20,22</sup> Unfortunately, the afterglow agents reported so far exhibit a short half-life of several minutes, and therefore

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**Radioluminescent Perovskite**

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**Circularly Polarized Radioluminescence from Chiral Perovskite Scintillators for Improved X-ray Imaging**

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Dedicated to Professor Zhifang Chai on the occasion of his 80th birthday

**Abstract:** Scintillators display radioluminescent properties when irradiated by high-energy photons and therefore play an essential role in radiation detection. The current inventory of scintillators is overwhelmingly represented by achiral structures, where the radioluminescence propagates isotropically after generation. Herein, we demonstrate that chiral perovskites of (R-3AP)PbBr<sub>2</sub>Cl·H<sub>2</sub>O (**R-3APP**) and (S-3AP)PbBr<sub>2</sub>Cl·H<sub>2</sub>O (**S-3APP**) emerge as a new type of scintillator displaying a distinct property of circularly polarized radioluminescence (**CPRL**). A high quantum yield of 27.6%, high luminescence dissymmetric factors ( $g_{\text{lum}}$ ) of  $4 \times 10^{-2}$ , and high X-ray absorption coefficients were observed for these compounds. As proof of concept, we fabricated a polarized scintillator pair by assembling chiral scintillator crystals, which provides a new strategy to attenuate optical crosstalk between the scintillators by precisely controlling the radioluminescence propagation and improves the X-ray imaging quality at the boundary region.

Scintillators that can convert the energy of X-ray photons into visible luminescence signals are core parts of an X-ray detector,<sup>[1]</sup> which play an essential role in medical imaging,

security checks, and industrial applications.<sup>[2]</sup> Generally, X-ray detectors are fabricated by coupling multiple scintillators with a photodetector array. Because the radioluminescence signal of scintillators propagates isotropically after generation, optical crosstalk is often present between adjacent scintillators and pixels, leading to the deterioration of the spatial resolution and imaging quality.<sup>[3–6]</sup> The common strategy against optical crosstalk is to reflect radioluminescence through packaging reflector materials (such as BaSO<sub>4</sub>, TiO<sub>2</sub>, MgO, etc.) between scintillators. However, these reflector materials are apt to absorb incident X-rays, producing noise and causing pixel vignetting.<sup>[6]</sup> Recent investigations indicate that the design of nanosized scintillators can minimize optical crosstalk by promoting light-to-charge carrier conversion in nanodomains.<sup>[7]</sup> In addition, optimizing the interconnected structure of scintillators forming optical waveguides is proposed to be a novel method to suppress light loss.<sup>[8]</sup> To this end, developing new scintillators with distinct radioluminescence is highly desirable for their practical applications.

Metal halide perovskites have recently received substantial attention due to their tunable structure, chemical composition, and superior optical properties.<sup>[9]</sup> In the past few years, perovskite-based scintillators have been greatly developed.<sup>[10]</sup> In particular, perovskite-based scintillators have demonstrated several synchronous merits, including a strong X-ray absorption coefficient, high light yield, and fast decay time, potentially meeting the general requirements for a decent scintillator.<sup>[10]</sup> For instance, eutectic nanocrystals of CsPbBr<sub>2</sub>@Cs<sub>2</sub>PbBr<sub>8</sub> have a light yield higher than 64000 photons/MeV and a decay time of 1.4 ns, which surpasses the vast majority of commercial inorganic scintillators.<sup>[11]</sup> The intrinsically large Stokes shift in these emerging materials facilitates the development of metal halide scintillators with negligible self-absorption and high light yield.<sup>[12]</sup> Furthermore, the solution-processing method is promising for rapid and facile crystal growth with low cost, a feature often not possessed by traditional inorganic scintillators, such as CsI:Tl and Bi<sub>4</sub>Ge<sub>3</sub>O<sub>12</sub>.

It is well documented that the luminescence properties of crystalline materials are determined by their molecular structure, symmetry, and morphology.<sup>[13]</sup> We note that all existing scintillators are structurally centrosymmetric, as shown in the statistical data in Table S1. Isotropic light propagation is a principal property of an achiral structure, and isotropic radioluminescence cannot be physically regulated for traditional scintillators. We thus seek a new

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**Metal–Organic Frameworks**

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**Metal–Organic Framework@Metal Oxide Heterostructures Induced by Electron-Beam Radiation**

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**Abstract:** Metal organic frameworks (MOFs) are a distinct family of crystalline porous materials finding extensive applications. Their synthesis often requires elevated temperature and relatively long reaction time. We report here the first case of MOF synthesis activated by high-energy (1.5 MeV) electron beam radiation from a commercially available electron-accelerator. Using ZIF-8 as a representative for demonstration, this type of synthesis can be accomplished under ambient conditions within minutes, leading to energy consumption about two orders of magnitude lower than that of the solvothermal condition. Interestingly, by controlling the absorbed dose in the synthesis, the electron beam not only activates the formation reaction of ZIF-8, but also partially etches the material during the synthesis affording a hierarchical pore architecture and highly crystalline ZnO nanoparticles on the surface of ZIF-8. This gives rise to a new strategy to obtain MOF@metal oxide heterostructures, finding utilities in photocatalytic degradation of organic dyes.

**M**etal organic frameworks (MOFs) are a large family of advanced crystalline hybrid materials constructed by ordered self-assembly between organic linkers and metal nodes,<sup>[1]</sup> and have many visible industrial applications owing to their high surface area, well-defined porous structure, and high chemical functionality.<sup>[2]</sup> Up to now, the vast majority

of MOFs are synthesized via hydrothermal/solvothermal method, where the reaction process often requires elevated temperature, closed system, increased autogenous pressure, and relatively long reaction time.<sup>[3]</sup> Therefore, the traditional synthesis of MOFs is quite energy-consuming when large-scale production is considered. Although new routes for MOF synthesis have been extensively studied in the past decade using mechanical grinding,<sup>[4]</sup> microwave,<sup>[5]</sup> ultrasound,<sup>[6]</sup> electricity,<sup>[7]</sup> and plasma,<sup>[8]</sup> search for new types of energy sources with merits of environmental friendliness and high efficiency (in terms of time and energy) for the activation of MOF synthesis remains to be a research goal in this area.

Ionization radiations are unique energy sources, finding extensive utilities in many areas of basic research and industrial production. Since the energy of ionization radiations such as gamma ray and electron beam can be much higher than those of any chemical bonds, they can very efficiently activate all existing species in a chemical reaction system to promote the reaction, which have been successfully applied in the synthesis of various inorganic nanoparticles and organic polymers.<sup>[9]</sup> Additionally, ionization radiations often display radiation etching effect on the solid products,<sup>[10]</sup> leading to defects within the crystalline material,<sup>[11]</sup> and even complete amorphization when the absorbed dose is sufficiently high. In this work, for the first time, we utilized high-energy (1.5 MeV) electron beam radiation for the synthesis of MOFs. Using ZIF-8 as a representative, we show this type of synthesis shows merits

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## RESEARCH ARTICLE

## Activatable NIR-II Fluorescent Reporter for in Vivo Imaging of Amyloid- $\beta$ Plaques

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Supporting information for this article is given via a link at the end of the document.

**Abstract:** Fluorescence imaging in the second near-infrared (NIR-II) window holds great promise for in vivo visualization of amyloid- $\beta$  (A $\beta$ ) pathology, which can facilitate characterization and deep understanding of Alzheimer's disease (AD); however, it has been rarely exploited. Herein, we report the development of NIR-II fluorescent reporters with a donor- $\pi$ -acceptor (D- $\pi$ -A) architecture for specific detection of A $\beta$  plaques in AD-model mice. Among all the designed probes, DMP2 exhibits the highest affinity to A $\beta$  fibrils and can specifically activate its NIR-II fluorescence after binding to A $\beta$  fibrils via suppressed twisted intramolecular charge transfer (TICT) effect. With suitable lipophilicity for ideal blood-brain barrier (BBB) penetrability and deep-tissue penetration of NIR-II fluorescence, DMP2 possesses specific detection of A $\beta$  plaques in in vivo AD-model mice. Thus, this study presents a potential agent for non-invasive imaging of A $\beta$  plaques and deep deciphering of AD progression.

### Introduction

Alzheimer's disease (AD) represents the most widespread neurodegenerative disease that is clinically characterized by memory loss, cognitive decline and dementia, which seriously threatens people's health.<sup>[1]</sup> As the typical pathomorphological hallmark of AD, amyloid- $\beta$  (A $\beta$ ) plaques derived from the assembly of monomeric A $\beta$  peptides into high-ordered A $\beta$  fibrils accumulate and deposit into brains to induce neurological disorders.<sup>[2]</sup> Up to now, there are no effective therapeutic strategies that can halt or reverse the progression of AD.<sup>[3]</sup> Early characterization creates an opportunity for well-timed intervention to delay the onset and progression of this disease. Among the diagnostic methods, the cerebrospinal fluid (CSF) test possesses high accuracy but the collection procedure (spinal tap) is invasive and hence not widely acceptable.<sup>[2, 4]</sup> An alternative strategy is to develop imaging probes for the detection of A $\beta$  plaques, which have been regarded as an important biomarker for AD and the prediction of AD progression.<sup>[5]</sup> Over the years, many probes with different modality such as positron emission tomography (PET), single photon emission computed tomography (SPECT) and

magnetic resonance imaging (MRI) have been exploited to detect A $\beta$  plaques.<sup>[6]</sup> However, these conventional imaging techniques have their drawbacks, for instance, relatively low sensitivity for MRI and high cost and hazardous ionizing radiation for PET and SPECT. Furthermore, these developed probes incessantly emit signals and thus are "always-on", which leads to high background signals and thereafter inadequate specificity and sensitivity.<sup>[7]</sup> In comparison with conventional imaging techniques, fluorescent imaging possesses numerous advantages such as low cost, non-invasiveness, high sensitivity, and real-time longitudinal imaging.<sup>[8]</sup> Furthermore, by employing activatable fluorescent probes that can specifically turn on signals in response to stimuli, fluorescence imaging enables real-time visualization and specific detection of molecular alterations at the early stage of diseases.<sup>[9]</sup> Currently, fluorescent probes that are commercially available for imaging of A $\beta$  plaques are thioflavin T (ThT) and thioflavin S (ThS). However, these probes can only be utilized in histological samples due to their short emission wavelength (480 nm) and poor blood-brain barrier (BBB) penetration ability to hamper their in vivo utility.<sup>[10]</sup> Though a series of activatable near-infrared (NIR) fluorescent probes have been developed for in vivo imaging of A $\beta$  plaques,<sup>[11]</sup> the fluorescence emission of these probes is generally located in the first NIR window (NIR-I, 650-900 nm) that suffers from severe tissue absorption, light scattering and autofluorescence. Such intense light-tissue interactions will result in shallow penetration depth and poor signal-to-noise ratio (SNR), thereby making them inadequate for deep-tissue brain imaging with high fidelity.<sup>[12]</sup> By contrast, fluorescence imaging in the second NIR window (NIR-II, 900-1700 nm) shows deeper tissue penetration, improved SNR and higher spatiotemporal resolution because it minimizes light scattering and absorption, as well as autofluorescence.<sup>[13]</sup> To date, activatable NIR-II fluorescent probes have been developed for diverse imaging applications including tumor,<sup>[14]</sup> hepatotoxicity,<sup>[15]</sup> brain injury,<sup>[16]</sup> inflammation<sup>[17]</sup> and so on.<sup>[18]</sup> However, NIR-II fluorescent probes have been rarely explored for imaging of A $\beta$  plaques previously.<sup>[14, 19]</sup>

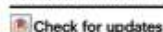


# A charged diatomic triple-bonded U≡N species trapped in C<sub>82</sub> fullerene cages

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Actinide diatomic molecules are ideal models to study elusive actinide multiple bonds, but most of these diatomic molecules have so far only been studied in solid inert gas matrices. Herein, we report a charged U≡N diatomic species captured in fullerene cages and stabilized by the U-fullerene coordination interaction. Two diatomic clusterfullerenes, viz. UN@C<sub>s</sub>(6)-C<sub>82</sub> and UN@C<sub>2</sub>(5)-C<sub>82</sub>, were successfully synthesized and characterized. Crystallographic analysis reveals U-N bond lengths of 1.760(7) and 1.760(20) Å in UN@C<sub>s</sub>(6)-C<sub>82</sub> and UN@C<sub>2</sub>(5)-C<sub>82</sub>. Moreover, U≡N was found to be immobilized and coordinated to the fullerene cages at 100 K but it rotates inside the cage at 273 K. Quantum-chemical calculations show a (UN)<sup>2+</sup>@(C<sub>82</sub>)<sup>2-</sup> electronic structure with formal +5 oxidation state (f<sup>1</sup>) of U and unambiguously demonstrate the presence of a U≡N bond in the clusterfullerenes. This study constitutes an approach to stabilize fundamentally important actinide multiply bonded species.

Fullerenes are known for their unique ability to encapsulate metal ions and clusters in their hollow interior. Clusterfullerenes, whose molecular structures are formed by the mutual stabilization between the entrapped metal clusters and the outer carbon cages, have become the most versatile and diverse category of endohedral metallofullerenes (EMFs) family<sup>1</sup>. Many of the entrapped clusters, including nitrides, carbides, oxides, sulfides, and cyanides, are otherwise unstable. Thus, besides their physical and chemical properties, cluster fullerenes also provide an ideal molecular model to study clusters that otherwise could not be prepared. Our recent studies showed that very diverse actinide clusters containing important actinide bonding motifs can be formed and stabilized inside the fullerene cages by electron transfer between the cluster and carbon cage and by the U-fullerene coordination. They can therefore be systematically characterized in the form of molecular compounds<sup>2</sup>. For example, a long-sought axial U=C bond with the shortest U-C bond distances discovered so far, was found to be stabilized in the form of an encapsulated U=C=U cluster in an actinide clusterfullerene, U<sub>2</sub>C@I<sub>h</sub>(7)-C<sub>80</sub><sup>2</sup>. Subsequent studies further

revealed the variety of the actinide clusterfullerene families, with the successful synthesis and characterization of U<sub>2</sub>C<sub>2</sub>@I<sub>h</sub>(7)-C<sub>80</sub> and UCN@C<sub>s</sub>(6)-C<sub>82</sub><sup>3,4</sup>. Encapsulated U<sub>2</sub>C<sub>2</sub>, which presents two U bridged by C≡C triple bond, and a triangular UCN cluster, which features η<sup>2</sup> (side-on) coordination of U by cyanide, show novel bonding motifs for U, broadening our understanding of the chemical properties of the actinide elements.

Covalent bonding with the 5f and 6d orbitals in actinide-ligand multiple bonds has been intensively studied, but remains incompletely understood both experimentally and theoretically<sup>5</sup>. The understanding of these bonding motifs is relevant for developing advanced nuclear fuel and managing radioactive waste. In particular, uranium nitrides have potential applications as nuclear fuel due to their high melting point and thermal conductivity<sup>6</sup>. Thus, a full understanding of U-N multiple bonding is essential for the future applications of uranium nitride compounds. From the aspect of synthesis, the terminal U-N multiple bond is very challenging because bond polarity is

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# Engineering micro oxygen factories to slow tumour progression via hyperoxic microenvironments

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While hypoxia promotes carcinogenesis, tumour aggressiveness, metastasis, and resistance to oncological treatments, the impacts of hyperoxia on tumours are rarely explored because providing a long-lasting oxygen supply in vivo is a major challenge. Herein, we construct micro oxygen factories, namely, photosynthesis microcapsules (PMCs), by encapsulation of acquired cyanobacteria and upconversion nanoparticles in alginate microcapsules. This system enables a long-lasting oxygen supply through the conversion of external radiation into red-wavelength emissions for photosynthesis in cyanobacteria. PMC treatment suppresses the NF- $\kappa$ B pathway, HIF-1 $\alpha$  production and cancer cell proliferation. Hyperoxic microenvironment created by an in vivo PMC implant inhibits hepatocarcinoma growth and metastasis and has synergistic effects together with anti-PD-1 in breast cancer. The engineering oxygen factories offer potential for tumour biology studies in hyperoxic microenvironments and inspire the exploration of oncological treatments.

Hypoxia is the most pervasive characteristic of microenvironments of solid tumours<sup>1,2</sup> and arises from an imbalance between insufficient oxygen supply and increased oxygen consumption by rapidly proliferating cancer cells. Consequently, cancer cells resort to multiple adaptive pathways and genomic changes for survival in hypoxic environments<sup>3</sup>. The transcription factor hypoxia-inducible factor 1 $\alpha$  (HIF-1 $\alpha$ ), the most recognized mediator of hypoxic responses, plays a central role in stimulating neovascularization in tumours to enhance oxygen and nutrient supply<sup>4</sup>. Paradoxically, these vessels are often irregularly organized (e.g., twisted, hyperpermeable and blind-ended structures) and have defects in oxygen diffusion or perfusion<sup>5</sup>, resulting in expansions of hypoxic regions in tumours. Concomitantly, the hypoxic microenvironment, a hallmark of malignant tumours, has been reported to be not only the primary barrier shielding the

tumour from various therapies by creating an immunosuppression environment<sup>6</sup>, activating the DNA repair pathway<sup>7</sup> and by enabling autophagic flux<sup>8</sup> but also a promoter of carcinogenesis<sup>9</sup>, tumour invasiveness and metastasis<sup>1,2</sup>. These findings inspired the exploration of technologies to convert hypoxic microenvironments into hyperoxic microenvironments for tumour biology or therapy studies.

It is a major challenge to construct a long-lasting hyperoxic microenvironment in tumours due to the lack of constant and biocompatible oxygen sources. Considering that algal microbes are the major suppliers of O<sub>2</sub> on Earth, photosynthesis in algal chloroplasts could potentially be explored for O<sub>2</sub> supplements in tumours. The photosynthetic machinery requires a matched light source emitting 650–700 nm photons. Since rare earth-based upconversion nanoparticles (UCNPs) have shown an extraordinary capability to convert

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ARTICLE



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OPEN

# A hydrogen sulphide-responsive and depleting nanoplatform for cancer photodynamic therapy

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Hydrogen sulfide (H<sub>2</sub>S) as an important biological gasotransmitter plays a pivotal role in many physiological and pathological processes. The sensitive and quantitative detection of H<sub>2</sub>S level is therefore crucial for precise diagnosis and prognosis evaluation of various diseases but remains a huge challenge due to the lack of accurate and reliable analytical methods *in vivo*. In this work, we report a smart, H<sub>2</sub>S-responsive and depleting nanoplatform (ZNNPs) for quantitative and real-time imaging of endogenous H<sub>2</sub>S for early diagnosis and treatment of H<sub>2</sub>S-associated diseases. We show that ZNNPs exhibit unexpected NIR conversion (F<sub>1070</sub> → F<sub>720</sub>) and ratiometric photoacoustic (PA<sub>680</sub>/PA<sub>900</sub>) signal responsiveness towards H<sub>2</sub>S, allowing for sensitive and quantitative visualization of H<sub>2</sub>S in acute hepatotoxicity, cerebral hemorrhage model as well as colorectal tumors in living mice. ZNNPs@FA simultaneously scavenges the mitochondrial H<sub>2</sub>S in tumors leading to significant ATP reduction and severe mitochondrial damage, together with the activated photodynamic effect, resulting in efficient suppression of colorectal tumor growth in mice. We believe that this platform may provide a powerful tool for studying the vital impacts of H<sub>2</sub>S in related diseases.

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## Review

## Reciprocal regulation of mesenchymal stem cells and immune responses

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## SUMMARY

Mesenchymal stem/stromal cells (MSCs) exist in almost all tissues and participate in tissue regeneration and homeostasis. *In-vitro*-expanded MSCs are employed as therapeutics for autoimmune diseases, organ failures, and many other chronic disorders. Remarkably, the reparative and homeostatic maintenance functions of MSCs rely on their interaction with the inflammatory microenvironment. Here, we discuss the characteristics and functions of MSCs under different pathophysiological conditions and highlight how the immunomodulatory functions of MSCs are altered in accordance with the inflammatory cues. We hope to provide new insights into the diverse immunoregulatory properties of MSCs during tissue regeneration and therapy.

## INTRODUCTION

Links between inflammation and tissue regeneration in metazoan species are highly conserved during evolution (Karin and Clevers, 2016). An appropriate immune response is essential for stem cell activation, proliferation, and differentiation during tissue damage repair and homeostatic maintenance (Aurora and Olson, 2014). The proposition of a crosstalk between immune responses and stem cells is derived from decades of investigation on mesenchymal stem/stromal cells (MSCs), a kind of tissue stem cells originally identified from bone marrow (BM) stroma in the late 1960s on account of their self-renewal and colony formation capabilities (Friedenstein et al., 1970; Moll et al., 2022; Viswanathan et al., 2019). The application of *in-vitro*-expanded MSCs in regenerative medicine does not only rely on their limited differentiation potentials ("cell replacement") but, more importantly, on their role in immunomodulation resulting in a favorable immune microenvironment and releasing growth factors to activate endogenous tissue repair ("cell empowerment") (Wang et al., 2014). Paradoxically, the immunoregulation of MSCs is not intrinsic, but initiated by inflammation (Ren et al., 2008). The immunomodulatory properties of MSCs are dynamically influenced by the kinds and amounts of inflammatory cytokines (Wang et al., 2014). Besides, cell replacement through conventional intravenous (i.v.) infusion is suboptimal since exogenous MSCs are rapidly destroyed by the instant blood-mediated inflammatory reaction (IBMIR) (Moll et al., 2019, 2022). A better understanding of the mechanisms governing the crosstalk between MSCs and immune cells should provide insights into how aberrant immune responses such as those in autoimmune diseases can be blocked, or how impaired immune responses such as those against tumor antigens in cancer patients can be evoked.

Recently, transcriptional and epigenetic profiling of MSCs from various tissues showed that MSCs in different tissues are

highly diverse in terms of tissue specific gene expression profiles and chromatin accessibility (Ho et al., 2018). Furthermore, populations and subpopulations of resident MSCs in the same tissue can also vary dramatically (Matsuzaki et al., 2014). Nevertheless, recent investigations have revealed that MSCs either *in situ* or expanded *in vitro* could actively respond to changes in tissue pathophysiological signals to mobilize various components in the tissue immune microenvironment to promote homeostasis, tissue repair, and regeneration (Gao et al., 2021; Solman et al., 2021; Wang et al., 2014). In the last few years, *in-vitro*-expanded MSCs have emerged as an important therapeutic candidate for the treatment of many human inflammatory diseases and tissue damages (Galicau and Sensébé, 2018; Levy et al., 2020; Shi et al., 2018). There has been an increasing diversification of MSC products in the past decade, from the preferential use of BM-derived MSCs (BM-MSCs) to the equal use of MSCs from BM, perinatal tissue, and adipose tissue (AD) (Moll et al., 2019, 2022). Unfortunately, the therapeutic effects are not always achieved and can be subverted by unfavorable inflammatory tissue microenvironment conditions and co-administrated drugs (Boland et al., 2022; Purtil et al., 2020; Ringóén et al., 2022). Thus, the biological properties and applications of MSCs, especially in inflammatory diseases, should be investigated by taking account of their interactions with the immune microenvironment.

The impact of inflammation on MSC differentiation has been discussed previously in several previous publications (Chen et al., 2016; Grassei and Ahmed, 2007). Therefore, the present review concentrates on the mechanisms by which different populations and subpopulations of MSCs either *in situ* or expanded *in vitro* adapt to tissue pathophysiological conditions and, reciprocally, how the responding MSCs actively modulate tissue immune microenvironments and tissue repair processes. We will emphasize on the heterogeneity of MSCs during tissue homeostasis maintenance as well as the diversity and functional







## REVIEW ARTICLE OPEN

# The secretion profile of mesenchymal stem cells and potential applications in treating human diseases

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Mesenchymal stromal/stem cells (MSCs) possess multi-lineage differentiation and self-renewal potentials. MSCs-based therapies have been widely utilized for the treatment of diverse inflammatory diseases, due to the potent immunoregulatory functions of MSCs. An increasing body of evidence indicates that MSCs exert their therapeutic effects largely through their paracrine actions. Growth factors, cytokines, chemokines, extracellular matrix components, and metabolic products were all found to be functional molecules of MSCs in various therapeutic paradigms. These secretory factors contribute to immune modulation, tissue remodeling, and cellular homeostasis during regeneration. In this review, we summarize and discuss recent advances in our understanding of the secretory behavior of MSCs and the intracellular communication that accounts for their potential in treating human diseases.

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## THE IDENTIFICATION OF MSCs

In 1970, Alexander J. Friedenstein and colleagues described an adherent and non-hematopoietic cell type present in the mouse bone marrow (BM) that could form fibroblast-like colonies *in vitro*, unlocking the door to the world of mesenchymal stem cells (MSCs).<sup>1</sup> While MSCs, which are later found to reside in various organs, can generally self-renew and exhibit stromal cell-like characteristics *in vitro*, the lineages that contribute to MSCs in each organ *in vivo* and their spatiotemporal changes during development have yet to be well explored. An early study of the hierarchy of BM-derived mesenchymal progenitors showed that Sca1<sup>+</sup> progenitors can differentiate into CD146<sup>+</sup> and CD166<sup>+</sup> progenitors sequentially.<sup>2</sup> While all three types of progenitors support bone formation, only Sca1<sup>+</sup> progenitors can home back to the BM through a chemotactic axis post-intravenous infusion. Another report showed that the niches formed by interleukin (IL)-7<sup>+</sup> mesenchymal progenitors could functionally regulate hematopoietic stem cell maintenance and multilineage differentiation.<sup>3</sup> These MSCs in BM highly express the intermediate filament protein nestin and are located around hematopoietic stem cells (HSCs).<sup>4</sup> The nestin<sup>+</sup> MSCs are proven to regulate the homing of transplanted HSCs to BM,<sup>4</sup> as well as guiding immune cells to egress to circulation.<sup>5</sup> In other organs, most of the mesenchymal progenitors are closely associated with capillaries and blood vessels.<sup>6–8</sup> These perivascular cells display phenotypes similar to those of MSCs derived from BM and dental pulps.<sup>9</sup> A population of stromal cells that resides among choroidal vascular endothelial cells was also recognized to display the MSC phenotype and possess the capacity for mesenchymal differentiation.<sup>10</sup> Thus, blood vessel walls in diverse human

tissues (such as BM, umbilical cord (UC), adipose, muscle, and placenta) are considered as the primary dwellings of progenitor cells that give rise to MSCs.

The first batch of MSCs during embryonic development could be traced to Sox1<sup>+</sup> neuroepithelium partly through a neural crest intermediate stage,<sup>11</sup> arguing for their ectodermal origin. The MSC lineages during organ development are being actively investigated and, owing to the widespread use of single-cell sequencing, imaging analysis, and tracing technologies, functionally distinct new subsets of MSCs are emerging rapidly.

## MSC ISOLATION AND CHARACTERIZATION

Well-characterized MSCs can now be isolated and propagated *in vitro* from multiple organs (such as BM, dental pulp, thymus, muscle, pancreas, and lung).<sup>12</sup> According to the International Society for Cellular Therapy (ISCT)-published minimal guidelines to define human MSC identity, the isolated cells are generally positive for CD105, CD73, and CD90, and negative for CD45, CD34, CD14, or CD11b, CD79a, or CD19 and MHC class II.<sup>13</sup> Additionally, these cells possess the potential of specific-lineage differentiation toward osteoblasts, adipocytes, or chondrocytes, as well as the capacity of plastic adherence when cultured *in vitro*.

### Tissue specificity

MSCs isolated from different sources can vary in their gene expression patterns and differentiation potentials.<sup>14</sup> There are several non-classical markers (such as CD36, CD163, CD271, CD200, CD273, CD274, CD146, CD248, and CD140b) that potentially distinguish MSCs of different sources.<sup>15</sup> For instance, CD271 is a surface marker for the majority of BM-derived MSCs

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# Patient-specific iPSC-derived cardiomyocytes reveal abnormal regulation of *FGF16* in a familial atrial septal defect

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## Aims

Congenital heart disease (CHD) frequently occurs in newborns due to abnormal formation of the heart or major blood vessels. Mutations in the *GATA4* gene, which encodes GATA binding protein 4, are responsible for atrial septal defect (ASD), a common CHD. This study aims to gain insights into the molecular mechanisms of CHD using human-induced pluripotent stem cells (iPSCs) from a family cohort with ASD.

## Methods and results

Patient-specific iPSCs possess the same genetic information as the donor and can differentiate into various cell types from all three germ layers *in vitro*, thus presenting a promising approach for disease modelling and molecular mechanism research. Here, we generated a patient-specific iPSC line (iPSC-G4<sup>T280M</sup>) from a family cohort carrying a hereditary ASD mutation in *GATA4* gene (T280M), as well as a human embryonic stem cell line (ESC-G4<sup>T280M</sup>) carrying the isogenic T280M mutation using the CRISPR/Cas9 genome editing method. The *GATA4*-mutant iPSCs and ESCs were then differentiated into cardiomyocytes (CMs) to model *GATA4* mutation-associated ASD. We observed an obvious defect in cell proliferation in cardiomyocytes derived from both *GATA4*<sup>T280M</sup>-mutant iPSCs (iPSC-G4<sup>T280M</sup>-CMs) and ESCs (ESC-G4<sup>T280M</sup>-CMs), while the impaired proliferation ability of iPSC-G4<sup>T280M</sup>-CMs could be restored by gene correction. Integrated analysis of RNA-Seq and CHIP-Seq data indicated that *FGF16* is a direct target of wild-type *GATA4*. However, the T280M mutation obstructed *GATA4* occupancy at the *FGF16* promoter region, leading to impaired activation of *FGF16* transcription. Overexpression of *FGF16* in *GATA4*-mutant cardiomyocytes rescued the cell proliferation defect. The direct relationship between *GATA4*<sup>T280M</sup> and ASD was demonstrated in a human iPSC model for the first time.

## Conclusions

In summary, our study revealed the molecular mechanism of the *GATA4*<sup>T280M</sup> mutation in ASD. Understanding the roles of the *GATA4*-*FGF16* axis in iPSC-CMs will shed light on heart development and provide novel insights for the treatment of ASD and other CHD disorders.

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EDITORIAL OPEN



## Novel SARS-CoV-2 therapeutic targets: RNA proofreading complex and virus-induced senescence

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative viral pathogen of the coronavirus disease 2019 (COVID-19), which has led to 250 million infections and more than 5.00 million deaths worldwide by the middle of October, 2021 (WHO). Although available vaccines can lower the risk of developing symptomatic COVID-19, the world is still under the threat of SARS-CoV-2 due to the lack of highly effective treatments [1, 2]. Suppressing intracellular viral replication and eliminating the infected cells are the two major strategies to limit the severities of SARS-CoV-2 infections. However, little success has been achieved and novel efficient therapeutic targets are yet to be identified. Two latest papers published in *Cell Death and Differentiation* [3] and *Nature* [4] showed that coronavirus RNA repair complex NSP14/NSP10 and SARS-CoV-2-induced cellular senescence are druggable targets for SARS-CoV-2 infections. Thus, SARS-CoV-2 RNA repair complex inhibitor sofalcone and senolytics could be applied to treat COVID-19 infections.

SARS-CoV-2 is single-stranded positive-sense RNA virus belong to the  $\beta$ -coronavirus genus [5], able to attack the immune system [6, 7]. Compared to other RNA virus, coronavirus have dramatically larger genomes (~30 kb). To maintain the integrity of their genome and prevent lethal mutagenesis, coronavirus developed a specialized RNA proofreading mechanism that, excises misincorporated nucleotides from the nascent RNA [8]. Such effects were mediated by the NSP14/NSP10 complex containing an exonuclease domain. The RNA proofreading complex not only ensured the replication fidelity but also impaired the therapeutic effects of anti-virus agents, especially nucleotide analogs, which are incorporated into the viral genome to induce premature replication termination [9].

Currently, remdesivir is the only anti-viral drug approved by FDA for the treatment of hospitalized COVID-19 patients. According to the phase III clinical trial report, remdesivir moderately speeds up the recovery of COVID-19 patients [10]. Such therapeutic efficacy does not fully meet the urgent medical demands imposed by SARS-CoV-2 infections and the approval of remdesivir also raised debates among the scientific community. It is important to note that most nucleotide analogs stop viral replication once they are incorporated into the viral genome. The incorporation of remdesivir, an adenosine nucleotide analog, could allow up to three correct nucleotides insertion into the virus genome [11]. Loss-of-function mutation of NSP14 in coronavirus significantly sensitized the virus to remdesivir, suggesting the existence of a drug resistance mechanism mediated by NSP14 [12]. The example set by remdesivir suggests that targeting the RNA proofreading complex NSP14/NSP10 may unleash the therapeutic effects of nucleotide analogs, which are the largest class of anti-virus drugs [13].

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Considering the beneficial effects of targeting RNA proofreading complex in control coronavirus, it is imperative to develop specific inhibitors targeting NSP14/NSP10. However, this is challenging since NSP14/NSP10 exonuclease activities are measured using gel-based assay, which is not compatible with large-scale screening of compound libraries. To overcome this obstacle, Rona et al. established a new assay modified from fluorescence resonance energy transfer (FRET) to determine the activities of NSP14/NSP10. Briefly, dsRNA with very low  $T_m$  were labeled with a fluorophore and a quencher. The exonuclease activities of NSP14/NSP10 recognize and remove the mismatched base pairs and eventually separate the two RNA strands, thus dissociating the quencher from the fluorophore. Therefore, the catalytic activities of NSP14/NSP10 exonuclease could be obtained by monitoring the changes of fluorescent intensity. After pre-selection by an in silico screen, 122 compounds were tested with the FRET system to evaluate their inhibitory effects on NSP14/NSP10. The identified NSP14/NSP10 inhibitors with low micromolar  $IC_{50}$  were further evaluated using HCoV-OC43 and SARS-CoV-2 infected cells individually or in combination with remdesivir. None of identified NSP14/NSP10 inhibitors alone could suppress the replication of HCoV-OC43 and SARS-CoV-2. However, three NSP14/NSP10 inhibitors showed synergistic effects with remdesivir to inhibit coronavirus replication in infected cells. The most potent identified inhibitor is sofalcone, which lowered the  $IC_{50}$  of remdesivir by ~5 fold. Sofalcone is an oral gastrointestinal medication used in Japan with validated safety [14], and this is expected to accelerate the translation of the current findings.

The replication of SARS-CoV-2 is the "root of all evil." However, what makes COVID-19 a deadly disease is the overwhelming immune responses triggered by the virus infected cells. Therefore, strategies that accelerate the clearance of virus-infected cells could also be considered for COVID-19 treatment, especially for patients suffering from severe COVID-19. Soyoung Lee et al. showed that the SARS-CoV-2 infection could induce typical cellular senescence phenotypes both in in vitro infected human diploid fibroblast and in SARS-CoV-2 lung sections [4]. Such virus-induced senescence (VIS) is indistinguishable from other forms of cellular senescence and is accompanied by a senescence-associated secretory phenotype (SASP) which drives the activation of macrophages. Taking advantage of the similarities between VIS and the well-studied types of senescence, the authors employed the currently available senolytics to eliminate the virus-infected cells. It was found that these senescence cells are indeed sensitive to senolytics such as Bcl-2 inhibitor Navitoclax and multiple kinases-inhibiting flavonoids Fisetin and Quercetin. Furthermore, oral administration of these senolytics to animal model of COVID-19 infections reduced systemic inflammation and mitigated the diseases.

The evolution of SARS-CoV-2 variants is now becoming a new challenge for controlling the COVID-19 pandemic. Combined strategies including blocking the entry of virus, suppressing virus

RESEARCH PAPER



## FLT4/VEGFR3 activates AMPK to coordinate glycometabolic reprogramming with autophagy and inflammasome activation for bacterial elimination

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### ABSTRACT

Macrophages rapidly undergo glycolytic reprogramming in response to macroautophagy/autophagy, inflammasome activation and pyroptosis for the clearance of bacteria. Identification of the key molecules involved in these three events will provide critical potential therapeutic applications. Upon *S. typhimurium* infection, FLT4/VEGFR3 and its ligand VEGFC were inducibly expressed in macrophages, and FLT4 signaling inhibited CASP1 (caspase 1)-dependent inflammasome activation and pyroptosis but enhanced MAP1LC3/LC3 activation for elimination of the bacteria. Consistently, FLT4 mutants lacking the extracellular ligand-binding domain increased production of the proinflammatory metabolites such as succinate and lactate, and reduced antimicrobial metabolites including citrate and NAD(P)H in macrophages and liver upon infection. Mechanistically, FLT4 recruited AMP-activated protein kinase (AMPK) and phosphorylated Y247 and Y441/442 in the PRKAA/alpha subunit for AMPK activation. The AMPK agonist AICAR could rescue glycolytic reprogramming and inflammasome activation in macrophages expressing the mutant FLT4, which has potential translational application in patients carrying *FLT4* mutations to prevent recurrent infections. Collectively, we have elucidated that the FLT4-AMPK module in macrophages coordinates glycolytic reprogramming, autophagy, inflammasome activation and pyroptosis to eliminate invading bacteria.

**Abbreviations:** 3-MA: 3-methyladenine; AICAR: 5-aminoimidazole-4-carboxamide- $\beta$ -D-ribofuranoside; AMP: adenosine monophosphate; AMPK: AMP-activated protein kinase; ATP: adenosine triphosphate; BMDM: bone marrow-derived macrophage; CASP1: caspase 1; CFUs: colony-forming units; FLT4/VEGFR3: FMS-like tyrosine kinase 4; GFP: green fluorescent protein; LDH: lactate dehydrogenase; LPS: lipopolysaccharide; MAP1LC3/LC3: microtubule-associated protein 1 light chain 3; PEM: peritoneal exudate macrophage; PRKAA1/AMPK $\alpha$ 1: protein kinase, AMP-activated, alpha 1 catalytic subunit; PYCARD/ASC: PYD and CARD domain containing; ROS: reactive oxygen species; SQSTM1/p62: sequestosome 1; TLR4: toll-like receptor 4; ULK1: unc-51 like autophagy activating kinase 1; VEGFC: vascular endothelial growth factor C; WT: wild type

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### Introduction

As the first line of host defense against invading pathogens, macrophages recognize pathogen-associated molecular patterns through pattern-recognition receptors to rapidly and efficiently remove pathogens [1]. Various processes are involved during clearance of the intracellular bacteria, including phagocytosis and autophagy, production of pro-

inflammatory cytokines or chemokines, as well as macrophage pyroptosis, which might be coordinated with changes of cell metabolism [2]. Upon infection with Gram-negative bacteria, macrophage activation by lipopolysaccharide (LPS) is accompanied by marked metabolic changes including upregulation of aerobic glycolysis and the pentose phosphate pathway, and disruption of the tricarboxylic acid cycle [3]. These metabolic pathways not only provide energy, but also support

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 Supplemental data for this article can be accessed here

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## Imaging-guided targeted radionuclide tumor therapy: From concept to clinical translation



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### ABSTRACT

Since the first introduction of sodium iodide I-131 for use with thyroid patients almost 80 years ago, more than 50 radiopharmaceuticals have reached the markets for a wide range of diseases, especially cancers. The nuclear medicine paradigm also shifts from solely molecular imaging or radionuclide therapy to imaging-guided radionuclide therapy, which is deemed a vital component of precision cancer therapy and an emerging medical modality for personalized medicine. The imaging-guided radionuclide therapy highlights the systematic integration of targeted nuclear diagnostics and radionuclide therapeutics. Regarding this, nuclear imaging serves to "visualize" the lesions and guide the therapeutic strategy, followed by administration of a precise patient specific dose of radiotherapeutics for treatment according to the absorbed dose to different organs and tumors calculated by dosimetry tools, and finally repeated imaging to predict the prognosis. This strategy leads to significantly enhanced therapeutic efficacy, improved patient outcomes, and manageable adverse events. In this review, we provide an overview of imaging-guided targeted radionuclide therapy for different tumors such as advanced prostate cancer and neuroendocrine tumors, with a focus on development of new radioligands and their preclinical and clinical results, and further discuss about challenges and future perspectives.

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Abbreviations: CAFs, tumor-associated fibroblasts; C12, lauric acid; C16, palmitic acid; CCK2R, Cholecystokinin 2 receptor; CCK, cholecystokinin; CXCR4, C-X-C chemokine receptor 4; DFO, Desferrioxamine; DOTA, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid; DOTAGA, 1,4,7,10-tetraazacyclododecane-1-(glutamic acid)-4,7,10-triacetic acid; DOTATATE, [DOTA<sup>0</sup>, Tyr<sup>3</sup>, Thr<sup>6</sup>]-octreotide; DOTATOC, [DOTA<sup>0</sup>, Tyr<sup>3</sup>]-octreotide; DSBs, double strand breaks; DTPA, Diethylenetriaminepentaacetic acid; EB, Evans blue; EMA, European Medicines Agency; FAP, fibroblast activation protein; FAPis, fibroblast activation protein inhibitors; FDA, Food and Drug Administration; PDX, patient-derived xenografts; GEP-NETs, gastroenteropancreatic neuroendocrine tumors; GRP, gastrin-releasing peptide receptor; IC<sub>50</sub>, half-maximal inhibitory concentration; LET, linear energy transfer; mCRPR, metastatic castration resistant prostate cancer; MC1R, Melanocortin 1 receptor; MTCs, medullary thyroid cancers; NETs, neuroendocrine tumors; NODAGA, 1,4,7-triazacyclononane,1-glutaric acid-4,7-acetic acid; NT, neurtensin; NTR1, Neurtensin receptor 1; ORR, objective response rate; PARP1, Poly (ADP-ribose) polymerase-1; PET, positron emission tomography; PFS, progression-free survival; PRRT, peptide-receptor radionuclide therapy; PSA, prostate-specific antigen; PSMA, prostate specific membrane antigen; RECIST, Response Evaluation Criteria in Solid Tumors; SA, squaric acid; SDF-1, stromal cell-derived factor-1; SIFAs, silicon-fluoride acceptors; SPECT, single photon emission computed tomography; SSBs, single strand breaks; SSTR, somatostatin receptor; SSTR2, somatostatin receptor subtype II; SSTR3, somatostatin receptor subtype III; SSTR5, somatostatin receptor subtype V; SUVmax, maximum standardized uptake value; SWOG, Southwest Oncology Group; TAT, Targeted alpha therapy; TATE, Octreotate; TOC, <sup>90</sup>Yr-octreotide; TRT, Targeted radionuclide therapy; 3,2-HOPO, 3,2-hydroxypropylidone.

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## Short Communication

**In vivo static and dynamic angiography of thrombosis by using multi-functional lanthanide nanoprobes**Feng Ren<sup>a,1</sup>, Qiang Yuan<sup>b,1</sup>, Mengxiao Han<sup>a</sup>, Zhilin Jiang<sup>a</sup>, Hongqin Zhu<sup>a</sup>, Baofeng Yun<sup>a</sup>, Zhen Li<sup>a,\*</sup><sup>a</sup>Center for Molecular Imaging and Nuclear Medicine, State Key Laboratory of Radiation Medicine and Protection, School for Radiological and Interdisciplinary Sciences (RAD-X), Soochow University, Collaborative Innovation Center of Radiation Medicine of Jiangsu Higher Education Institutions, Suzhou 215123, China<sup>b</sup>The Second Affiliated Hospital of Soochow University, Suzhou 215004, China

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The cardiovascular system composed by the heart and the blood vessels is responsible for continuously transporting nutrients and oxygen to major organs [1]. The thrombosis in the arteries and veins could impede the blood flow to the heart and brain and cause the serious cardiovascular and cerebrovascular diseases [2]. Arterial thrombosis derived from thromboembolism or the complication of atherosclerosis can lead to myocardial infarction and ischemic stroke, while venous thromboembolism can trigger the increasing systolic pressure of pulmonary artery and the right ventricular failure [3]. Therefore, it is of great importance to assess the vascular patency and hemodynamics for precise diagnosis and therapy of cardiovascular diseases (CVDs).

The angiography is a highly effective and powerful method for clinical evaluation of vascular structure and function. The combined use of computed tomographic angiography (CTA) and magnetic resonance angiography (MRA) of whole-body arterial patency with assistance of different contrast agents (CAs) enable the assessment of thrombolytic treatment of stroke patients [4]. Both MRA and CTA have unlimited penetration depth in evaluating vascular patency, however, they face difficulties in assessing hemodynamics due to the long-scanning or post-processing time [5].

In this context, optical imaging shows merits of fast feedback, high sensitivity, spatio-temporal resolution, and portability, especially the optical imaging in the second near-infrared window (NIR-II, 1000–1700 nm), which is featured with deeper penetration up to millimeter scale, lower autofluorescence and less photon scattering in comparison with the imaging in the visible (400–700 nm) and first near-infrared (NIR-I, 700–900 nm) range [6–8].

The real-time and dynamic NIR-II fluorescence angiography (NIR-II FLA) has been competent in evaluating hemodynamics of animals (such as mouse and marmoset) with ischemic reperfusion, middle cerebral artery occlusion and traumatic brain injury [9]. However, the intrinsic limitation of optical imaging in penetration depth hinders the visualization of deep-seated vasculature. Therefore, the integration of different angiographic modalities could obtain imaging dimensions and dynamics. In addition, all the enhanced angiographic imaging is strongly dependent on the performance of exogenous CAs and it is significant to develop high-performance CAs to simultaneously meet the requirement of angiographies in different application scenarios. In term of CAs, lanthanide-based nanoparticles (Ln-based NPs) have shown great potential in multimodal imaging, such as optical imaging, magnetic resonance imaging (MRI), and computed tomography (CT) [10,11]. Their imaging performance is strongly dependent on their components and structures, which have to be finely engineered to achieve the optimum multimodal imaging without sacrifice of individual performance [12].

To simultaneously optimize the multimodal imaging performance, sub-20 nm NaNdF<sub>4</sub>@NaGdF<sub>4</sub> core-shell nanoparticles with tunable shell thickness and high crystallinity (Fig. 1a) were prepared through the nanocluster-mediated synthetic method as described elsewhere [13]. The spherical nanoclusters are in a diameter of 2.0 ± 0.3 nm (Fig. S1a, b online). The thickness of NaGdF<sub>4</sub> shells (0, 2.1, 2.8, 4.0, 5.1, 8.0 nm) can be finely tuned by controlling the amount of nanoclusters (Fig. 1b, c and Fig. S1a–c online). The elemental maps of NaNdF<sub>4</sub>@NaGdF<sub>4</sub> (5.1 nm) core-shell nanoparticles demonstrate homogeneous distribution of Nd<sup>3+</sup> ions in the core and Gd<sup>3+</sup> ions in the shell (Fig. S1d online). The effects of shell thickness on the NIR-II fluorescence and magnetic properties of NaNdF<sub>4</sub>@NaGdF<sub>4</sub> nanoparticles were investigated after they were modified with amphiphilic DSPE-PEG<sub>40</sub>-COOH polymer to

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

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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  $\text{Cu}_{2-x}\text{Se}$  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  $\text{CD8}^+$  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  $\text{Cu}_{2-x}\text{Se}$  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.<sup>[1,2]</sup> 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.<sup>[3–5]</sup> 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.<sup>[6]</sup> Modulating the immunosuppressive tumor immune microenvironment (TIME) to reconstruct immune surveillance system is one of the most promising ways for tumor immunotherapy.<sup>[7]</sup>

Training of macrophages to be immunosuppressive TAMs by abnormal TME is an impactful immune escape pattern during the tumor progression, because TAMs are the major tumor-infiltrating immunosuppressive cells in the TIME.<sup>[8–9]</sup>

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.<sup>[9]</sup> 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,<sup>[8,7,10,11]</sup> 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.<sup>[8,7,12,13]</sup> They also inhibit adaptive immunity by suppressing T cells activity.<sup>[14,15]</sup> 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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## Biogenic platinum nanoparticles on bacterial fragments for enhanced radiotherapy to boost antitumor immunity

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### ABSTRACT

Being widely utilized in clinic to treat solid tumors, the efficacy of radiotherapy (RT) is usually restricted by insufficient deposition of radiation energy and hypoxia-associated tumor radio-resistance. Moreover, as a local treatment technique, RT is ineffective against tumor metastases, the main cause of cancer death. Herein, biogenic platinum nanoparticles (Pt NPs) are *in situ* synthesized on the surface of *Shewanella oneidensis* MR-1 (*S. oneidensis* MR-1), followed by sonication to acquire Pt NPs decorated membrane fragments (PtMFs) for reinforcing the treatment outcome of RT. Thanks to the high-Z element intrinsic property and the catalytic property of Pt NPs in decomposing tumor endogenous H<sub>2</sub>O<sub>2</sub> to produce oxygen, PtMFs not only effectively amplify radiation-induced DNA damages, but also significantly enhance tumor oxygenation to overcome the hypoxia-induced radio-resistance and reprogram the immunosuppressive tumor micro-environment, thereby enhancing antitumor efficacy *in vivo*. After PtMFs-mediated RT to trigger the immunogenic cell death (ICD), the generated tumor antigens subsequently elicit potent anti-tumor immune responses in the presence of bacterial membrane fragments as natural immunologic adjuvants. Via combination with programmed death-ligand 1 (PD-L1) checkpoint blockade, strong abscopal effects are achieved to effectively inhibit tumor metastases, whereas a long-term immune memory effect to reject rechallenged tumors is further observed. Therefore, such biogenic Pt-based therapeutic platforms present a unique approach for enhanced RT to inhibit tumor metastasis and recurrence by triggering strong anti-tumor immunity.

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### Introduction

Radiotherapy (RT) has been demonstrated to be one of the most reliable tools to fight against cancer [1–3]. During the RT, high energy ionizing radiation (such as X-rays,  $\gamma$ -rays, and protons) are locally applied to destruct tumors by directly destroying DNA or

indirectly producing reactive oxygen species to kill tumor cells [4]. Although RT has been frequently used in the clinic, its therapeutic efficacy is limited by several factors. When exposed to the highly ionized radiation beam, only a fraction of the radiation energy would be absorbed by tumors, while it can cause severe side effects by damaging adjacent normal tissues [5–7]. Besides, the inadequate oxygen supply that commonly exists in solid tumors has been considered to be the cause of tumor resistance to RT [8–13]. Thus, developing effective strategies to concentrate radiation energy into the tumor region and relieve tumor hypoxia would be beneficial to enhance RT treatment. Moreover, recent studies have uncovered that

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## Engineering catalytic dephosphorylation reaction for endotoxin inactivation



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### ABSTRACT

Although lives have been saved due to the discovery of endotoxin removal methods including solvent extraction and affinity adsorption, they have limitations in treatment capacity, efficiency or costs. Endotoxin contaminations still result in a large number of deaths in global every year. This necessitates a mechanistic breakthrough for endotoxin removal or inactivation. Herein, we engineered a dephosphorylation reaction on endotoxins by a synthetic nanozyme (CeO<sub>2</sub>) to attenuate the toxicity. CeO<sub>2</sub> prepared in phosphate-free hydrothermal reaction selectively and efficiently catalyzed the breaking of P-O bonds in endotoxins. Catalytic depletion of phosphates from endotoxins attenuated their binding with Toll-like receptors, NF- $\kappa$ B activation and pro-inflammatory cytokine release. Airborne LPS was, for the first time, inactivated (98%) by this facile dephosphorylation reaction. A CeO<sub>2</sub> integrating column displayed a 16-fold higher treatment capacity than commercial resins to aqueous endotoxins (water and protein solution). Overall, our findings offer a different mechanistic insight for removal of endotoxins.

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### Introduction

Endotoxin, also known as lipopolysaccharide (LPS), is a toxin discovered in lysed bacteria by Richard Pfeiffer in 1982 [1]. LPS contamination of products or air is a big health issue as it closely relates to endotoxemia [2], sepsis [3] and respiratory diseases (e.g., fibrosis [4] and inflammation response [5]). Strict thresholds of acceptable LPS levels have been set in diet and biomedical products [6]. This has aroused substantial research interests in the

development of methods to separate or inactivate endotoxins, according to their structure characteristics. LPS consists of lipid A and polysaccharide moieties, which are composed of O-antigen, outer core and inner core with phosphate groups. In 1952, Westphal et al. reported the first phenol-water extraction method to remove endotoxins by stability differences between proteins and lipopolysaccharide in hot phenol [7,8]. Subsequently, the discovery of specific interactions between polymyxin B and lipid A of endotoxins enabled the explorations of affinity adsorption methods [9], which have become the mainstream technique for efficient endotoxin removal [10,11]. However, such methods are relatively onerous and expensive, which has limited their broad applications, especially in less developed area [12]. According to the WHO report, there were still 48.9 million sepsis cases and 11 million deaths worldwide in

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# Antibiotic-Like Activity of Atomic Layer Boron Nitride for Combating Resistant Bacteria

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**ABSTRACT:** The global rise of antimicrobial resistance (AMR) that increasingly invalidates conventional antibiotics has become a huge threat to human health. Although nanosized antibacterial agents have been extensively explored, they cannot sufficiently discriminate between microbes and mammals, which necessitates the exploration of other antibiotic-like candidates for clinical uses. Herein, two-dimensional boron nitride (BN) nanosheets are reported to exhibit antibiotic-like activity to AMR bacteria. Interestingly, BN nanosheets had AMR-independent antibacterial activity without triggering secondary resistance in long-term use and displayed excellent biocompatibility in mammals. They could target key surface proteins (e.g., FtsP, EnvC, TolB) in cell division, resulting in impairment of Z-ring constriction for inhibition of bacteria growth. Notably, BN nanosheets had potent antibacterial effects in a lung infection model by *P. aeruginosa* (AMR), displaying a 2-fold increment of survival rate. Overall, these results suggested that BN nanosheets could be a promising nano-antibiotic to combat resistant bacteria and prevent AMR evolution.

**KEYWORDS:** 2D materials, nanotoxicity, proteomics, molecular dynamic simulation, antimicrobial resistance



## INTRODUCTION

Antimicrobial resistance (AMR) is one of the biggest public health challenges of our time.<sup>1</sup> The emergence of resistant microbes (a.k.a. superbugs) is threatening our ability to treat common infectious diseases, resulting in increasingly high healthcare costs, prolonged illnesses, and increasing mortality.<sup>2</sup> In response to this crisis, researchers have devoted significant efforts to develop antibiotics against resistant cells, such as G0775 and teixobactin.<sup>3,4</sup> In contrast, research and development (R&D) of conventional antibiotics have been scaled down in more and more pharmacy incorporations.<sup>5</sup> Worse still, AMR cells may quickly develop secondary resistance to invalidate the antibiotics.<sup>6</sup> Considering that we are on the cusp of the “postantibiotic” era, alternatives to current antibiotics, especially those with a different mode of action, are highly desired to combat the AMR crisis.

Currently, diverse antimicrobial agents have been explored, including antimicrobial polysaccharides, peptides, glycopeptide polymers, and engineered nanomaterials (ENMs).<sup>7,8</sup> Among them, metallic and carbonaceous ENMs have exhibited distinct killing mechanisms and tunable antibacterial activity in Gram-positive/negative ( $G^+/G^-$ ) strains.<sup>9</sup> However, these nano-antimicrobial agents often display similar killing pathways in microbes and mammalian cells, irrespective of their different biological identifications.<sup>10</sup> For example, although potent

antibacterial activities of graphene oxides (GOs) have been reported in several bacteria strains,<sup>11</sup> they exhibit a similar killing mechanism in mammalian cells including lipid peroxidation and membrane damages.<sup>12</sup> This has become the key obstacle to the clinical translation of nanoantimicrobial agents. Considering the extraordinary features (*in vivo* and *in vitro* effectiveness, negligible toxicity in mammals, and specific targets of microbe identifications) of antibiotics toward infectious diseases,<sup>13</sup> the bottleneck problems in clinical translation of nanoantimicrobial agents necessitate the exploration of candidates with antibiotic-like activities.

In this study, we identified an antimicrobial nanomaterial, two-dimensional boron nitride (BN) nanosheets, by extensively screening 16 ENMs in a multiresistant *E. coli* strain tolerant to 24 antibiotics (Table S1). The antibacterial efficiency of the BN nanosheets was examined in five AMR bacteria strains, and its toxicity was assessed in three mammalian cell lines and animals. The susceptibility of the

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# Immunotherapy of Malignant Glioma by Noninvasive Administration of TLR9 Agonist CpG Nano-Immunoadjuvant

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Immunotherapy with toll like receptor 9 (TLR9) agonist CpG ODN offers an emergent strategy to treat life-threatening malignant glioma. CpG is typically applied invasively by intracranial and intrathecal administration which induces not only poor compliance and lessened potency but also possibly strong adverse effects and immunotoxicity. Here, it is reported that immunotherapy of murine LCPN glioma is greatly boosted by polymersome-steered intravenous and intranasal brain delivery of CpG. CpG is efficiently loaded in apolipoprotein E peptide-directed polymersomes to give blood-brain barrier permeable and glioma and cervical lymph node-homing CpG nano-immunoadjuvant (t-NanoCpG) which strongly stimulates the maturation of dendritic cells, antigen cross-presentation, and production of proinflammatory cytokines in vivo. Intriguingly, both intravenous and intranasal administration of t-NanoCpG brings about significant survival benefits in murine LCPN glioma-bearing mice while free CpG and nontargeted CpG nano-immunoadjuvant (NanoCpG) afford modest therapeutic effects. Moreover, combination of t-NanoCpG with radiotherapy further boosts the immunotherapeutic effects leading to more improved survival rate of mice. This intelligent brain-permeable nano-immunoadjuvant provides a new, minimally invasive and highly potent strategy for immunotherapy of glioma.

## 1. Introduction

Malignant glioma with a highly invasive nature has poor prognosis with a five-year survival rate of less than 5% worldwide.<sup>[1]</sup> Tumor immunotherapy by activating host's immune response to repress tumor and improve survival has brought revolutionary breakthroughs for cancers including melanoma and non-small cell lung cancer.<sup>[2]</sup> However, there has been little progress in the immunotherapy of glioblastoma, as evidenced by the failure of recent phase III clinical trials with anti-PD-1 therapy.<sup>[3]</sup> On the one hand, the existence of blood-brain barrier (BBB) sets a blockade for therapeutic drugs including immunotherapeutic agents from reaching glioma sites.<sup>[4]</sup> On the other hand, malignant glioma is an immunologically "cold" tumor which is infiltrated with a large number of immune-suppressive cells such as tumor-associated macrophages (TAM) and myeloid-derived suppressor cells (MDSC) in the highly innate and adaptive

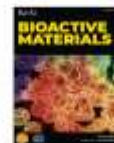
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## Polymersome-mediated cytosolic delivery of cyclic dinucleotide STING agonist enhances tumor immunotherapy

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### ABSTRACT

Cyclic dinucleotides (CDNs) as stimulator of interferon genes (STING) agonists capable of inducing strong antitumor innate immune response are highly promising for tumor immunotherapy. The efficacy of these CDNs is, however, reduced greatly by their fast clearance, poor cell uptake and inefficient cytosolic transportation. Here, we report that reduction-responsive biodegradable chimeric polymersomes (CPs) markedly enhance tumor retention and cytosolic delivery of a synthetic CDN, ADU-S100, and bolster STING pathway activation in the tumor microenvironment and tumor draining lymph nodes, giving significantly better tumor repression and survival of B16F10 melanoma-bearing mice compared with free CDN control. The superiority of CPs-mediated CDN delivery is further verified in combination therapy with low-dose fractionated radiation, which brings about clearly stronger and longer-term immunotherapeutic effects and protection against tumor re-challenge. The development of nano-STING agonists that are able to overcome the delivery barriers of CDNs represents an effective strategy to potentiate cancer immunotherapy.

### 1. Introduction

Immunotherapy has turned out to be an attractive way to cure cancer or defer tumor evolution, characterizing long-term effects [1–3]. In recent years, immune checkpoint blocking (ICB) therapy using CTLA-4 antibodies [4,5], PD-1 antibodies [6–8] or PD-L1 antibodies [9,10] has been approved for the treatment of melanoma, lung cancer, and liver cancer. However, the response rate is only about 20% [11–13]. Many researchers have focused on further improving ICB therapy by combining chemotherapy drugs, stereotactic radiosurgery or other immune checkpoint inhibitors [16–19]. Recently, much attention has focused on stimulator of interferon genes (STING), which is the major innate immune pathway involved in the generation of spontaneous antitumor T cell response. The activation of STING pathway by STING agonists, such as cyclic dinucleotides (CDN) including c-diGMP, c-diAMP, and cGAMP, drives the production of type I IFN and other

cytokines, and stimulates the maturation of dendritic cells (DCs) and cross-presentation of tumor antigens for subsequent T cell priming [20, 21], leading to effective anti-cancer therapy via intratumoral (i.t.) injection [22–24]. A synthetic CDN, ADU-S100, combining with PD-1 antibody has moved to clinical trials in patients with triple-negative breast cancer or relapsed/refractory melanoma. CDNs activate STING pathway by binding to STING protein on endoplasmic reticulum (ER). However, CDNs are anionic and hydrophilic, which renders fast clearance following intratumoral injection and poor internalization by antigen presenting cells (APCs), leading to low bioavailability and reduced efficacy [25].

Local delivery and nanodelivery systems have been investigated to improve the performance of STING agonist CDNs [26]. Hartgerink et al. reported that STINGel implanted subcutaneously could sustain CDN release and achieve enhanced cancer immunotherapy in murine oral tumor model [27], though cell entry problem was still not addressed.

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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	2021-J-JG-R1	无	其他省部级奖励	其他	阮长耿
2	2021-D-300198P1-1	/	其他省部级奖励	国际科学技术合作奖	Tom K. Hei
3	2022-YJ-01-10-01	高分子结构设计与精准合成	国家级协会奖项	基础研究成果一等奖	张正彪
4	20216229	多模态医学影像分析方法研究与应用	产学研创新成果奖	优秀奖	陈新建
5	2021-JB-2-07-	放射性皮肤损伤救治新技术的研究	其他省部级奖励	二等奖	曹建平
6	/	亚洲辐射研究协会青年科学家奖	国际地区级		第五娟

## 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	GZN1202201	李玉龙	教授	核与辐射外照射评估体系及诊疗技术规范的建立	150	2022.06-2024.12

## 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	GZC00401	基于加速器制备的 $^{225}\text{Ac}$ 生物学效应及其评价标准的构建	杨 凯	50	2022.11-2023.10
2	GZC00402	多维度低剂量辐射量-效关系模型的构建及验证	焦 旻	50	2022.11-2023.10

### 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	GZK1202201	周晓中	苏州大学附属第二医院	Gai1/3 在放射性骨损伤中的作用机制及治疗研究	5	2022.08-2023.12
2	GZK1202202	周乐源	苏州大学附属独墅湖医院	高低剂量组合照射促进抗肿瘤免疫的实验研究	5	2022.08-2023.12
3	GZK1202203	王 燕	苏州大学附属第一医院	131I 偶联 B7-H3 抗体联合 CD40 激发型抗体在脑胶质瘤治疗中的药效及机制研究	5	2022.08-2023.12
4	GZK1202204	林 健	西安交通大学	核辐射剂量可视化探测的研究	5	2022.08-2023.12
5	GZK1202205	曹津铭	苏州大学附属第一医院	Wnt3a 调控具有 MARVEL 跨膜结构域的紧密连接蛋白家族对放射性皮肤损伤的影响及机制研究	5	2022.08-2023.12
6	GZK1202206	张淑英	苏州大学附属第二医院	低频超声介导靶向微泡击破技术增敏肝癌放射治疗的疗效评价及分子机制研究	5	2022.08-2023.12
7	GZK1202207	董凤林	苏州大学附属第一医院	新型荧光探针 5'(Cy5.5)-MALAT1 ASO 对 PTC 颈部转移性淋巴结的精准检测	5	2022.08-2023.12
8	GZK1202208	车 俊	江南大学附属医院	仿皮肤疏密梯度结构脂肪干细胞支架对放射性皮肤损伤的修复研究	5	2022.08-2023.12
9	GZK1202209	于亚峰	苏州大学附属第一医院	氧化应激响应型铁蛋白纳米试剂的抗放射性中耳炎研究	5	2022.08-2023.12
10	GZK1202210	徐全晓	南阳市第一人民医院	藏红花酸对肺癌放疗敏感性的影响及机制研究	5	2022.08-2023.12

序号	项目编号	负责人	工作单位	课题名称	金额(万)	执行时间
11	GZK1202211	邓立峰	苏州大学附属第二医院	RNA 结合蛋白 IGF2BP3 通过 m6A 甲基化修饰调控肾癌辐射抗拒的作用及其分子机制研究	5	2022.08-2023.12
12	GZK1202212	张 荣	苏州大学附属第二医院	低剂量辐射通过 PI3K/Akt 通路缓解卵巢癌顺铂耐药的机制研究	5	2022.08-2023.12
13	GZK1202213	陈 伟	苏州大学附属第二医院	主动靶向肝癌的放射性纳米载药系统的研究	5	2022.08-2023.12
14	GZK1202214	胡端敏	苏州大学附属第二医院	牛磺酸在放射性肠损伤防护中作用的实验研究	5	2022.08-2023.12
15	GZK1202215	李柳炳	苏州大学附属第二医院	Fam20C/DMP1 在放射性锶诱发骨质破坏中的功能及机制研究	5	2022.08-2023.12
16	GZK1202216	桑永华	苏州大学附属第二医院	Notch2 的 SUMO 化通过促进 IL-4 分泌调控肺癌辐射抵抗的机制研究	5	2022.08-2023.12
17	GZK1202217	卞海溢	淮阴工学院	食道癌放疗评价与预测技术研究	5	2022.08-2023.12
18	GZK1202218	马 麒	苏州大学附属第二医院	阻断 TGF- $\beta$ 1 信号下调 B7-H3 表达对甲状腺未分化癌 131I 放疗增敏的机制研究	5	2022.08-2023.12
19	GZK1202219	朱玉春	昆山市第一人民医院	靶向 Her2 与 CXCR4 新型放射性异二聚小分子	3	2022.08-2023.12
20	GZK1202220	华 松	南阳市中心医院	基于影像-剂量-病理组学特征预测放射性肺损伤的智能化模型研究	3	2022.08-2023.12
21	GZK1202221	曹志飞	苏州大学附属第二医院	维甲酸诱导蛋白 2 对胰腺癌细胞辐射敏感性的作用及其分子机制研究	3	2022.08-2023.12

序号	项目编号	负责人	工作单位	课题名称	金额(万)	执行时间
22	GZK1202222	毛卫东	苏州大学附属第二医院	碳离子辐射诱导的 LNC CRYBG3 靶向 Actin-MTA3 通路调控肺癌细胞转移	3	2022.08-2023.12
23	GZK1202223	张园	苏州大学附属第二医院	LncRNA-XR595534.2 调控 5-HT3A 表达介导放射损伤性疼痛及机制研	3	2022.08-2023.12
24	GZK1202224	陈伟	苏州思萃同位素技术研究有限公司	放射性同位素 14C 的全流程一体化循环利用体系开发	3	2022.08-2023.12
25	GZK1202225	秦华龙	苏州大学附属第一医院	探讨核转录因子 RelB 在非小细胞肺癌放疗敏感性中的作用及其分子机制	3	2022.08-2023.12
26	GZK1202226	蒋东	苏州大学附属第一医院	E2F1/RRP9 通过调控 CDK1 促进食管癌放疗抵抗作用及机制研究	3	2022.08-2023.12
27	GZK1202227	丁玖乐	苏州大学附属第三医院	糖尿病肾病进展的 MRI 肾周淋巴成像定量评价	3	2022.08-2023.12
28	GZK1202228	毕金玲	安徽医科大学附属合肥医院	p53 通过 GDF15 介导电离辐射引起骨丢失的作用机制研究	3	2022.08-2023.12
29	GZK1202229	刘杰	海安市中医院	电离辐射引起的睾丸精原干细胞 RNA 氧化损伤研究	3	2022.08-2023.12
30	GZK1202230	杨毅	苏州大学附属第一医院	基于 PET-MRI 双模态纳米探针靶向脑胶质瘤免疫成像的研究	3	2022.08-2023.12
31	GZK1202231	陈蕾	苏州大学附属第二医院	MTSS1 调控 CXCL12/CXCR4 信号轴活性对结直肠癌细胞放疗敏感性的影响及其机制研究	3	2022.08-2023.12
32	GZK1202232	陈庆	南阳师范学院	计算模拟和实验验证放射性铯污染黏土净化研究	3	2022.08-2023.12



序号	项目编号	负责人	工作单位	课题名称	金额(万)	执行时间
33	GZK1202233	马孝明	苏州大学附属第二医院	FeWOx 纳米片对胰腺癌放疗敏感性的影响及分子机制探讨	3	2022.08-2023.12
34	GZK1202234	肖莉	苏州大学附属第二医院	基于人工神经网络的辐射损伤相关甲基化位点模型的建立	3	2022.08-2023.12
35	GZK1202235	章远江	常熟市第二人民医院	乳腺癌细胞外泌体靶向调控巨噬细胞诱导免疫抑制微环境的作用机制及可视化研究	3	2022.08-2023.12
36	GZK1202236	赵佳慧	连云港市妇幼保健院	鞘氨醇-1-磷酸通过上调 GCLC 抑制铁死亡防治卵巢辐射损伤的机制研究	3	2022.08-2023.12
37	GZK1202237	崔红霞	苏州大学附属第二医院	放射性认知障碍中神经营养素受体通路及关键靶点研究	自筹	2022.08-2023.12
38	GZK1202238	邢鹏飞	苏州大学附属第二医院	CD103+树突状细胞在放疗联合免疫治疗结肠癌腹膜转移中的作用及机制探讨	自筹	2022.08-2023.12
39	GZK1202239	俞辰逍	苏州大学附属第二医院	METTL14/m6A/miRNA let7e-5p 通路调控 IL-10 水平对放射性皮肤损伤的防治作用及机制研究	自筹	2022.08-2023.12
40	GZK1202240	洪智慧	苏州大学附属第二医院	免疫 PET 可视化评估布拉格治疗结肠癌疗效及其作用机制研究	自筹	2022.08-2023.12
41	GZK1202241	陈强	苏州大学附属第二医院	CXCR4 特异性 <sup>68</sup> Ga-Pentixafor 核	自筹	2022.08-2023.12
42	GZK1202242	李叶骋	苏州大学附属第二医院	脱氧胆酸在直肠癌放射治疗中的作用机制研究	自筹	2022.08-2023.12
43	GZK1202243	吴勇	苏州大学附属第二医院	GOLM1-NCAPD3-PDK4 信号轴影响大肠癌放射敏感性的机制研究	自筹	2022.08-2023.12

序号	项目编号	负责人	工作单位	课题名称	金额 (万)	执行 时间
44	GZK1202244	伍丽君	苏州大学附属 第二医院	FTO/m6A/SLC7A11 调控血管内皮细胞 铁死亡在放射性皮肤 损伤修复中的机制 研究	自筹	2022.08- 2023.12
45	GZK1202245	王 波	苏州大学附属 第二医院	IGFBP6 蛋白复合物 作为胶质瘤放疗 增敏剂的机制及 应用研究	自筹	2022.08- 2023.1

## 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 22 台大型仪器设备，设备总金额六千余万元。

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	DMi8	倒置荧光显微镜	德国	2020.12	29.128	29.128
14	AX	高分辨多光谱亚细胞激光辐照仪	日本	2021.01	239.5	192

15	HDX-MS	氢-氘交换质谱	英国	2021.01	360	288
16	VIVO Intravital Imaging System	微循环活体成像显微系统	美国	2021.03	372.62	372.62
17	DDLH2.0/30-500	低能电子加速器	中国	2021.07	555	555
18	自研	辐射探测大体积单晶器件制备及表征测试平台	中国	2021.11	274.4	274.4
19	IVIS Lumina III	小动物活体成像系统	美国	2021.01	161.6	161.6
20	HM 525 NX U	冷冻切片机	中国	2021.01	24.9318	24.9318
21	自研	磁粒子二维成像系统			360	
22	研发定制	蒸汽自循环节能高通量含氚废水处理装置			300	
<b>合计</b>					<b>6620.3</b>	<b>5310.0</b>

## 十五、2022 大事记



2022年9月19日，全国人大常委会副委员长、中国红十字会会长陈竺调研



2022年11月5日-国防科工局黄平副司长和中核孟琰彬书记一行调研国重室



2022年11月12日，国家药监局药品审评检查长三角分中心主任杨进波一行调研



2022年4月21日，苏州市科技局专家论证会成功召开



2022年7月8日，上海复弘医疗服务有限公司与国重室合作协议签订仪式



2022年7月8日，浙江省海盐县政府、秦山核电站领导一行来访

## 十六、2022 年国重室科普工作总结

2022 年度，在喜迎党的二十大召开之际，国重室科普工作迈向新的台阶，成功获批全国科普教育基地、全国核科普教育基地及苏州市科学家精神教育基地，成功申报江苏省科学家精神宣讲团。为全面贯彻落实《全民科学素质行动计划纲要》精神，国重室科普团队在“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，年度累计参与人数达 5110 万人次，得到了社会的高度好评，获得“魅力之光”全国核科普讲解员大赛、全国高校学生课外“核+X”大赛等 20 项国家、省、市级荣誉。



1. 专家谈核有权威：5 月，实验室开展了“创新强核，科学报国—全国科技周暨全国科技工作者日系列开放活动”，国重室王爻凹教授、国际宇航科学院院士周光明教授作为特邀嘉宾参与主持讲座活动，胡士军教授在以题为《筑梦苍穹——揭秘太空生命科学研究》的讲座报告，张乐帅教授为大家带来《认识你身边的辐射》的讲座，孙亮老师通过《氡的基本性质和环境迁移特点》为大家深入浅出的讲解了氡对环境健康影响的重要性和现实紧迫性。崔凤梅老师在《氡的毒理知多少》中进一步为大家展开了氡的毒性分级、生物转运、损伤效应以及安全防护等相关知识。8 月，实验室承办了“魅力之光”科普夏令营，柴之芳院士、国际宇航科学院院士周光明分别作了题为《低剂量辐射是有益的？》《空间辐射——外星移民的隐性障碍》的专题讲座，为营员们深入浅出地介绍了辐射的相关知识，并解答了营员代表有关核能发展、电离辐射对设备仪表的影响效应等。讲座在科普中国、凤凰网，中核集团、中国核电微信和视频号、微博、抖音、快手等平台全网直播，线上观看量超百万。柴之芳院士设立“教师科普奖”，鼓励国重室在职



人员参与科普工作，荣获“典赞·科普苏州”2022年度科普人物。



2. 协同科普有成效：4月，实验室成功申请到由团中央青年志愿者行动指导中心、中国核工业集团有限公司、中国青年志愿者协会秘书处联合举办的“强国有我，‘核’你一起”大学生志愿讲团5月-8月，面向我校师生和社会公众开展了16场宣讲活动，参观了华克智能科技有限公司、周庄生命奥秘馆等，面向中小學生举行开放活动，与四川大凉山富强小学同学们互动，以核圆梦，筑梦起航。本次宣讲活动引导社会公众和广大青年学生深刻认识碳达峰碳中和目标的重大意义，宣传绿色核能发展理念。此外，实验室联合中国核学会、中核集团旗下上市公司中国核能电力股份有限公司主办，江苏核电在8月成功举办第十届“魅力之光”杯全国核科普夏令营，本次活动线上传播及微博话题累计阅读量达3900万。苏大重室荣获第十届“魅力之光”杯全国核科普活动组织工作卓越贡献奖。



3. 科创竞赛创佳绩：在第十届“魅力之光”杯第二届全国核科普讲解大赛中，苏大放医国重室再创佳绩，贾云怡获二等奖、刘雨桐获三等奖、李张欣获优秀奖，苏州大学放射医学与辐射防护国家重点实验室获优秀组织奖。在第七届全国高校学生课外“核+X”创意大赛总决赛中，《平地惊“镭”》作品从全国51所高校的1003件参赛作品中脱颖而出，荣获全国一等奖第一名，实现了一等奖零突破，取得了参赛以来最好成绩，本年度还获得全国三等奖4项、全国优秀奖3项，苏

州大学荣获大赛优秀组织奖。此外，《中国大百科全书——核技术》出版发行。《辐射与健康科普丛书》入选江苏省“十四五”时期重点出版规划项目。



2022 年度，国重室科普工作硕果累累。新年新征程，国重室科普团队将继续围绕“与核同行”主题，全面贯彻落实《全民科学素质行动计划纲要》精神，宣传绿色核能在生命健康领域的突出贡献，绽放出“放射医学”特色的科普之花。

## 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。

# 2018-2022 五年情况总结



## 十八、2018-2022 五年情况总结

### 1, 新增人才

人才名称	姓名	获得年份
欧洲科学院院士	时玉舫	2020
俄罗斯工程院外籍院士	路建美	2020
国际宇航科学院院士	周光明	2019
教育部长江学者特聘教授	王旻凹	2019
国家杰青	陈华兵	2021
国家杰青	张正彪	2019
国家杰青	王旻凹	2018
外籍杰青	邵常顺	2021
国家万人计划	高明远	2020
教育部长江学者青年	第五娟	2021
教育部长江学者青年	湛宁	2019
国家优青	王亚星	2022
国家优青	曾剑锋	2022
国家优青	李培山	2022
国家优青	汪勇	2021
国家优青	葛翠翠	2020
国家优青	杨凯	2018
海外优青	崔家斌	2021
青年千人	苗庆庆	2020

人才名称	姓名	获得年份
青年千人	畅磊	2020
青年千人	何亦辉	2020

## 2. 项目-总体情况

项目类型	2018 (万元)	2019 (万元)	2020 (万元)	2021 (万元)	2022 (万元)	合计 (万元)
国家重点实验室	3300	3000	3000	3000	3000	15300
江苏省协同创新中心	800	800	800	940	940	4280
江苏省优势学科		1180	590	590	280.25	2640.25
国家级项目数	17	20	14	35	27	113
国家级项目金额	5395	6772	2129	6259	9967	30522
省部级项目数	8	6	4	9	4	31
省部级项目金额	777	398	859	580	610	3224
市厅级及其它项目数	5	8	15	8	8	44
市厅级项目及其它金额	86	360	1334.47	1510	308	3598.47
横向项目数	6	9	13	18	11	57
横向项目金额	206.445	1632.836	1168.6	613.85	1273	4894.731
GF 项目数		1	1			3
GF 项目金额		400	1000			4701

### 3, 重要项目汇总

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	15300
2	国家重点研发计划	有机框架材料及气体传感技术	2021YFB3200400	王爻凹	1100
3	国家重点研发计划	“高效富集/催化氧化/自降解”三功能纳米新材料构建及原位净化场地有机物的研究	2020YFC1818401	路建美	878
4	国家重点研发计划	建立小鼠发育代谢表型库	2018YFA0801100	徐 璿	4126
5	国家重点研发计划	人工智能元学习新理论与新技术及其在医学影像大数据的示范应用	2018YFA0701700	陈新建	1349
6	国家重点研发计划	新型纳米氧化铁磁共振造影剂的宏量制备及临床转化研究	2018YFA0208800	高明远	1944
7	国家重点研发计划	炎症微环境中间充质干细胞对肝肾纤维化的调控作用及干预策略	2018YFA0107500	时玉舫	2962
8	国家重点研发计划	特定环境条件下干细胞对组织器官发育和功能重塑的调控	2022YFA1104300	胡士军	2796
9	国家重点研发计划	聚乳酸的规模化制备及关键单体丙交酯的一步法产业示范	2022YFB3704900	张正彪	2200
10	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
11	国家重点研发计划政府间国际科技创新合作	新型填料材料研究及其在含氚废水精馏处理技术中的应用	2022YFE0105302	王爻凹	300
12	国家重点研发计划政府间国际科技创新合作重点专项	金属基纳米颗粒毒理学构效关系探索及其安全设计与合成的研究	2018YFE0120400	李瑞宾	103
13	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



序号	项目类别	项目名称	项目编号	项目负责人	总经费 (万元)
14	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
15	国家重点研发计划子课题	完善消化肿瘤 HFRT 的放射防护与损伤控制体系	2022YFC2503702	曹建平	300
16	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
17	国家自然科学基金杰青项目	环境放射化学	21825601	王爻凹	350
18	国家自然科学基金国际(地区)合作与交流项目	层粘连蛋白调控巨噬细胞和脂肪基质细胞影响肥胖脂肪组织重塑的机制	31961133024	时玉舫	300
19	国家自然科学基金联合基金重点项目	多离子印迹硅基材料用于高盐低放废水深度净化的应用基础研究	U1867206	华道本	268
20	国家自然科学基金联合基金重点项目	流出物中放射性核素对敏感水生动物的辐射影响	U1867204	涂 彧	268
21	国家自然科学基金联合基金重点项目	新型双功能铀促排剂研究	U2167222	第五娟	255
22	国家自然科学基金联合基金重点项目	基于人工智能影像组学的视网膜色素变性诊断及其临床应用	U20A20170	陈新建	259
23	国家自然科学基金联合基金重点项目	选择性吸附分离水溶性裂变产物的金属有机框架材料的设计与机理研究	U1967217	周如鸿	269
24	国家自然科学基金联合基金重点项目	多组学联合的生物辐射敏感分子标志物研究	U1967220	曹建平	267
25	国家自然科学基金联合基金重点项目	海藻酸钠/咪喹莫特微球在肿瘤重离子免疫联合治疗中应用基础研究	U1932208	杨 凯	300
26	国家自然科学基金联合基金重点项目	钙钛矿半导体探测器中信息载流子的传输及收集机理研究	U2267211	何亦辉	280
27	国家自然科学基金联合基金重点项目	核工业职业照射致晶状体损伤先进评估模型构建及机制研究	U2267220	刘玉龙	280

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
28	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
29	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
30	国家自然科学基金重点项目	肠道菌群在 aGVHD 中的免疫调控机制及临床干预研究	82020108003	吴德沛	248
31	国家自然科学基金重点项目	炎症调控下间充质干细胞的异质性影响肿瘤发生发展的机制研究	81930085	时玉舫	297
32	国家自然科学基金重点项目	多功能囊泡纳米疫苗用于高效肿瘤免疫治疗	52233007	钟志远	269
33	国家自然科学基金重点项目	血小板 GPIb $\alpha$ 对肿瘤血行转移的调控作用及其机制研究	82230003	戴克胜	261
34	国家自然科学基金重点项目	骨髓微环境促炎巨噬细胞介导巨核前体细胞过甲基化在移植后巨核系重建不良中的机制研究	82230005	韩悦	261
35	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
36	国家自然科学基金优青项目	活体成像分析	22122407	汪勇	200
37	国家自然科学基金优青项目	脂质代谢与炎症反应调节	32222025	李培山	200
38	国家自然科学基金优青项目	纳米分子影像探针及活体成像	82222033	曾剑峰	200
39	国家自然科学基金优青项目	铜系核素分离与资源化	22222606	王亚星	200
40	国家自然科学基金优青项目	纳米环境健康效应	K112800820	葛翠翠	120
41	国家自然科学基金优青项目	功能纳米材料在肿瘤放疗中的应用探索	31822022	杨凯	130
42	国家级其他项目	海外高层次人才青年项目	无	畅磊	200
43	国家级其他项目	海外高层次人才青年项目	无	何亦辉	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)
44	国家级其他项目	海外高层次人才青年项目	无	苗庆庆	200
45	科工局项目	低活度含氚废水浓缩去除新材料与新工艺研究	#####	王爻凹	3301
46	军委科技委	XXXX	#####	王爻凹	1000
47	国家级其他项目	空间辐射致肺细胞转化效应及其机理和生物标志物研究	科总字【2020】12	周光明	240
48	国家级其他项目	XXX 加固项目研究	41424060204	周光明	400
49	省协同创新中心	省放射医学协同创新中心	SX12800117	柴之芳	4280
50	省优势学科	省特种医学优势学科	YX12800211	柴之芳	2640

53924.5

#### 4、授权发明专利、SCI 论文

类别	2018	2019	2020	2021	2022	合计
授权发明专利	28	28	42	29	85	212
SCI 收录	115	152	182	227	261	937

#### 5、省部级及以上获奖情况统计及明细

获奖类型	2018	2019	2020	2021	2022	合计	备注
国家级科技奖二等奖			2	1		3	1 项非第一
何梁何利				2		2	
省部级重大贡献奖					1	1	

获奖类型	2018	2019	2020	2021	2022	合计	备注
省部级科技奖一等奖		2		2		4	
省部级科技奖二等奖		1	1			2	1项非第一
省部级科技奖三等奖	1	1		1		3	
中国青年五四奖				1		1	

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	2019-F-304-2-01-R01	多元催化剂嵌入法富集去除低浓度VOCs增强技术及应用	国家科学技术发明奖	二等奖	路建美
2	2019-J-233-2-01-R01	血液系统疾病出凝血异常诊疗新策略的建立及推广应用	国家科学技术进步奖	二等奖	吴德沛 阮长耿 韩悦 武艺 黄玉辉 戴克胜
3	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	国家科学技术进步奖	二等奖	胡士军
4	2021	何梁何利基金科学与技术创新奖	国家奖励-其他	其他	路建美
5	2021	何梁何利基金科学与技术进步奖	国家奖励-其他	其他	吴德沛
6	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
7	2018-1-43-R1	移植相关性出凝血疾病及其关键机制研究	江苏省科学技术奖	一等奖	韩悦 吴德沛 阮长耿
8	2020-031-R02	肿瘤多模态诊疗一体化探针相关基础研究	教育部科技进步	一等奖	高明远 李楨 汪勇 史海斌 曾剑峰
9	2018-216	造血干细胞移植后出凝血异常的发生机制	教育部科技进步	一等奖	韩悦 吴德沛

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)
		与诊疗新策略研究	步		阮长耿
10	2019-236	肿瘤辐射生物效应作用机制及临床应用	教育部科技进步	二等奖	刘芬菊 俞家华
11	2018-2-2-R1	多模态医学影像处理与分析及其在疾病诊断中的应用	江苏省科学技术奖	二等奖	陈新建
12	2018-3-140-R5	电离辐射所致海马依赖性认知功能障碍的机制研究	江苏省科学技术奖	三等奖	田野 杨红英
13	2020GFJBJ3006-R01	认知功能辐射损伤机制和防治的新技术研究	国防科学技术进步奖	三等奖	田野
14	2018HGY004	大规模核事故高通量生物剂量评价及伤员分类	国防科学技术进步奖	三等奖	刘玉龙
15	2021-J-JG-R1	无	江苏省科学技术奖	基础研究重大贡献奖	阮长耿

## 6、重要成果转化

### 技术转让

序号	技术成果名称	类型	固定人员	转让对象	合同签订时间	合同登记号	合同金额 (万元)	到账金额 (万元)
1	XXXXXX	A	钟志远	博瑞生物医药(苏州)股份有限公司	2019.1	/	1000	500
2	基于生物材料的肿瘤放射免疫核药( <sup>131</sup> I-CM)研制	A	柴之芳(杨凯)	陕西健康医疗集团有限公司	2019.1	/	2000	/

序号	技术成果名称	类型	固定人员	转让对象	合同签订时间	合同登记号	合同金额(万元)	到账金额(万元)
3	伽马/荧光双模分子影像设备研发	A	王璐瑶	陕西健康医疗集团有限公司	2019.1	35243	100	60
4	XXXXXX	A	王旻凹	中国工程物理研究院材料研究所	2018.1	/	120	60
5	一种靶向PSMA 抗原的配体化合物及其制备方法与用于前列腺癌的诊断和治疗	A	钟志远	/	2021.12	/	15	15

#### 技术入股

序号	技术成果名称	技术持有人(固定人员)	企业	技术入股合作协议签订时间	技术估价(万元)	合同登记号	总股本(万元)
1	新型纳米氧化铁磁共振造影剂	高明远	苏州欣影生物医药技术有限公司	2018.11	17500	/	1250
2	CD19/CD138双特异抗体	杨林	博生吉医药科技(苏州)有限公司	2018.11	/	/	441.2
3	一次性使用介入治疗辐射防护手套	许玉杰 王敬东	苏州嘉乐威企业发展有限公司	2019.12	/	/	6000

## 7、仪器和平台建设

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	DMi8	倒置荧光显微镜	德国	2020.12	29.128	29.128
14	AX	高分辨多光谱亚细胞激光辐照仪	日本	2021.01	239.5	192
15	HDX-MS	氢-氘交换质谱	英国	2021.01	360	288
16	VIVO Intravital Imaging System	微循环活体成像显微系统	美国	2021.03	372.62	372.62
17	DDLH2.0/30-500	低能电子加速器	中国	2021.07	555	555
18	自研	辐射探测大体积单晶器件制备及表征测试平台	中国	2021.11	274.4	274.4
19	IVIS Lumina III	小动物活体成像系统	美国	2021.01	161.6	161.6

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)
20	HM 525 NX U	冷冻切片机	中国	2021.01	24.9318	24.9318
21	自研	磁粒子二维成像系统			360	
22	研发定制	蒸汽自循环节能高通量含氚废水处理装置			300	
合计					<b>6620.3</b>	<b>5310.0</b>

## 8、体制机制改革和创新措施

- 1) **办室方针：**民主办室、协同兴室、人才强室、与实俱进；
- 2) **人员流动机制：**连续 2 年绩效考核均为 0 者，将自动回到本学院；新加盟成员前 2 年免考核；
- 3) **课题申请：**随时申请创新课题，鼓励青年成员开展重大原创性基础研究。