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

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目　录

前　言

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

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

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，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。

2020年在科学研究、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。实验室在2020年在省科技厅组织的江苏省重点实验室评估中评为“优秀”。现有成员97人，其中院士2人，杰青6人，优青5人。本年度放射医学与辐射防护创新团队入选科技部创新人才推进计划重点领域创新团队，时玉舫教授入选欧洲科学院院士，高明远教授入选国家“万人计划”科技创新领军人才，同时引进一名国家自然科学基金杰青获得者张正彪教授。柴之芳院士获得中国科学院杰出科技成就奖（突出贡献者）；阮长耿院士获得吴阶平医学奖以及中华医学会血液学分会终身成就专家奖；路建美教授获得何梁何利基金科学与技术创新奖；吴德沛教授获

得何梁何利基金科学与技术进步奖。

在科研方面，2020 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 46 项，总金额逾 1 亿元。值得指出的是，路建美分别获国家重点研发计划资助，苗庆庆和畅磊获得中组部海外高层次人才基金资助，陈新建和吴德沛获得国家自然科学基金委重点项目资助，葛翠翠获得国家自然科学基金优秀青年基金资助。依托重点实验室，共发表 SCI 研究论文 182 篇，其中影响因子大于 10 的 32 篇，大于 5 的 113 篇，SCI 引用逾万次。获得授权发明专利 43 项，其中欧洲发明专利 1 项、美国发明专利 9 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。获得了军委科技委、国防科工局、国家核应急办等军民合作项目；与中广核、好医生医药集团、中陕核、鞍山肿瘤医院、华克、华益等公司的合作稳步向前。

2020 年国家重点实验室举办了系列会议和科普活动。11 月 20 日国家重点实验室第一届学术委员会第三次会议成功举行。策划、举办了**“重”志成城、放医战“疫”**、**“以核济世护健康”**—全国科技创新周等一系列大型科普活动，累计参与受益达 3 万人次。

2020 年 2 月以来，苏大放医国重室主动作为开展“助力企业，共渡难关”系列活动，包括：委派专家对接企业解决技术难题、合作项目研发、平台免费向企业开放、科技成果转化发布会、学术交流会、技术培训讲座、科普知识宣讲会等，采用“走出去”和“请进来”、“线上+线下相结合” 多措并举——“助力企业，共渡难关”。2020 年度实验室共助力全国企业 20 余家；参加服务企业人员 100 余人次；国重实验平台为企业提供样品检测服务近 1300 个；累计开放仪器 66 台；组织了科技成果转化发布会，全年累计参加活动近 7000 人次。

同时实验室共有 59 人次被邀请在国际国内学术会议上作报告或者交流；共有 25 人次被邀请来作学术报告。另外，实验室成功举办了中华医学会第 16 次全国血液学学术会议（9.24），2020 年中国生理学会学术年会（8.22）和中国医药教育协会感染疾病专业委员会第六届学术大会（9.10）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 97 人，其中院士 2 人，杰青 6 人，优青 5 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
1	柴之芳	男	194209	放射化学/放射医学	主任（院士、教授）
2	时玉舫	男	196010	肿瘤学	副主任（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（教授）
6	周如鸿	男	196612	定量生物医学	教授
7	张学光	男	195111	免疫学	教授、杰青
8	吴庆宇	男	195710	血液与血管生物学	教授
9	周光明	男	197007	放射医学/特种医学	特聘教授
10	曹建平	男	196205	放射医学/特种医学	教授
11	刘芬菊	女	195412	放射医学/特种医学	教授
12	胡士军	男	198002	细胞生物学	教授
13	杨红英	女	197211	放射医学	教授
14	武　艺	男	196503	血栓与血管生物学	教授
15	何玉龙	男	196701	淋巴管与肿瘤	教授、新世纪人才
16	黄玉辉	男	197212	病理学与病理生理学	教授、省特聘教授
17	周泉生	男	195505	病理学与病理生理学	教授
18	王建荣	男	196205	细胞生物学	教授
19	杨　林	男	196408	免疫学	教授、省“双创”

序号	姓　名	性别	出生年月	专业	技术职务
20	陈　秋	女	197608	辐射免疫学	教授
21	孙　巧	女	197407	定量生物医学	教授
22	邵常顺	男	196210	遗传学	特聘教授
23	杨再兴	男	198209	定量生物医学	副研究员
24	孟烜宇	女	198306	定量生物医学	副研究员
25	王　畅	女	197601	放射医学	教授
26	阮长耿	男	193908	血液学	院士、教授
27	吴德沛	男	195802	血液学	教授、主任医师
28	钟志远	男	197404	药物化学	特聘教授、杰青
29	陈新建	男	197905	分子影像学	特聘教授、优青
30	陈华兵	男	197811	纳米毒理学	教授、优青
31	李　桢	男	197608	分子影像与核医学	特聘教授、江苏双创人才
32	史海斌	男	197803	分子影像与核医学	教授
33	许玉杰	男	196311	放射医学与核医学	教授
34	夏利军	男	196203	血液学	教授
35	赵　利	男	198302	放射医学	副教授
36	俞家华	男	198102	放射医学/特种医学	副教授
37	崔凤梅	女	197510	放射毒理学	教授
38	余自强	男	196311	血液学	主任医师
39	韩　悦	女	197002	血液学	主任医师
40	汪　勇	男	198309	放射医学	副教授
41	焦　旸	女	197711	放射医学	教授
42	尚增甫	男	198209	放射医学	副教授
43	朱　巍	男	197009	放射医学	副教授
44	朱　然	女	197508	放射医学	副教授
45	朱秀林	男	195510	材料化学	教授
46	路建美	女	196010	材料化学/辐射防护	教授
47	王殳凹	男	198506	放射化学	特聘教授、长江学者、杰青、优青

序号	姓　名	性别	出生年月	专业	技术职务
48	涂　彧	男	196507	放射医学/辐射防护	教授
49	郭正清	男	198105	放射医学	副教授
50	李瑞宾	男	198209	辐射纳米毒理学	特聘教授
51	第五娟	女	198604	放射化学	教授、江苏省杰青
52	张乐帅	男	198002	毒理学	教授
53	刘玉龙	男	196608	放射损伤临床	教授、主任医师
54	葛翠翠	女	198311	辐射纳米毒理学	特聘教授、优青
55	杨　凯	男	198308	放射医学	特聘教授、优青
56	万　骏	男	196411	放射医学/辐射防护	副教授
57	孙　亮	男	197410	放射医学/辐射防护	副教授
58	胡　亮	男	198402	核科学与技术	特聘副教授
59	刘志勇	男	198101	放射化学	教授
60	王杨云	女	198610	放射医学	副教授
61	苗庆庆	女	198907	化学	特聘教授、省特聘教授
62	畅　磊	男	198705	生物与医药	特聘教授
63	曾剑峰	男	198706	化学	副教授
64	胡文涛	男	198408	物理学	副教授
65	屈卫卫	男	198808	物理学	副教授
66	田　欣	男	198506	生物学	副教授
67	代　星	男	198710	物理学	副研究员
68	王艳龙	男	198604	化学	副教授
69	杨　巍	男	197609	特种医学	教授
70	田　野	男	196501	特种医学	教授
71	张正彪	男	197411	化学	教授、杰青
72	宋耀华	男	196103	化学	教授
73	董宁征	女	197001	临床医学	研究员
74	邓　超	男	197511	化学	教授
75	徐加英	女	197201	肿瘤放射生物	研究员

序号	姓　名	性别	出生年月	专业	技术职务
76	何伟伟	男	198710	高分子化学与物理	副教授
77	赵　琳	女	198710	放射医学	副教授
78	刘汉洲	男	198505	化学	副教授
79	白　霞	女	196809	血液学	高级实验师
80	王敬东	男	197004	放射医学	实验师
81	吴安庆	男	198706	放射免疫学	实验师
82	商冰雪	女	198612	免疫学	助理研究员
83	陈永井	男	197712	免疫学	助理研究员
84	聂　晶	女	197304	生物化学	实验师
85	盛道鹏	男	198507	放射化学	助理研究员
86	封　琼	女	198710	放射医学	助理研究员
87	王春宏	女	198001	生物学	助理研究员
88	陈兰花	女	198707	放射化学	实验师
89	吴　艳	女	198107	免疫学	高级实验师
90	刘胜堂	男	198702	放射医学	助理实验师
91	闫思齐	女	198905	核物理	实验师
92	王成奎	男	197108	心理学	副教授
93	朱本兴	男	197012	机关管理办公自动化	实验师
94	易　剑	女	196403	机关管理办公自动化	主管技师
95	彭　蓉	女	197704	机关管理办公自动化	科员
96	燕　倩	女	199409	商务管理	财务秘书
97	佟　鑫	女	199108	新闻与传播	行政秘书

二、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 12 台大型仪器设备，设备总金额近四千万元。

序号	设备型号	设备名称	设备价格(万元)	国重室出资（万元）	产地国
1	Talos F200S G2	高分辨场发射透射电镜	794.38	794.38	美国
2	Invivo2 1000	低氧工作站	182.94	182.94	英国
3	ASAP2460	多站拓展式全自动快速比表面与孔隙度分析仪	60.10	60.10	美国
4	Fluidigm Hyperion Imaging System	组织质谱成像系统	779.90	479.90	加拿大
5	CPL-300	全波长圆偏振光谱联用仪	298.34	240.00	日本
6	SPL-SC-Pro-7	双波段眼科 OCT 成像系统	144.00	116.00	中国
7	E500-10/12	电子自旋（顺磁）共振波谱仪	297.78	297.78	德国
8	D8VENTURE	X 射线单晶衍射仪	259.00	259.00	德国
9	TS10K	高性能计算集群	307.76	240.00	中国
10	非标定制	空间零磁环境模拟设备	186.78	186.78	中国
11	自研	辐射敏感器官剂量测量体模	430.00	430.00	中国
12	FV3000	激光共聚焦显微镜	192.88	154.30	日本
合计			**3933.85**	**3441.18**	

三、研究方向

2018 年 6 月 13 日下午，江苏省科技厅会同科技部基础研究司对省部共建放射医学与辐射防护国家重点实验室建设运行实施方案组织专家论证。与会专家从实验室定位、研究方向和研究内容设置等方面提出建设性的意见和建议。实验室以放射生物效应为基础、以放射诊治和辐射防护为目标，开展高水平的基础研究和应用基础研究。具体如下：

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

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

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

四、代表性科研成果

（一） 放射生物效应及机理

1、COVID-19 感染中的关键点：免疫反应

在 1918 年流感大爆发 100 多年之后的今天，我们再次面临另一场流行病的大考。新型冠状病毒(COVID-19)感染的爆发正蔓延到每一个大陆，如没有有效的疫苗或特效药，人类或许在很长一段时间内都要与这种病毒进行博弈。科学家和临床医生已经发现并非所有接触 COVID-19 的人都被感染，存在无症状感染者，但部分受感染的病人发展成严重的呼吸道疾病。

基于临床研究数据，我们提出了一些简单但基本被忽视的 COVID-19 患者的治疗方案。新冠肺炎患者的病程可以划分为两个阶段：第一阶段是基于免疫防御的保护阶段，第二阶段是炎症驱动的损伤阶段。医生可以在第一阶段尝试增强免疫反应，而在第二阶段抑制免疫反应。细胞因子释放综合征（CRS）和肺损伤是新冠肺炎严重患者康复的主要障碍。不同阶段应该采取不同的治疗方式。该论文对目前席卷全球的新型冠状病毒感染的肺炎中关键点——免疫反应，进行了独到的解析，并提出了一些可供参考的治疗思路。成果发表在在 **Cell Death and Differentiation**, 2020, 27, 1451-1454。

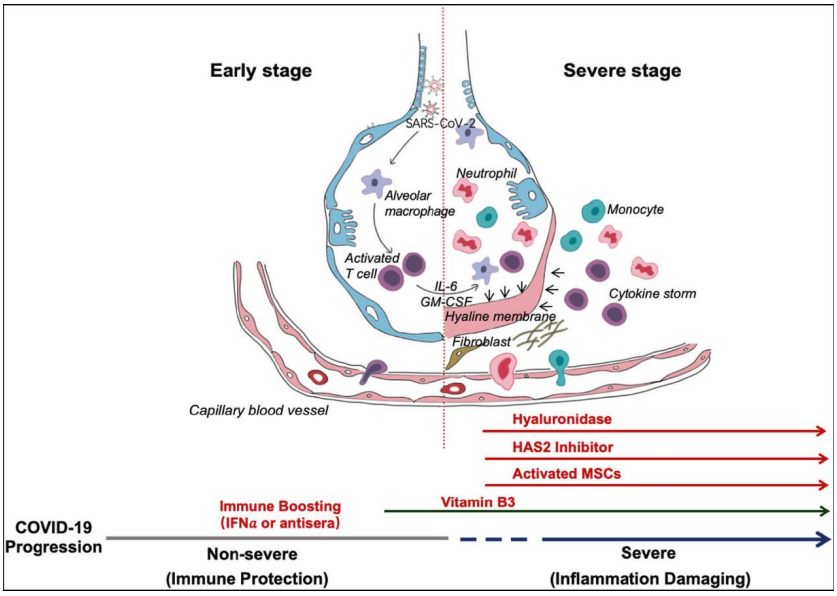

图 1.1 COVID-19 感染进程和潜在辅助干预措施示意图。

潜伏期过后，入侵的 COVID-19 病毒会引起非严重症状并引发保护性免疫反应。在此阶段，可以应用增强免疫反应的策略。如果感染者不能消除病毒，则患者会进入严重阶段，即发生强烈的破坏性炎症反应，尤其是在肺部。

2、X 射线对人血清白蛋白载体体内运输的影响

心血管疾病是人类健康的最大威胁。由于成体心脏再生能力差，心肌损伤后难以自我修复。多能干细胞（包括胚胎干细胞和诱导多能干细胞）可分化为心肌细胞，在心脏修复方面有巨大应用潜力，还可为体外心脏疾病模型构建、药物筛选和毒性测试等提供丰富的人源心肌细胞资源，对心脏再生医学研究和心脏疾病临床治疗均具有重要意义。但是，多能干细胞分化的心肌细胞在结构、电生理和代谢等特征上尚未发育成熟，与成人心肌有很大区别，这也是多能干细胞在心脏疾病治疗、成年疾病模型和药物开发等领域应用的主要障碍。因此，控制心肌细胞分化成熟是解决这些问题的关键。

现阶段，人血清白蛋白(HSA)作为抗肿瘤药物的载体已经在临床上被广泛的使用。研究 X 射线辐照对 HSA 的体内行为的影响，有利于临床上优化联合放化疗的设计。我们发现与 HSA 的细胞摄取息息相关的 Caveolin-1 蛋白在 X 射线照射下表达明显增加，进而导致了①肿瘤细胞对 HSA 的摄取增加，②肿瘤组织经 X 射线预照射后，125I（131I）标记的 HSA 在肿瘤组织的滞留时间延长了。同时，为了进一步提高 HSA 对放疗后肿瘤组织的靶向性，本课题将具有靶向凝血功能的 A15 多肽偶联到 HSA 上，使得 HSA 靶向至 X 射线辐照引发的肿瘤组织凝血部位，实现 X 射线照射辅助下的 131I-HSA 的高肿瘤蓄积。因此，本研究利用 X 射线可同时诱导肿瘤细胞高表达 Caveolin-1 蛋白和肿瘤组织的凝血形成的优势，使得 HSA 在放疗后的肿瘤组织具有更高的富集率和更长的滞留时间，优化了 HSA 的递送，对临床上基于蛋白载体的放化疗联合治疗提供一定的参考价值。相关成果发表在 **Biomaterials**, 2020, 233, 119764。

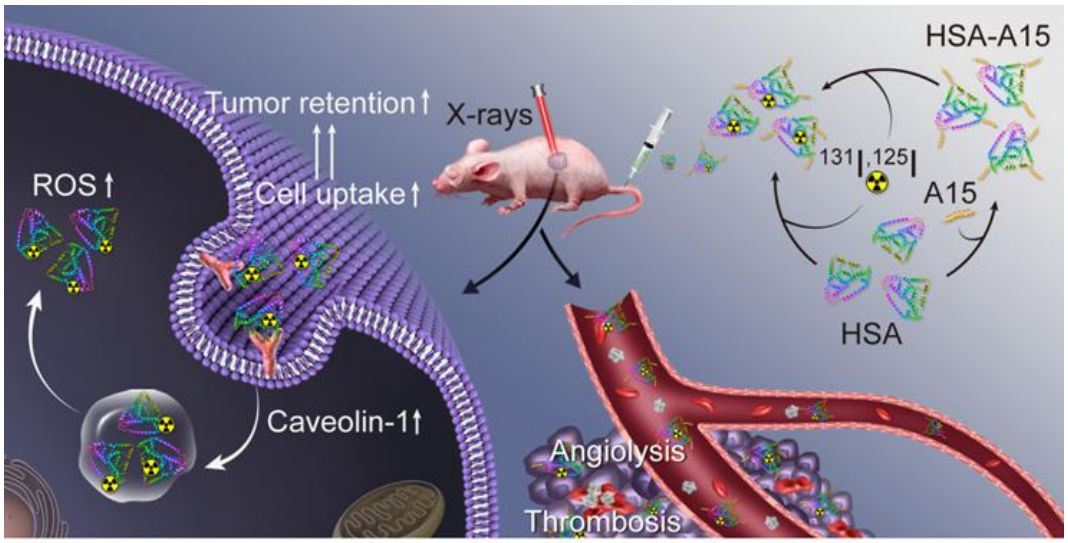

图 1.2 X 射线对人血清白蛋白载体体内运输的影响机制。

3、红光介导探针锚定于细胞质 RNA 分子诱发肿瘤凋亡的新途径

增加肿瘤药物或探针在肿瘤组织的积聚和延长其滞留是提高药物诊疗效果的有效途径。近年来，为了提高药物在肿瘤细胞内的摄取量与滞留时间，科学家们发展了许多先进的策略使药物或探针分子特异性靶向并滞留于肿瘤部位以达到提高肿瘤诊疗效果的目的。临床上一般通过使用大剂量或者多次给药的方式来提高诊疗疗效，这往往会给机体带来较大的毒副作用。纳米材料由于其较大的尺寸以及独特的 EPR 效应，虽然能一定程度上延长探针在肿瘤病灶的滞留时间，但大量纳米材料在体循环过程中会被内皮网状系统（RES）摄取，不可避免会给机体带来一定的伤害。因此，开发新型高效的肿瘤诊疗一体化新技术对于实现临床癌症的精准诊治意义重大。

在最新研究中，我们创新性地提出一种利用红光引发探针 *f*-CR 特异性与肿瘤细胞内 RNA 分子共价交联的新策略。一个新型的近红外荧光探针 *f*-CR 被策略性设计与构建，其主要由三部分组成：近红外荧光染料 Cy7 为信号基元，环肽 cRGD 作为肿瘤细胞靶向基团，单线态氧敏感的 Furan 基团可以与 RNA 分子侧链选择性发生交联。当探针被高表达的整合素 v3 受体蛋白介导内吞入肿瘤细胞后，在 660nm 光照射亚甲基蓝（MB）光敏剂产生单线态氧的条件下，探针通过 Furan 与细胞质 RNA 中的腺嘌呤、胞嘧啶或鸟嘌呤核苷等碱基之间的环加成反应锚定于肿瘤细胞内，这有效地降低了探针的外排，实现了在体肿瘤的长窗口期近红外成像，同时

还意外地发现，大量肿瘤细胞被诱发凋亡，活体肿瘤的生长得到显著的抑制。因此，我们首次发现了红光介导探针锚定于细胞质 RNA 分子诱发肿瘤凋亡的新途径，并建立了一种基于细胞质 RNA 分子修饰的肿瘤诊疗一体化新策略，为临床开展肿瘤的精准诊治提供了新思路。相关成果发表在 **Journal of the American Chemical Society**, 2020, 142, 21502–21512。

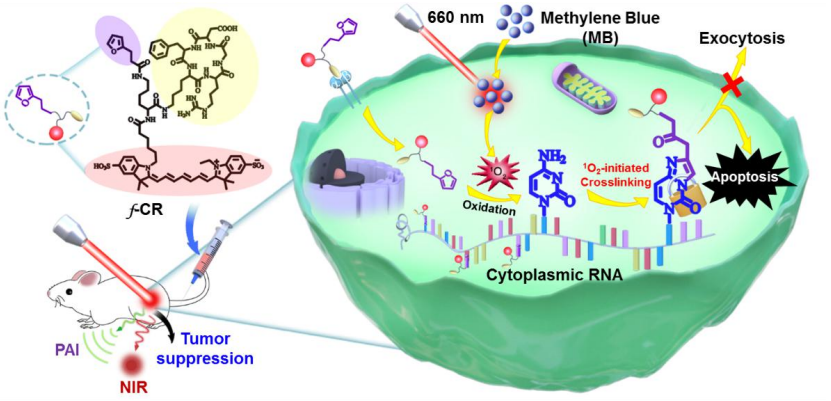

图 1.3 红光引发的探针 *f*-CR 与细胞质 RNA 的共价交联用于长窗口期肿瘤成像和治疗。

（二） 先进放射诊断和治疗

1、聚钼酸盐纳米团簇用于放射-放射动力治疗

为了解决近红外光在光动力治疗（PDT）中穿透性较弱和高剂量 X 射线对正常组织的毒副作用，低剂量 X 射线诱导的放射和放射动力学治疗在癌症治疗领域掀起一场革命。研究团队首次合成了具有 X 射线触发光动力（X-RPDT）和 X 射线诱导辐射（X-RT）双重功能的聚钼酸盐纳米团簇（POMo NCs）。

我们将光敏剂二碘曙红（RB）装载于这种大草莓形状的 POMo NCs 上，并通过带羧基的聚乙二醇和功能化的壳聚糖进行修饰。这种聚乙二醇化 POMo@CS RB 纳米制剂能够在肿瘤部位取得高积聚和长时间滞留。在低剂量 X 射线照射下，POMo NCs 与 RB 的放射增敏和闪烁共同作用可减少放疗的副作用，提高放疗和 PDT 的效率。这是因为 POMo NCs 不仅可以通过产生俄歇电子直接刺激 DNA 损伤来增强 RT 的功效，还可以通过将高能 X 射线转化为光来刺激 RB 产生单态氧（1O2）来增强 PDT 的功效。体内实验结果表明，在低剂量 X 射线照射下，POMo NCs 能显著抑制肿瘤生长。更重要的是，经组织学检查，合成聚乙二醇化的 POMo

NCs 对主要正常器官无明显副作用。

本工作描述了一种简单的策略来设计有效的 X-RRDT 药物，具有多种特性，包括 X 射线辐射敏化、X 射线闪烁和低剂量 X 射线照射下的 X-RRDT 光敏化。因此，我们所制定的策略将进一步提高低剂量 X 射线照射下肿瘤的治疗效果，为临床肿瘤治疗带来希望。相关成果发表于 **Nanoscale Horizons**, 2020, 5, 109。

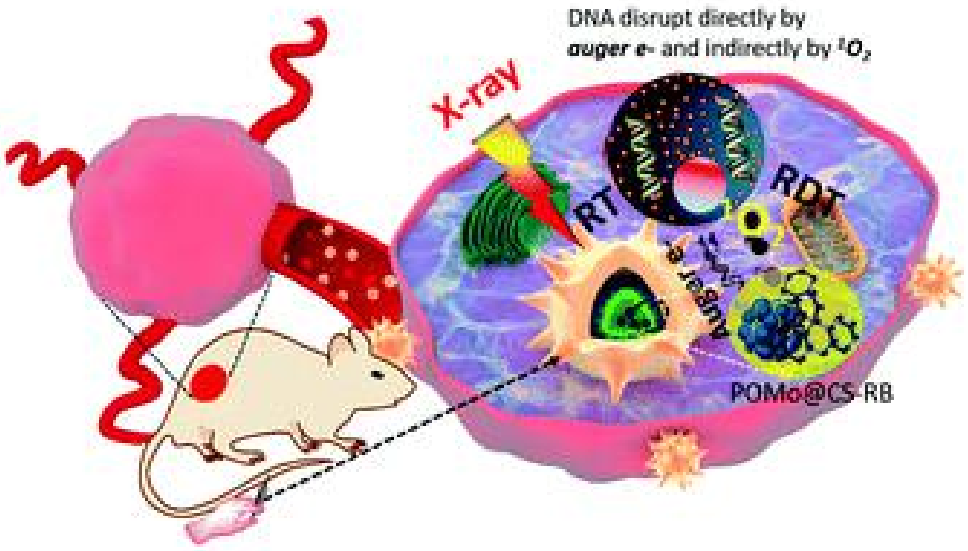

图 2.1 聚钼酸盐纳米团簇用于放射-放射动力治疗机制图。

2、近红外二区荧光成像用于脑胶质瘤手术引导

脑肿瘤边界的清晰定位是实现其精准诊断和治疗的关键。在荧光成像引导肿瘤手术（FGS）过程中，受限于组织穿透较深的荧光探针以及血脑屏障（BBB），实现高灵敏、高特异性地区分脑肿瘤与周围实质边界仍然是一个巨大的挑战。近年来发展的近红外二区荧光成像技术不仅相较于可见光和近红外一区波段的组织穿透性更强，而且能实时动态地对观察生物过程。

针对深层组织穿透特性的荧光纳米探针的设计，我们基于具有近红外二区荧光特性的 Er 基稀土纳米颗粒，引入 NaYbF4 活性层、Ce3+掺杂剂以及染料聚合物实现能量限域、交叉驰豫和发射敏化，从而构建出能量级联下转换（ECD）方式，将 808 nm 激发下 1525 nm 发射相较于 Er 基核心增强了~ 675 倍。在小鼠全身血管造影以及肿瘤血管新生过程的观察的实验结果都显示出所制备探针优异的近红外二区造影性能。

我们为了实现脑肿瘤的精准定位和有效切除，首先通过术前 T2 加权磁共振成像对脑肿瘤进行定位，再结合脑胶质瘤细胞靶向多肽（Angippeptide-2）的特异性修饰和聚焦定位区域超声打开 BBB 的策略，高效递送近红外二区荧光纳米探针后实现荧光成像引导下的脑肿瘤手术切除。本研究在稀土纳米探针荧光强度调控策略上具有一定启示性意义，同时阐述了近红外二区荧光成像技术在手术引导方面的潜力。相关成果发表在 **Nano Today**, 2020, 34, 100905。

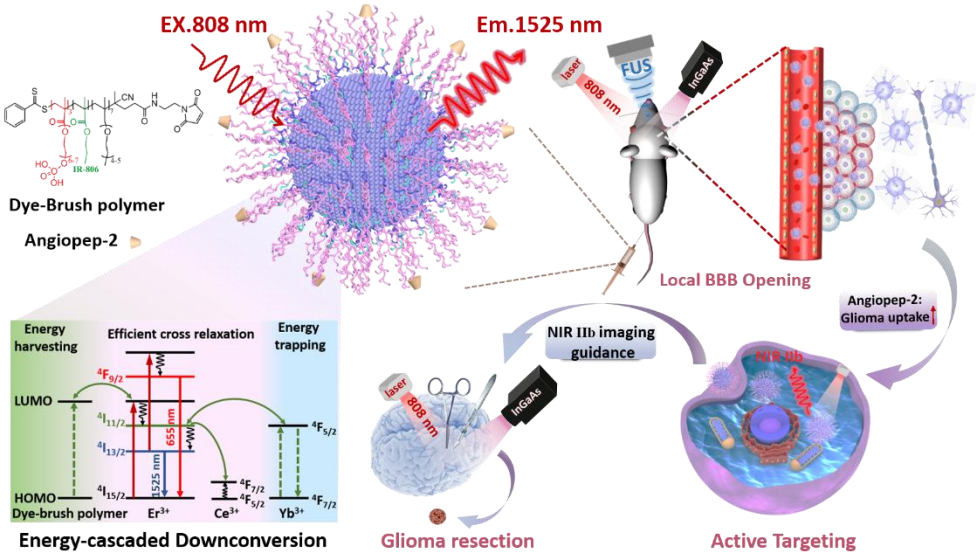

图 2.2 能量级联下转换近红外二区稀土纳米颗粒的构建及联合主动靶向和聚焦超声实现近红外二区成像引导下的脑肿瘤切除。

3、一种可激活聚合物探针用于浸润性肿瘤的近红外荧光和光声成像

乳腺癌是发生在乳腺腺上皮组织的一种恶性肿瘤，在全球女性肿瘤发病率中位居首位，严重威胁着女性的身心健康。乳腺癌有多种亚型，如 luminal 型、HER2 型、三阴性乳腺癌（TNBC）型等，其中，三阴性乳腺癌是一种侵袭性亚型，预后较差，死亡风险较高。这就需要对其进行早期诊断和对其病理过程进行深入了解。因此，开发智能探针用于区分性检测浸润性和非浸润性乳腺癌对于其有效治疗和预后至关重要。

在最近的研究进展中，我们创新地发展了一种可激活的聚合物探针（P-Dex）（图 2.4），该探针在浸润性乳腺癌中过表达的尿激酶型纤溶酶原激活剂（uPA）作用下，特异性地开启近红外（NIR）荧光和光声（PA）信号。P-Dex 由四个部分

组成：1.可肾清除的葡聚糖主链，葡聚糖的引入不仅增强了 P-Dex 的亲水性和肾脏清除率，还促进了 P-Dex 被酶的裂解；2. NIR 染料；3.自消除剂-氨基苄醇；4. uPA 识别底物（Cbz-GlyGly-Arg-OH）。P-Dex 能够被动靶向浸润性乳腺癌肿瘤，并在 uPA 酶特异性识别和切除 P-Dex 上的肽链 Gly-Gly-Arg 后，经 1，6-消除反应，打开 NIR 染料的荧光和光声信号。细胞实验和动物实验证实，P-Dex 能够有效地鉴别检测侵袭性 MDA-MB-231 乳腺肿瘤和非侵袭性 MCF-7 乳腺肿瘤。据我们所知，这是首个能够鉴别诊断乳腺浸润性和非浸润性的聚合物探针。由于 uPA 在肿瘤中的表达水平与较低的总生存期及无复发生存期密切相关，P-Dex 不仅可用于评估肿瘤的恶性和预后，还能用于监测和评估以 uPA 表达为指标的恶性肿瘤的全身治疗策略。同时，由于 uPA 被发现高表达于转移性乳腺肿瘤区，P-Dex 还可以用于乳腺癌转移灶的成像。因此，该聚合物探针对于恶性乳腺癌的诊断具有广阔的前景。相关成果以封面形式发表在 **Angewandte Chemie International Edition**，2020, 59, 7018。

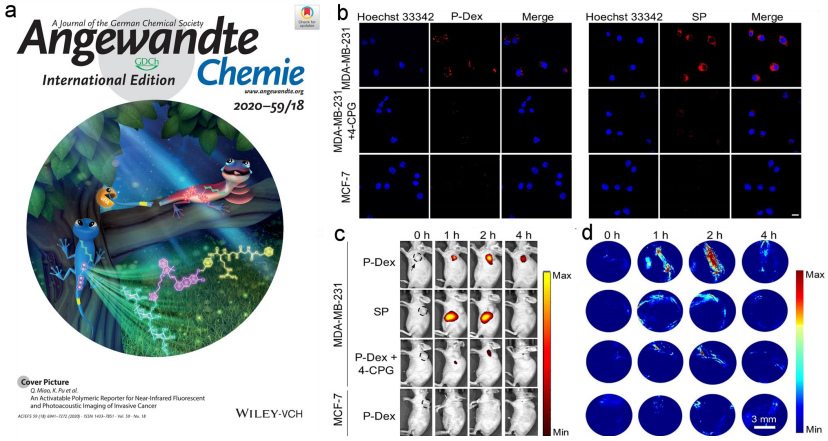

图 2.3 用 P-Dex 和 P-Dex+酶抑制剂（4-CPG）处理后得到细胞的荧光成像图（b）、小动物的荧光成像图（c）和小动物的光声成像图（d）。

4、GSH 响应磁共振探针的制备及脑胶质瘤活体成像

肿瘤微环境与肿瘤的发生发展密切相关，比如基质金属蛋白酶不仅和肿瘤转移相关，还与细胞凋亡、血管新生、肿瘤生长有关，肿瘤弱酸性不仅会增加肿瘤转移和入侵，也会诱导对化疗药的耐药性等等。因此对肿瘤微环境进行监测，对于肿瘤的疗效评估和预后具有重要意义。

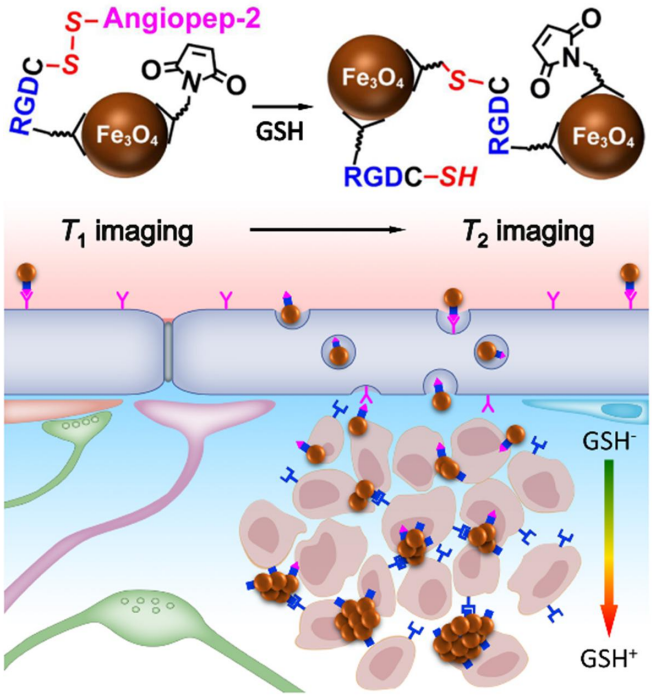

图 2.4 肿瘤微环境谷胱甘肽响应的磁共振信号互锁纳米探针示意图。

为了获取与肿瘤恶性生物学行为相关的分子病理信息，我们以临床中危害重大、但生化检测困难的脑胶质瘤为研究模型，设计并构建了一种对肿瘤微环境中高浓度还原性谷胱甘肽（GSH）具有特异性响应的，T1/T2 比率计量 MRI 探针，以实现肿瘤内 GSH 分布的无创可视化检测：将具有穿越血脑屏障功能的 angiopep-2 肽段和具有靶向脑胶质瘤细胞的 RGD 肽段通过二硫键相连，构成 GSH 响应肽；并进一步通过 RGD 一端的氨基将多肽加载到 Fe3O4 纳米颗粒表面，构建肿瘤 GSH 响应 T1/T2 比率计量 MRI 探针。细胞实验表明，当 GSH 对多肽进行裁切后，裸露出的 RGD 区段可以有效增加探针对肿瘤细胞的结合能力。原位荷瘤小鼠模型 MRI 成像结果显示，通过尾静脉给药后，在探针表面 angiopep-2 链段的协助下，探针可有效跨越血脑屏障，并在脑胶质瘤内蓄积。而随着多肽的二硫键被瘤内微环境高浓度的 GSH 裁切，暴露出的 RGD 区段可以促进探针靶向肿瘤细胞，从而延长探针在瘤内的滞留时间。更重要的是，二硫键裁切生成的巯基，与探针表面残余马来酰亚胺基反应，使探针发生原位交联，在提高探针瘤内滞留效果的同时，使得聚集体中 Fe3O4 纳米颗粒磁耦合作用增强，实现探针造影效果由 T1 信号向 T2 信号的转换。进一步我们结合聚集反应动力学和外球弛豫模型进行了理论推导，建立了弛豫率变化的比值与环境中谷光氨肽的浓度的定量关系。通过这两种磁共

振信号的比率成像，就可以显示出脑胶质瘤内 GSH 的空间分布。因此，探针不仅实现了对脑胶质瘤精确诊断，而且成功实现了瘤内 GSH 的分布可视化，对脑瘤分级的评估和预后策略都有潜在的价值。相关成果发表在 **Angewandte Chemie International Edition**, 2020, DOI: 10.1002/anie.202014348。

（三） 辐射防护

1、锕系固体化学用于辐射探测

金属有机笼（MOC），也称为金属有机多面体（MOP），是由金属节点和有机配体通过配位键组装而成的离散型分子笼。MOC 材料多利用主客体相互作用，在催化、手性分离和生物医学等诸多领域均有广泛的应用。然而由于笼体之间缺少相互作用而难以形成合适的电子传导路径，导致 MOC 材料在电催化，能量存储，光电子设备等方面应用甚少。

该工作中铀酰离子通过平面六配位和原位形成的二齿柔性配体巧妙地形成了罕见的 M_4L_6 八面体型分子笼。单晶结构分析表示笼之间通过机械互锁拓展延伸，其中每个笼体与六个晶体学相同的笼子相连，继而延展成为三维的多孔结构（图一）。另外，孔隙里原位形成的六甲蜜胺大分子与 MOC 骨架之间形成的长程连续的π-π堆积为 SCU-14 提供了有效的电子传输路径，使得 SCU-14 成为首例宽带隙锕系半导体 MOC 材料。

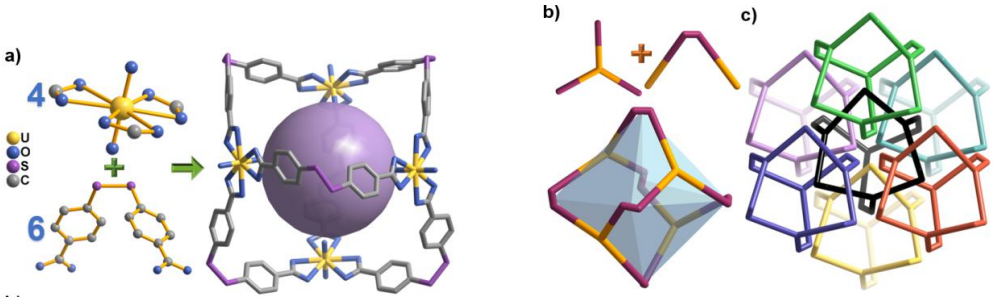

图 3. 1 SCU−14 的结构示意图。

SCU-14 以自然界中最重的铀元素作为金属中心，同时笼间彼此紧密互锁带来较高的密度，这两点的共同作用使得其具有较高的 X 射线阻滞效率。与此同时，SCU-14 的高电阻率带来较低的漏电流，可有效控制噪声从而提升信噪比。基于以上两大优势，探索了其作为直接 X 射线探测器的应用。实验结果表明 SCU-14 在 X 射线照射下有明显的光电导效应。该材料还具有较高的载流子迁移效率，其探测性能（$\mu\tau = 6.30 \times 10^{-4}\ cm^2\ V^{-1}$）优于之前本团队报道的 MOF 材料，可与商业探测

材料媲美。此外，该材料的 X 射线探测灵敏度可达 54.93 μCGy_{air}^{-1} cm^{-2}。在长时间的 X-ray 照射下，其光电响应也几乎没有变化，体现了该材料在长时间应用工况下的稳定性。该研究成果发表在在 **Journal of the American Chemical Society,** 2020, 142, 16218-16222。

2、基于电化学发光技术的痕量铀酰便携式监测器

随着核工业及核技术应用的发展，世界各国在过去几十年中产生了共计超过十亿吨各类贫铀废弃物，其长达 45 亿年的半衰期及污染地域之广，成了广为关注的环境问题。世界卫生组织（WHO）明确规定饮用水中 UO_2^{2+}含量不得超过 1 ppb。同时，对环境中的痕量 UO_2^{2+}进行快速实时实地精确监测，也是核应急公共突发事件应对能力建设的重要内容。

针对这一挑战，我们将电化学发光（ECL）技术应用于痕量放射性物质监测，对铀酰的检测限低达 10.6 pM/2.5 ppt 且具有良好选择性，并设计成便携式装备成功应用于自然水样的实际监测（图 3.2）。同时，该研究亦首次发现了铀酰的阳极 ECL 现象并阐明其机理。为证明该便携式痕量 UO_2^{2+} ECL 监测技术的实际应用价值，该方法分别被用来检测来自渤海（天津）、骆马湖（徐州）、独墅湖（苏州）和千岛湖（杭州）的实际水样中 UO_2^{2+}的含量，其结果与使用 ICP-MS 法的测定结果非常接近，证明了该技术的实际应用前景。与 ICP-MS 法相比，ECL 检测系统具有成本低、便携式的突出优势，更有利于野外条件下的环境监测工作。该工作为环境中 UO_2^{2+}离子的实时监测和饮用水质量监控提供了有效而精确的手段，也为该领域今后的工作提供了全新的思路。该研究成果发表在在 **Advanced Functional Materials,** 2020, 30, 2000220。

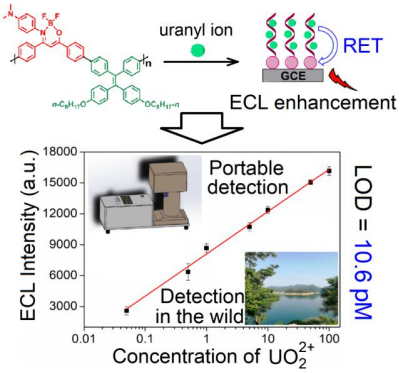

图 3.2 聚集诱导发光(AIE)活性聚合物点（Pdots）ECL 探针用于环境中铀酰的高灵敏度便携式监测。

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	800
3	省优势学科	省特种医学优势学科	YX12800211	柴之芳	590
4	军委科技委	XXXX		王殳凹	1000
5	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
6	国家级其他项目	暂无	暂无	畅　磊	300
7	国家级其他项目	暂无	暂无	苗庆庆	300
8	国家自然科学基金	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
9	国家自然基金	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
10	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
11	国家重点研发计划	生物界面蛋白质冠原位表征与主动调控	2020YFA070079	葛翠翠	132.8
12	国家自然科学基金	纳米环境健康效应	K112800820	葛翠翠	120
13	国家自然科学基金	放射性疫苗 89Sr-CpG 的乳腺癌骨转移免疫响应监测与放射免疫治疗研究	12075164	汪　勇	64
14	国家自然科学基金	光触发锚定型多功能分子探针的构建及其肿瘤诊疗研究	22077092	史海斌	63
15	国家自然科学基金	211At 标记的 GIP 靶向纳米载体用于神经内分泌肿瘤的治疗研究	22076132	朱　然	63
16	国家自然科学基金	TnC/TPM4 信号通路在氚水诱导心脏发育异常中的调控作用	22076133	涂　彧	60
17	国家自然科学基金	空间辐射与微重力通过 β-arrestin1-FN1-YAP 通路协同诱导肿瘤发生的机理研究	32071243	胡文涛	58
18	国家自然科学基金	TNFα通过骨髓氧化微环境参与移植后血小板减少的调控机制研究	82070143	韩　悦	56

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
19	国家自然科学基金	乳铁蛋白通过调节乏氧微环境改善放射性肠损伤	82073482	徐加英	55
20	国家自然科学基金	肝 X 受体促进胰腺癌转移及其分子机制研究	82073225	周泉生	55
21	国家级其他项目	LNC CRYBG3 通过生物力学传导通路调控肿瘤增殖 /转移的研究	171017	畅　磊	18
22	省部级项目	“高效吸附/催化氧化/自降解”三功能新材料构筑及其原位净化土壤有机污染物研究	BK20202012	路建美	500
23	江苏省双创团队	纳米生物安全性评价	暂无	李瑞宾	300
24	省部级项目	基于放射性核素储放的金属有机骨架研究	BK20200102	王艳龙	50
25	省部级项目	核与辐射突发事件急性放射损伤救治指南编制项目合同	无（见合同）	刘玉龙	9.9
26	市厅级项目	以血小板信号分子 CalDAG-GEFI 为靶点的抗血栓新机制研究	——	夏利军	30
27	市厅级项目	磁共振/核医学双模态纳米分子影像探针应用基础研究	20KJA150006	曾剑峰	30
28	市厅级项目	选择性吸附 TcO4-的含氮阳离子型 MOFs 材料先导设计及机理研究	20KJA150010	杨再兴	30
29	市厅级项目	新型纳米氧化铁静脉补铁剂开发	SYG202036	曾剑峰	5
30	市厅级项目	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	苏财教【2020】45 号	陈新建	100
31	市厅级项目	研究肿瘤微环境因素导致耐药、转移机制与干预策略	苏财教【2020】45 号	黄玉辉	1.15
32	市厅级项目	肿瘤诊疗与原位疗效评价一体化探针构建及应用研究	苏财教【2020】45 号	史海斌	1.8
33	市厅级项目	特异性探针的构建及体内成像应用评估	苏财教【2020】45 号	朱　然	11.11
34	市厅级项目	乏氧肿瘤多线束放疗的生物效应和分子机制研究	苏财教【2020】45 号	周光明	2.41
35	市厅级项目	问答辐射与健康	苏财教【2020】38 号	涂　彧	10
36	市厅级项目	通过高能 12C+12C 散射研究原子核中三体力效应		屈卫卫	3
37	横向项目	战略合作框架协议		曹建平	500
38	横向项目	PSQ 对血小板功能的影响	202009	戴克胜	480

序号	项目类别	项目名称	项目编号	项目负责人	总经费(万元)
39	横向项目	瑞喹莫德（R848）白蛋白制剂的开发		陈华兵	50
40	横向项目	红色诺卡氏菌细胞壁骨架治疗放射性皮肤损伤临床前有效性实验	H200397/1P12891120	陈　秋	40
41	横向项目	江苏省核应急紧急医学救援应急应战平台	涉密	刘玉龙	30
42	横向项目	苏灵止血机制研究	KC-HCA-200901	武　艺	25
43	横向项目	微粒肺部作用规律数据库及典型微粒载药吸入示踪分析	HM2020FH4110-WX	李瑞宾	15.6
44	横向项目	靶材光子产额分布测算及实际应用转化率评测	P112800920	孙　亮	15
45	横向项目	重大疫情下核电站及其他核设施营运单位操纵人员的心理危机情况调查及干预效果研究	委托书	刘玉龙	10
46	横向项目	一种创新药物制剂的药效学研究	P112801320	杨　凯	3
合计					**10612.77**

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	国家重点实验室粒子加速器论证会	区域性	主办	2020-05-12	36	苏州
2	first international forum on MSAM	全球性	主办	2020-09-20	50	苏州
3	中能多粒子超导医学研究加速器用户研讨会	全国性	主办	2020-10-17	100	苏州
4	加速器终端研讨会	全国性	主办	2020-12-25	33	苏州
5	造血干细胞移植治疗血液系统疾病研究进展	区域性	主办	2020-06-20	90	苏州
6	造血干细胞移植过程中的出血与血栓	区域性	主办	2020-07-11	100	苏州
7	2020 中国血液病大会暨第十四届中国医师协会血液科医师年会	全国性	承办	2020-08-14	500	苏州
8	2020 年中国生理学会学术年会	全国性	承办	2020-08-22	500	线上会议
9	中国医药教育协会感染疾病专业委员会第六届学术大会	全国性	承办	2020-09-10	500	苏州
10	中华医学会第 16 次全国血液学学术会议	全国性	承办	2020-09-24	1000	杭州
11	血液学的基础理论与诊疗技术新进展	区域性	主办	2020-10-09	300	苏州
12	第十二届泛太湖白血病/淋巴瘤流式及遗传学进展与标准化 协作组研讨会	区域性	主办	2020-11-06	300	苏州
13	第五届中国微循环周	全国性	承办	2020-11-20	300	广州
14	淋巴系统肿瘤诊治新进展	区域性	主办	2020-11-26	100	苏州
15	淋巴系统肿瘤的基础与临床研究进展	区域性	主办	2020-12-05	50	苏州
16	骨髓瘤诊治进展	区域性	主办	2020-11-10	100	苏州

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
17	核和辐射损伤医学应急演练与临床处理培训班	全国性	主办	2020-09-22	150	苏州市
18	中国核学会核应急医学分会成立大会暨第一届理事会第一次会议	全国性	承办	2020-09-22	180	苏州市
19	东吴心血管健康论坛	区域性	主办	2020-11-21	120	苏州

2、专家来访

序号	时间	报告人	主题	单位
1	2020-11-04	李占军	基因编辑技术优化及其在人源化兔模型中的应用	吉林大学
2	2020-11-05	李小平	云计算在生物信息分析中的应用	中山大学
3	2020-10-30	魏志祥	—纳米抗菌剂：可穿戴器件的能源解决方案：柔性太阳能电池与储能器件	国家纳米科学中心
4	2020-10-28	王忠良	肿瘤微环境的调控与可视化	西安电子科技大学
5	2020-10-28	王乐余	多功能纳米探针用于活体深度组织多模成像分析	北京化工大学
6	2020-10-27	申有青	高效抗肿瘤纳米药物的设计	浙江大学
7	2020-08-13	赵东元	功能介孔材料的界面组装与应用	复旦大学
8	2020-11-02	张承东	纳米抗菌剂：治病 and 致病	北京师范大学
9	2020-01-08	张红雨	火星探测和探测保障	华中农业大学
10	2020-09-16	雷　鸣	核医药合作	北京大学
11	2020-09-02	杨　辉	加速器项目	姑苏实验室
12	2020-11-10	罗金才	脑部淋巴管-淋巴结系统，放射线疗法与免疫疗法的连接点？	北京大学
13	2020-10-27	李培山	中性粒细胞在肿瘤肺转移中的功能研究	山东大学基础医学院
14	2020-09-25	王振义	克隆性嗜酸细胞增高伴肾病综合征	上海交通大学医学院附属瑞金医院

序号	时间	报告人	主题	单位
15	2020-09-25	陈　竺	对急性早幼粒细胞白血病发病原理、分型和治疗的最新认识	上海交通大学医学院附属瑞金医院
16	2020-09-25	施一公	基础研究推动创新制药	西湖大学
17	2020-09-25	陈赛娟	急性 B 淋巴细胞白血病发病机制研究	上海交通大学医学院附属瑞金医院
18	2020-09-25	于金明	免疫治疗十大挑战	山东省肿瘤医院
19	2020-10-09	沈洪兵	大数据时代的临床医学研究	南京医科大学
20	2020-10-09	王广基	精准医学背景下药代动力学新技术在新药及临床研究中的探索	中国医学科学院
21	2020-10-09	顾晓松	组织工程创新与再生医学	南通大学
22	2020-08-07	张灼华	Molecular Dissection of Parkinson's Disease	南华大学
23	2020-08-07	刘　东	鉴定全新的血管新生调控因子	南通大学
24	2020-11-03	任　骏	线粒体稳态与心血管病	复旦大学
25	2020-11-03	王书艺	脸红基因，自噬和心肌病	上海大学

3、外出交流

序号	时间	出访单位	报告人	主题
1	2020-10-29	301 医院	畅　磊	肿瘤发生中的生物力学
2	2020-10-22	同济大学	畅　磊	
3	2020-10-12	同济大学	畅　磊	生物力学和 long noncoding RNA
4	2020-09-10	上海交通大学	畅　磊	放射中的生物力学
5	2020-08-13	中广核公司	周光明	凤凰项目论证
6	2020-08-25	苏州市新区管委会	周光明	“多粒子加速器”项目
7	2020-10-30	南通新区管委会	周光明	“多粒子加速器”项目
8	2020-11-02	苏州市吴江平望镇政府	周光明	“多粒子加速器”项目
9	2020-10-09	中核动力设计院	崔凤梅	邀请讲座

4、参加会议

序号	会议类别	报告人	会议名称	会议地点
1	全国性	涂　彧	“环境氡污染监测、评价与防治技术”学术讨论会	北京
2	区域性	杨红英	第五届临床放射生物学新进展研讨会	
3	区域性	杨红英	2020 姑苏肿瘤放射免疫治疗论坛暨江苏省免疫学会放射与免疫专业委员会成立大会	苏州
4	全国性	李　桢	2020 年生物医学交叉青年论坛	宁波
5	全国性	李　桢	第二届全国生物磁学与磁性纳米材料学术会议	南京
6	区域性	李　桢	2020 苏州市医学会放射学分会学术年会	苏州
7	全国性	李瑞宾	第四届环境污染与健康会议	天津
8	全国性	王殳凹	辐射化学与辐照应用学术研讨会	苏州市
9	全国性	周光明	核闪光放射治疗学术交流会	成都
10	全国性	周光明	深空探测辐射防护技术与应用	北京
11	全国性	周光明	中国生命电子学术年会	佛山
12	全国性	周光明	空间环境与物质科学研究院战略研讨会	哈尔滨
13	全球性	时玉舫	COVID 19 Pandemic: Challenges and Recent Advancements	新德里（视频会）
14	全球性	时玉舫	ISCT 2020 Paris Virtual - COVID-19 Session I "The Force Awakens"	巴黎（视频会）
15	全国性	时玉舫	浙江省免疫学会 2020 年度学术大会	杭州市
16	全国新	时玉舫	第一届中国西部“干细胞与再生医学”科技创新论坛	西安市
17	全国性	时玉舫	2020 兽医科技发展论坛暨上海兽医公共卫生论坛	上海市
18	全国性	戴克胜	2020 年中国生理学会学术年会	线上会议
19	全国性	戴克胜	第五届中国微循环周	广州
20	全国性	吴德沛	2020 中国医师协会血液科医师分会年会	苏州
21	全国性	韩　悦	中华医学会第 16 次全国血液学学术会议	杭州

序号	会议类别	报告人	会议名称	会议地点
22	全球性	杨　林	EHA（虚拟会议）	法兰克福
23	全国性	杨　林	CSCO	北京
24	全国性	胡士军	第十届寒地心脏病学会议	哈尔滨市
25	全国性	胡士军	中国干细胞第十届年会	贵阳市
26	全国性	胡士军	第七届武汉国际心血管病大会	武汉市
27	全国性	胡士军	长城心脏病学大会 2020/ 亚洲心脏学会大会 2020	北京市
28	全国性	胡士军	第三届武当国际医学论坛（干细胞）	十堰市
29	全国性	刘玉龙	第九期全国核应急干部管理培训班	苏州市
30	全国性	陈新建	第三届中国模式识别与计算机视觉大会(3rd Chinese Conference on Pattern Recognition and Computer Vision, PRCV 2020)	南京市
31	全球性	陈华兵	4th Nanomachine Meeting	东京
32	全球性	陈华兵	2020 IEEE Nanotechnology Materials and Devices Conference (NMDC)	南京市
33	全国性	畅　磊	中国毒理学会-第九次全国毒理学大会	太原
34	全国性	畅　磊	中国细胞生物学学会 2020 年全国学术大会·苏州暨 学会成立 40 周年庆	苏州
35	全国性	畅　磊	2020 中国肿瘤学大会	广东广州
36	全国性	胡文涛	中国核学会核应急医学分会成立大会暨第一届理事会第一次会议	苏州
37	全国性	胡文涛	重点研发计划数字诊疗装备研发重点专项项目讨论会	上海
38	全国性	胡文涛	深空探测空间辐射研讨会	北京
39	全国性	刘志勇	第六届辐射与环境专题研讨会	绵阳
40	全国性	杨红英	2020 中国肿瘤学大会	广东广州
41	全国性	胡士军	第十届寒地心脏病学会议	哈尔滨市
42	全国性	周光明, 胡文涛	深空探测空间辐射研讨会	北京

序号	会议类别	报告人	会议名称	会议地点
43	全国性	周光明	载人月球探测“关深”阶段科学研究与应用任务	北京
44	全国性	周光明	核闪光放射治疗学术交流会	四川
45	全国性	周光明	中国生命电子学术年会	广东
46	全国性	周光明	空间环境与物质科学研究院战略研讨会	黑龙江
47	全国性	周光明	中国辐射防护学会放射生态分会 2020 年度年会	四川成都
48	全国性	周光明	第六届“辐射与环境”专题研讨会	四川成都
49	全国性	周光明	四川省原子能农学会 2020 年度年会	四川成都
50	全国性	时玉舫	中国杭州湘湖国际生命将康产业创新区成立一周年暨发展研讨会	杭州
51	全国性	时玉舫	中国干细胞第十届年会	贵阳
52	全国性	时玉舫	云南省灵长类生物医学重点实验学术委员会会议	昆明
53	周边性	阮长耿	江苏省第二十四次血液学学术会议	常州
54	周边性	阮长耿	第九届广州国际血液肿瘤与免疫高峰论坛	广州
55	全国性	阮长耿	第 12 届 WFH 全国血友病大会	贵阳
56	周边性	阮长耿	2019 海峡两岸血液病学术会议 暨姑苏造血干细胞移植和免疫治疗精英论坛	苏州
57	全球性	杨　林	EHA（虚拟会议）	德国 法兰克福
58	全国性	杨　林	CSCO	北京
59	全国性	陈华兵	药学学报前沿论坛	烟台

七、授权专利目录

序号	专利号	专利名称	授权公告日	国家	完成人（固定人员）
1	ZL 201810867119.7	一种紫外光触发交联型近红外分子探针及其制备方法与应用	2020-05-08	中国	史海斌
2	ZL 201810867119.7	叶酸修饰的金纳米颗粒及其制备方法与在制备放射增敏治疗药物中的应用	2020-10-12	中国	史海斌, 高明远
3	ZL 201910696937.X	一种肿瘤微环境H2O2响应交联型近红外分子探针及其应用	2020-10-16	中国	史海斌
4	ZL 201910551670.5	r-谷氨酰转肽酶响应型分子探针及其应用	2020-10-29	中国	史海斌
5	ZL 201910550078.3	作用于小肠的辐射防护纳米药物及其制备方法	2020-05-15	中国	华道本
6	ZL 201910988730.X	用于检测痕量铀酰离子的探针及基于其的便携式 ECL 检测器	2020-07-24	中国	华道本
7	ZL 201710621505.3	含配体的共轭微孔聚合物及其应用	2020-08-11	中国	华道本
8	ZL 201611075209.X	铋化合物在制备细胞自噬引发剂及细胞自噬模型中的应用	2020-08-25	中国	张乐帅, 王杨云
9	US 10,711,324 B2	Method For Removing Radioactive Element Thorium In Rare Earth	2020-07-14	美国	王殳凹
10	ZL 2018 1 0264190.6	含铀化合物作为闪烁体的应用	2020-05-22	中国	王殳凹
11	ZL 2017 1 0099851.X	一种羟基吡啶酮配体及其应用	2020-04	中国	第五娟
12	ZL 2018 1 0922561.5	具有三重发光通道的镧系发光材料及其制备方法	2020-06-30	中国	王殳凹
13	ZL 2019 1 0048805.6	羟基吡咯酮类化合物修饰的碳量子点及其制备和应用	2020-09-18	中国	王殳凹, 第五娟
14	CN 108400360B	一种磷酸锆基质子导体材料及其在燃料电池中的应用	2020-06-18	中国	王殳凹
15	US 10625214 B2	Titanium Dioxide / Sulfonated Graphene Oxide / Ag Nanoparticle Composite Membrane, And Preparation And Application Thereof	2020-04-21	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）
16	US 10618813 B2	Carbon Nitride Modified With Perylenetetracarboxylic Dianhydride / Graphene Oxide Aerogel Composite Material, Preparation Method And Application Thereof	2020-04-14	美国	路建美
17	US 10714690 B2	Auto-polymerization electric storage material based on Dopamine, preparation method thereof and application to Electric storage device thereof	2020-07-14	美国	路建美
18	US 10710915 B2	Graphene aerogel metallic organic frame composite material loaded with microorganism as well as preparation method and application thereof in the treatment of azo dye	2020-07-14	美国	路建美
19	US 10737240 B2	3d ruthenium / graphene aerogel composite loaded with metal-organic frameworks, preparation method thereof, and its application in continuous treatment of co	2020-08-11	美国	路建美
20	US 10730759 B2	Inverse opal material for visible-light-driven photocatalytic degradation of organic pollutants and its preparation method	2020-08-04	美国	路建美
21	US 10773247 B2	Hollow Porous Carbon Nitride Nanospheres Composit Loaded With Agbr Nanoparticles, Preparation Method Thereof, And Its Application In Dye Degradation	2020-09-15	美国	路建美
22	US 10780370 B2	Material used for rapid separation of oil and water And preparation method and application thereof	2020-09-22	美国	路建美
23	ZL 2016 1 0339108.2	低氧处理的间充质干细胞及其应用	2020-08-04	中国	时玉舫

序号	专利号	专利名称	授权公告日	国家	完成人（固定人员）
24	EP 14 795 387.1	Application of mesenchymal stem cells in prophylaxis or treatment of stress response-induced weaken immunity	2020-01-10	欧洲	时玉舫
25	ZL 201610143773.4	RIP3 抑制剂在制备抗血小板血栓药物中的用途	2020-05-18	中国	戴克胜
26	ZL 2017 1 1065730.X	肉豆蔻酸和甘油组合物在评估慢性粒细胞白血病 TKI 疗效的应用	2020-11-24	中国	吴德沛
27	ZL 2017 1 0757969.7	多聚核苷酸-5’激酶-3’磷酸酶的新应用/NEW USE OF POLYNUCLEOTIDE-5' KINASE-3' PHOSPHATASE	2020-11-10	中国	周泉生
28	ZL 201710323138.9	单克隆抗体 6C9G4 及其在制备治疗内毒素血症的药物中的应用	2020-09-08	中国	武　艺
29	ZL 2017 1 1332144.7	囊泡纳米药物在制备脑肿瘤治疗药物中的应用	2020-07-14	中国	钟志远
30	ZL 2017 1 1333193.2	一种单靶向还原响应囊泡纳米药物在制备脑肿瘤治疗药物中的应用	2020-09-25	中国	钟志远
31	ZL 2017 1 1332154.0	囊泡纳米药物在制备脑肿瘤治疗药物中的应用	2020-07-21	中国	钟志远
32	ZL 2018 1 0137028.8	聚合物囊泡在制备治疗多发性骨髓瘤药物中的应用	2020-07-14	中国	钟志远
33	ZL 2018 1 0137029.2	可逆交联不对称囊泡在制备治疗急性白血病药物中的应用	2020-07-14	中国	钟志远
34	ZL 2018 1 0597955.8	抗肿瘤药物及其制备方法	2020-08-14	中国	钟志远
35	ZL 2017 1 0529848.7	四碘甲腺原氨酸-N-羧基内酸酐，聚四碘甲腺原氨酸及其制备方法与应用	2020-09-08	中国	钟志远，邓　超
36	ZL 2018 1 0792522.8	聚乙二醇-b-聚酪氨酸-硫辛酸共聚物，聚多肽胶束及其制备方法与应用	2020-12-05	中国	钟志远，邓　超
37	ZL 201810122820.6	促进多能干细胞分化为心肌细胞成熟的方法	2020-10-09	中国	胡士军
38	ZL 201710057562.3	一种用于肾皮质定位的非均匀图搜索分割算法	2020-06-05	中国	陈新建
39	ZL 201710481505.8	基于随机森林与复合活性曲线的 OCT 图像层分割方法	2020-08-11	中国	陈新建
40	ZL 201710480352.5	基于神经网络与约束图搜索算法的 OCT 图像层分割方法	2020-02-05	中国	陈新建

序号	专利号	专利名称	授权公告日	国家	完成人（固定人员）
41	ZL 201611005068.4	三维大视野扫频光学相干断层成像中脉络膜的分割方法	2020-04-03	中国	陈新建
42	ZL 201711308033.2	基于微液滴的全柔性无源压力传感器及其制造方法及其检测方法	2020-06-23	中国	陈新建
43	ZL 201710829251.4	具有近红外光热效应和多模态成像功能的超小蛋白复合纳米粒及其制备方法和应用	2020-10-02	中国	陈华兵

八、论文目录

序号	论文名称	期刊名称	所有作者	卷、期、页
1	Heavy-Atom-Modulated Supramolecular Assembly Increases Antitumor Potency against Malignant Breast Tumors via Tunable Cooperativity	Advanced Materials	Zhengqing Guo, Hui He, Yi Zhang, Jiaming Rao, Tao Yang, Ting Li, Lu Wang, Mengke Shi, Mengya Wang, Shihong Qiu, Xue Song, Hengte Ke, Huabing Chen	2020, 2004225
2	Construction of an Ion Pathway Boosts Uranium Extraction from Seawater	Chem	Shuo Zhang, Hui Li, ShuaoWang	2020, 6(7):1504-1505
3	A Nitrogen-rich Covalent Organic Framework for Simultaneous Dynamic Capture of Iodine and Methyl Iodide	Chem	Linwei He, Long Chen, Xinglong Dong, Shitong Zhang, Mingxing Zhang, Xing Dai, Xiajie Liu, Peng Lin, Kunfeng Li, Cailing Chen, Tingting Pan, Fuyin Ma, Junchang Chen, Mengjia Yuan, Yugang Zhang, Lei Chen, Ruhong Zhou, Yu Han, Zhifang Chai, Shuao Wang	DOI: 10.1016/j.chempr.2020.11.024
4	Proteasome activity regulated by charged gold nanoclusters: Implications for neurodegenerative diseases	Nano Today	Xiaochuan Ma, Sangyun Lee, Xingshu Fei, Ge Fang, Tien Huynh, Chunying Chen, Zhifang Chai, Cuicui Ge, RuhongZhou	2020, 35:100933
5	Engineering NIR-IIb Fluorescence of Er-Based Lanthanide Nanoparticles for Through-skull Targeted Imaging and Imaging-guided Surgery of Orthotopic Glioma	Nano Today	Feng Ren, Hanghang Liu, Hao Zhang, Zhilin Jiang, Bing Xia, Cécile Genevois, Tao He, Mathieu Allix, Qiao Sun, Zhen Li, Mingyuan Gao	2020, 34, 100905
6	Improved AIE-Active Probe with High Sensitivity for Accurate Uranyl Ion Monitoring in the Wild Using Portable Electrochemiluminescence System for Environmental Applications	Advanced Functional Materials	Ziyu Wang, Jianbin Pan, Qian Li, Yi Zhou, Sen Yang, JingJuan Xu, Daoben Hua	2020, 30, 2000220

序号	论文名称	期刊名称	所有作者	卷、期、页
7	Red Light-initiated Crosslinking of NIR Probes to Cytoplasmic RNA: An Innovative Strategy for Prolonged Imaging and Unexpected Tumor Suppression	Journal of the American Chemical Society	Shuyue Ye, Chaoxiang Cui, Xiaju Cheng, Meng Zhao, Qiulian Mao, Yuqi Zhang, Anna Wang, Jing Fang, Yan Zhao, and Haibin Shi	2020, 142 (51), 21502–21512.
8	Targeting Microglia for Therapy of Parkinson's Disease by Using Biomimetic Ultrasmall Nanoparticles	Journal of the American Chemical Society	Hanghang Liu, Yaobao Han, Tingting Wang, Hao Zhang, Qi Xu, Jiaxin Yuan, Zhen Li	2020, 142, 52, 21730–21742
9	Engineering Fe−N Doped Graphene to Mimic Biological Functions of NADPH Oxidase in Cells	Journal of the American Chemical Society	Di Wu, Jingkun Li, Shujuan Xu, Qianqian Xie, Yanxia Pan, Xi Liu, Ronglin Ma, Huizhen Zheng, Meng Gao, Weili Wang, Jia Li, Xiaoming Cai, Frede ric Jaouen, and Ruibin Li	2020;142,19602-19610
10	Electron Beam Irradiation as a GeneralApproach for the Rapid Synthesis of Covalent organic Frameworks under AmbientConditions	Journal of the American Chemical Society	Mingxing Zhang, Junchang Chen, Shitong Zhang, Xiaoqi Zhou, Linwei He, Matthew V. Sheridan, Mengjia Yuan, Maojiang Zhang, Long Chen, Xing Dai, Fuyin Ma, Jingdong Wang, Jiangtao Hu, Guozhong Wu, Xueqian Kong, Ruhong Zhou, Thomas E. Albrecht-Schmitt, Zhifang Chai, Shuao Wang	2020, 142(20):9169-9174
11	Three-Dimensional Polycatenation of a Uranium-Based Metal-Organic Cage: Structural Complexityand Radiation Detection	Journal of the American Chemical Society	Liwei Cheng, Chengyu Liang, Wei Liu, Yaxing Wang, Bin Chen, Hailong Zhang, Yanlong Wang, Zhifang Chai, Shuao Wang	2020, 142(38):16218-16222
12	Asynchronous actions of immune responses in COVID-19 patients	Signal Transduction and Targeted Therapy	Yufang Shi, Guoqiang Zhou, Qing Li	2020, 5(1), 284

序号	论文名称	期刊名称	所有作者	卷、期、页
13	Robust and smart polypeptide-based nanomedicines for targeted tumor therapy	Advanced Drug Delivery Reviews	Chao Deng , Qiang Zhang, Jiakun Guo, Xiaofei Zhao, Zhiyuan Zhong	2020;160:199-211.
14	Bacteria-triggered tumor-specific thrombosis to enable potent photothermal immunotherapy of cancer	Science Advances	Xuan Yi, Hailin Zhou,Yu Chao, Saisai Xiong, Jing Zhong, Zhifang Chai, Kai Yang, Zhuang liu	2020; 6 : eaba3546
15	IGF2R-initiated proton rechanneling dictates an anti-inflammatory property in macrophages	Science Advances	Xuefeng Wang, Liangyu Lin, Bin Lan, Yu Wang, Liming Du, Xiaodong Chen, Qing Li, Keli Liu, Mingyuan Hu, Yueqing Xue, Arthur I. Roberts, Changshun Shao, Gerry Melino, Yufang Shi, Ying Wang	2020; 6 : eabb7389
16	An Activatable Polymeric Reporter for Near-Infrared Fluorescent and Photoacoustic Imaging of Invasive Cancer	Angewandte Chemie-International Edition	Qing Li, Shenhua Li, Shasha He, Wan Chen, Penghui Cheng, Yan Zhang, Qingqing Miao, Kanyi Pu	2020, 59, 7018 – 7023
17	Two-Dimensional Tin Selenide (SnSe) Nanosheets Capable of Mimicking Key Dehydrogenases in Cellular Metabolism	Angewandte Chemie International Edition	M Gao, Z Wang, H Zheng, L Wang, S Xu, X Liu, W Li, Y Pan, W Wang, X Cai, R Wu, X Gao, R Li	2020;59,3618-3623
18	Engineering the Protein Corona Structure on Gold Nanoclusters Enables Red-Shifted Emissions in the Second Near-infrared Window for Gastrointestinal Imaging	Angewandte Chemie International Edition	W Wang, Y Kong, J Jiang, Q Xie, Y Huang, G Li, Di Wu, H Zheng, M Gao, S Xu, Y Pan, W Li, R Ma, Mei X Wu, X Li, H Zuilhof, X Cai, R Li	2020;59, 22431-22435
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67	The role of electrostatic potential polarization in the translocation of graphene quantum dots across membranes	Nanoscale	Xiaofeng Tang, Shitong Zhang, Hong Zhou, Bo Zhou, Shengtang Liu, and Zaixing Yang	2020, 12, 2732-2739
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Heavy-Atom-Modulated Supramolecular Assembly Increases Antitumor Potency against Malignant Breast Tumors via Tunable Cooperativity

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

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

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

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

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Previews

Construction of an Ion Pathway Boosts Uranium Extraction from Seawater

Shuo Zhang,[1] Hui Li,[1] and Shuao Wang[1,*]

Uranium extraction from seawater (UES) is critical for the sustainable development of nuclear energy but faces tremendous scientific and technical challenges. In this issue of *Chem*, Zhu and colleagues propose an advanced UES strategy incorporating an extended electric field that can facilitate the migration of uranium species in the channels of sorption materials, leading to record-breaking kinetics, selectivity, and capacity of UES.

Nuclear power remains one of the most desirable and mature choices of energy sources that can reduce carbon emission.[1] However, at the current rate of uranium consumption, the known geological reserves of uranium will be exhausted in less than a century—perhaps even sooner given the many new nuclear power plants that are either under construction or planned in several countries.[2,3] Alternatively, the ocean contains approximately 4.5 billion tons of uranium, accounting for 99.9% of the total uranium inventory on Earth, but the concentration of 3.3 ppb is unfortunately extremely low, and the uranium coexists with many different types of metal ions in huge excess. This makes uranium extraction from seawater (UES) one of the "seven chemical separations to change the world," but it comes with intrinsic challenges.[4] The current development of UES is dominated by the search for high-performance sorbent materials that can enrich uranium in the solid phase through a chemical sorption reaction. In order to show real applications to potentially replace the uranium mining industry, a target sorbent material should meet the requirements of a one-run uptake capacity of 30 mg g^{-1} or a service life of ten adsorption-desorption cycles with a 6 mg g^{-1} uptake capacity and an average 3% capacity loss per cycle.[5,6]

Although a significant amount of effort has been paid to this field in the past decade, almost no uranium sorbent materials can meet the above requirements because of their limited extraction efficiencies.[5] Specifically, in these traditional sorbent materials, where the chemical sorption reaction is the sole thermodynamic driving force, the amount of uranium uptake is predominately determined by the chemical equilibrium between the solid and solution states. Therefore, the extremely low concentration of uranium in seawater directly leads to low uptake capacity in solids, and the complete elimination of uranium from seawater is quite challenging without additional driving forces. Moreover, the small uranium concentration gradient at the solid-solution interface and the extensive sorption competition induced by coexisting metal ions (especially vanadium and iron) result in notably slow uranium-uptake kinetics. These are bottleneck issues of traditional sorbent materials, calling for new UES strategies.[7]

In this issue of *Chem*, Zhu's team proposes an interesting idea whereby a new type of driving force is added to the sorbent material, leading to much elevated UES capabilities.[8] They inserted conductive chains (poly phenylacetylene [PPA]) into the channels of the channel- and specific-site-abundant porous aromatic framework (PAF) MISS-PAF-1 (PAFs bearing bissalicyladoxime as adsorption sites) and obtained PPA@MISS-PAF-1 (Figure 1) to potentially introduce an extended electric field that could cover the whole PAF particles. This contrasts sharply with the recently developed electrochemical UES strategy using the ordinary electrode mode that works in Deby length (λ_D < 1 nm) only.[7] The asymmetrical alternating current electrochemical (AACE) method significantly facilitates the migration of uranium into the PAF, leading to a dramatic increase in the uranium-uptake kinetics. In addition, amidoxime is the state-of-the-art ligand for UES, but its affinity to uranium is often challenged by vanadyl ions, especially in the form of polyamidoximes.[9] Interestingly, PPA@MISS-PAF-1 showed excellent selectivity via the AACE method in that it achieved a selectivity coefficient (mass ratio) of 43.9 for UO_2^{2+}/VO_3^-, 20-fold higher than those of state-of-the-art UES sorbents.[5] This excellent selectivity most likely originates from a combination of the unique uranium molecularly imprinted spatial structure of MISS-PAF-1[10] and the charge-differentiation capability induced by the extended electric field, both of which exclude the accumulation of VO_3^- in the sorbent.

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A Nitrogen-rich Covalent Organic Framework for Simultaneous Dynamic Capture of Iodine and Methyl Iodide

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SUMMARY

The capture of radioiodine species during nuclear fuel reprocessing and the nuclear accidents is crucial for nuclear safety, environmental protection, and public health. Previously reported emerging materials for iodine uptake cannot outperform commercial zeolites and active carbon under the practical dynamic scenario. Herein we present a new design philosophy aiming at significantly enhanced specific host-guest interactions and obtain a nitrogen-rich covalent organic framework material by introducing a bipyridine group into the building block for the simultaneous capture of both iodine gas through enhanced electron-pair effect and organic iodide via the methylation reaction. These efforts give rise to not only an ultrahigh uptake capacity of 6.0 g g^{-1} for iodine gas and a record high value of 1.45 g g^{-1} for methyl iodide under static sorption conditions, but also more importantly a record high iodine loading capability under dynamics conditions demonstrated from the breakthrough experiments.

covalent organic frameworks; pyridine; iodine; sorption; breakthrough experiment

INTRODUCTION

Iodine isotopes make up approximately 0.69 mass% in the fission products of uranium-235 in the nuclear fuel cycle, representing a large inventory in the nuclear waste.[1] A large amount of radioiodine is released from reprocessing facilities when used nuclear fuel (UNF) is dissolved in concentrated nitric acid. The dominant chemical species in the dissolver off-gas (DOG) stream is highly volatile diatomic elemental iodine (I_2, 90~100%) along with a small fraction of organic iodides (e.g. methyl iodide and ethyl iodide, 0~10%).[2-3] The primary concerned iodine isotope is ^{129}I due to its extremely long half-life (1.6×10^7 years), toxicity, and high mobility in most geological environment.[1] ^{131}I also draws tremendous amount of public attention especially in an event of nuclear accident owing to its much higher specific activity with a short half-life of 8.02 d. It represents the major contribution to the short-term radiotoxicity to human beings given radioiodine can accumulate in the thyroid gland affecting the metabolism process.[4] After discharged from a fast breeder reactor, the amount of ^{129}I is 239 g with the radioactivity of 3.9×10^{-2} Ci. For ^{131}I, the value is 11.3 g but with extremely high radioactivity of 1.4×10^6 Ci (according to 1 metric ton of UNF). After one year, the amount of ^{131}I is negligible (2.54×10^{-15} g with 3.15×10^{-8} Ci) while the content of ^{129}I is almost unchanged (242 g with 3.94×10^{-2} Ci).[5] Therefore, development of functional materials to efficiently control the emission of radioiodine vapors is of great significance but remains to be a challenge,[6-7] originating from the complicated scenario in fuel reprocessing off-gases, where iodine is present in low concentrations along with large excess of moisture and oxidizing acidic gas at elevated temperatures.[1]

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Proteasome activity regulated by charged gold nanoclusters: Implications for neurodegenerative diseases

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ABSTRACT

The 20S proteasome, the catalytic core particle of 26S proteasome, degrades a wide range of intracellular proteins, which is essential for many cellular processes. Herein, we have found that the 20S proteasome activity is either up- or down-regulated by introducing gold nanoclusters (AuNCs) coated with nine peptide tails in two different forms, AuNC(−) and AuNC(+), each encoding five consecutive negatively or positively charged amino acids. Molecular dynamics simulations reveal that AuNC(−) and AuNC(+) bind to different surfaces of the 20S proteasome, and respectively facilitate or hinder the opening of the central gate of 20S proteasome for substrate access to the internal active site for protein degradation. Furthermore, the addition of AuNC(-) induces protective effects in a cell model of Parkinson's disease, by up-regulating the proteasome activity under the condition of reduced ATP production, and enhancing the degradation of overexpressed α-synuclein, thereby attenuating the loss of cell viability. Our findings suggest the potential application of gold nanoclusters for treating neurodegenerative diseases.

Introduction

Nanomaterials are capable of binding strongly to various biomolecules due to their higher surface free energy. Studies on the interaction of nanomaterials with proteins have received much attention in recent years due to their wide potential in biomedical applications, not only revealing the new biological identity of the nanomaterials [1–3] and underlying mechanism of how they affect protein structures and functions [4–10], but also providing novel methods to characterize the nanoparticle biomolecular interactions [11–13]. In this work, we focus on the ubiquitin–proteasome system (UPS) which serves as part of a major cellular proteolytic machinery that maintains the protein homestasis [14–16]. The 26S proteasome is a catalytic center in the UPS containing multiple active sites which mediates the degradation of misfolded, damaged, unnecessary and short-lived regulatory proteins tagged by poly-ubiquitin chains [17,18]. The 26S proteasome is composed of two 19S regulatory unit and one 20S catalytic core particle. The 20S proteasome is distributed in various cellular compartments, while contributing to about one percent of the total protein content in cells [19,20]. A decline of the proteasome activity, correlating with the progressive accumulation of damaged protein aggregates, has been recognized as the major contributor in the pathogenesis of neurodegenerative disorder diseases [21–25].

Here, we report the first experimental evidence that proteasome activity is either up- or down-regulated by two different forms of gold nanocluster (AuNC) coated by peptide tails encoding either negatively or positively charged amino acids in their sequences, named as AuNC(−) and AuNC(+), respectively. Our molecular dynamics (MD) simulations showed that the central gate opening in the α ring of the 20S proteasome, for substrate entry and product release, was either facilitated or hindered, when AuNC(−) or AuNC(+) binds to different regions of the surface of 20S proteasome. Furthermore, with a cell model for Parkinson's disease (PD), we found a protective role of AuNC(−), recovering the proteasome

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Engineering NIR-IIb fluorescence of Er-based lanthanide nanoparticles for through-skull targeted imaging and imaging-guided surgery of orthotopic glioma

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ABSTRACT

Highly sensitive and specific discrimination of brain tumor margins from the surrounding parenchyma remains a formidable challenge. Limited by the short of photostable probes with deep tissue penetration and high efficiency of crossing the blood-brain-barrier (BBB), the development of fluorescence-guided surgery (FGS) of brain tumors was markedly constrained. Herein, we report the capability of the strong second near-infrared-IIb (NIR IIb, 1500–1700 nm) fluorescence from Er-based lanthanide nanoparticles in imaging-guided surgery of orthotopic glioma. We designed an energy-cascaded Er^{3+}-Ce^{3+}-A^{3+} (A = Yb, Ho, Tm) system and prepared a series of $NaErF_4$:Ce@$NaAF_4$@$NaLuF_4$ down-conversion nanoparticles (DCNPs) for optimizing the influence of $NaAF_4$ interlayer and Ce^{3+} dopants. We modified the optimal $NaErF_4$:2.5 %Ce@$NaYbF_4$(0.9 nm)@$NaLuF_4$ DCNPs with Dye-brush polymer (Dye-BP) to facilitate $^4I_{13/2} \rightarrow {}^4I_{15/2}$ transition, which leads to an impressive 675-fold enhancement of 1525 nm fluorescence in aqueous solution under 808 nm excitation due to the excellent energy-cascaded downconversion (ECD), in comparison with that of $NaErF_4$ nanoparticles. We further modified these highly bright nanoparticles with tumor-targeting angiopep-2 peptide, and efficiently delivered them to the glioma by using the focused ultrasound sonication (FUS) to temporarily open the BBB. We obtained the highest tumor-to-background ratio (TBR = 12.5) ever reported in the targeted NIR IIb fluorescence imaging of small orthotopic glioma (size < 3 mm, depth> 3 mm) through intact skull and scalp, which was drastically improved to ~150 after cardiac perfusion and craniotomy to ensure the precise resection of tumor. More importantly, the size of glioma measured from the width of fluorescence profile is very close to that from T_2-weighted MRI images. Our work provides the insights into engineering NIR IIb fluorescence of lanthanide nanoparticles, and demonstrates the great potential of NIR IIb fluorescence imaging-guided surgery of tumor.

Introduction

Finely and clearly visualizing the margins of brain tumors, especially for glioblastoma (GBM), which is the most common malignant brain tumor, from the surrounding parenchyma is the lynchpin for their precise diagnosis and surgery [1–3]. Although the typical use of visual inspection and imaging guidance can provide valuable information for clinicians, the intrinsic limitations of currently available imaging methods, such as low sensitivity, non-dynamical inspection, and hazardous ionizing radiation, can cause intraoperative failure in completely resecting tumor tissues [1,4–6]. In addition, for fluorescence-guided surgery (FGS) of brain tumors, photostable probes with strong capability of crossing the blood-brain-barrier (BBB) are crucial for precise delineation glioma margin and the subsequent curative resection. The intrinsic drawbacks of clinically used probes (5-aminolevulinic acid (5-ALA) [7,8] and indocyanine green (ICG) [9,10]), such as insufficient photostability [11] and short excitation/emission wavelength-induced low

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Improved AIE-Active Probe with High Sensitivity for Accurate Uranyl Ion Monitoring in the Wild Using Portable Electrochemiluminescence System for Environmental Applications

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The development of highly sensitive and selective uranyl ion (UO_2^{2+}) probes has attracted significant attention owing to the threat to human health caused by high toxicity, radioactivity, and long half-life. Herein, the development of aggregation-induced emission (AIE) active polymer dots (Pdots) is described for an accurate UO_2^{2+} monitoring using a portable electrochemiluminescence (ECL) system. An AIE-active polymer containing tetraphenylethene and boron ketoiminate moieties is prepared into Pdots and modified with ssDNA to capture UO_2^{2+}, which can amplify the ECL signal of the Pdots through a resonance energy transfer mechanism. This probe provides an ultralow detection limit of 10.6 pM/2.5 ppt, which is at least two orders of magnitude lower than the known UO_2^{2+} luminescent probes. Only UO_2^{2+} can provide an obvious ECL enhancement among the various metal ions, indicating the excellent selectivity of this probe. Furthermore, a portable ECL analyzer is designed to realize UO_2^{2+} measurements in the wild. The anodic ECL mechanism of UO_2^{2+} is discovered and ECL technology is first applied in monitoring radioactive substances. This study provides a novel strategy for the development of accurate UO_2^{2+} probes and a practical UO_2^{2+} monitoring method, indicating its potential application in the environmental and energy fields.

1. Introduction

Nuclear power has become a significant technology for supplying electricity while avoiding greenhouse gases, providing 13% of the electricity worldwide from 2000 to 2013.[1] Uranium, a key element in nuclear fuel, is regarded as a hazardous substance with a high chemical toxicity, radioactivity, as well as long half-life, and has become a major threat to human health and a serious environmental problem.[2] Owing to the extreme limits to uranyl ions (UO_2^{2+}) (the most stable form of uranium) in the environment imposed by the World Health Organization and various national governments, the development of accurate UO_2^{2+} monitoring technologies for application in the environmental and energy fields is important.[2] Therefore, various researchers have focused on designing UO_2^{2+} probes with high sensitivity and selectivity[3] and have developed different methods for UO_2^{2+} determination, such as DNAzyme,[3] luminescent probes,[4] and colorimetric determination.[5] Compared to other UO_2^{2+} probes, UO_2^{2+} luminescent probes are an excellent tool owing to their low cost and convenience.[6]

Unfortunately, most traditional UO_2^{2+} luminescent probes often suffer from aggregation-caused quenching, which results in low quantum yields in aqueous solutions. The development of aggregation-induced emission (AIE)-active probes can overcome this drawback. AIE-active luminogens exhibit obviously enhanced luminescence signals in aggregated states, such as in aqueous solutions, owing to their restriction of intramolecular motions mechanism.[7] Because of this advantage, many studies on the design of different AIE-active luminescent probes have been reported during the past few years,[8] including efficient AIE-active UO_2^{2+} luminescent probes. To date, several small molecular AIE-active UO_2^{2+} probes have been reported.[9] However, the sensitivity of these probes is still insufficient for accurately monitoring trace UO_2^{2+} in the environment.

To obtain a UO_2^{2+} probe with high sensitivity, electrochemiluminescence (ECL) technology is an outstanding choice, involving electron transfers on the surface of the electrodes,

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Red Light-Initiated Cross-Linking of NIR Probes to Cytoplasmic RNA: An Innovative Strategy for Prolonged Imaging and Unexpected Tumor Suppression

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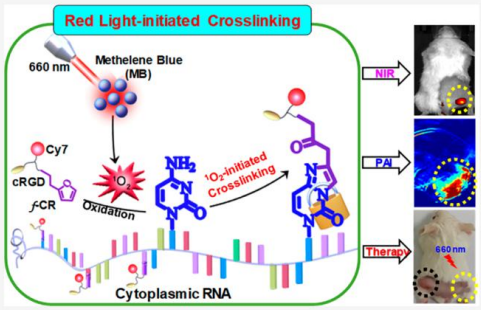
ABSTRACT: Improving the enrichment of drugs or theranostic agents within tumors is very vital to achieve effective cancer diagnosis and therapy while greatly reducing the dosage and damage to normal tissues. Herein, as a proof of concept, we for the first time report a red light-initiated probe-RNA cross-linking (RLIPRC) strategy that can not only robustly promote the accumulation and retention of the probe in the tumor for prolonged imaging but also significantly inhibits the tumor growth. A near-infrared (NIR) fluorescent probe *f*-CR consisting of a NIR dye (Cyanine 7) as a signal reporter, a cyclic-(arginine-glycine-aspartic acid) (cRGD) peptide for tumor targeting, and a singlet oxygen ($^1O_2$)-sensitive furan moiety for RNA cross-linking was rationally designed and synthesized. This probe possessed both passive and active tumor targeting abilities and emitted intense NIR/photoacoustic (PA) signals, allowing for specific and sensitive dual-modality imaging of tumors in vivo. Notably, probe *f*-CR could be specifically and covalently cross-linked to cytoplasmic RNAs via the cycloaddition reaction between furan and adenine, cytosine, or guanine under the oxidation of $^1O_2$ generated in situ by irradiation of methylene blue (MB) with 660 nm laser light, which effectively blocks the exocytosis of the probes resulting in enhanced tumor accumulation and retention. More excitingly, for the first time, we revealed that the covalent cross-linking of probe *f*-CR to cytoplasmic RNAs could induce severe apoptosis of cancer cells leading to remarkable tumor suppression. This study thus represents the first red light-initiated RNA cross-linking system with high potential to improve the diagnostic and therapeutic outcomes of tumors in vivo.



INTRODUCTION

As an important part of molecular imaging techniques, the molecular probe is becoming a fascinating tool for accurate cancer diagnosis and effective treatment.[1] To date, various types of molecular probes including small molecules,[2−5] macromolecules,[6−8] inorganic nanomaterials,[9,10] aptamers,[11,12] etc.[13−18] have been successfully developed for tumor imaging and therapeutic applications in living subjects.[19,20] Nevertheless, the limited accumulation of probes at targeted disease regions always causes unsatisfactory diagnostic and therapeutic outcomes.[21−27] To address this issue, a high dose of theranostic agents was usually administered[28] or utilizing bionanomaterials with long blood circulation, low renal clearance, and capillary leakage to improve their enrichment at the disease site,[29−32] which inevitably causes severe side effect to the body. Recently, stimuli-mediated self-assembly approaches have been reported to maximize the accumulation and retention of theranostic agents within tumors for improving the tumor diagnostic and therapeutic efficacy.[33−38] Many tumor microenvironment (TME)-responsive molecules that can be induced by certain stimuli such as cancer-associated enzymes,[39,40] acidic pH,[41] redox,[42] hypoxia,[43] etc.[44−49] to locally form aggregates or nanoparticles within tumors resulting in enhanced imaging signals and therapeutic efficacy were developed.[50−53] Despite the evident improvement achieved, the complicated biological environment may unavoidably pose unwanted particle aggregation and significant entrapment by the reticuloendothelial system (RES) leading to unsatisfactory theranostic outcomes.[54,55]

Light as a promising and controllable external stimulus has been widely applied in various biomedical applications due to its simplicity, low-cost, spatiotemporal addressability, and minimal invasiveness.[56] For example, the photo-cross-linking technique as an effective tool for covalent attachment of

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Targeting Microglia for Therapy of Parkinson's Disease by Using Biomimetic Ultrasmall Nanoparticles

Hanghang Liu, Yaobao Han, Tingting Wang, Hao Zhang, Qi Xu, Jiaxin Yuan, and Zhen Li*

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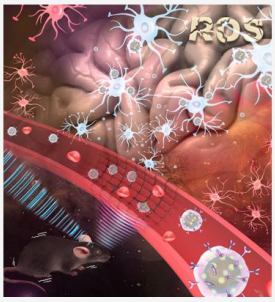
ABSTRACT: Microglia as an important type of innate immune cell in the brain have been considered as an effective therapeutic target for the treatment of central nervous degenerative diseases. Herein, we report cell membrane coated novel biomimetic $Cu_{2-x}Se$-PVP-Qe nanoparticles (denoted as CSPQ@CM nanoparticles, where PVP is poly(vinylpyrrolidone), Qe is quercetin, and CM is the cell membrane of neuron cells) for effectively targeting and modulating microglia to treat Parkinson's disease (PD). The CSPQ nanoparticles exhibit multienzyme activities and could effectively scavenge the reactive oxygen species and promote the polarization of microglia into the anti-inflammatory M2-like phenotype to relieve neuroinflammation. We reveal that biomimetic CSPQ@CM nanoparticles targeted microglia through the specific interactions between the membrane surface vascular cells adhering to molecule-1 and $\alpha 4\beta 1$ integrin expressed by microglia. They could significantly improve the symptoms of PD mice to result in an excellent therapeutic efficacy, as evidenced by the recovery of their dopamine level in cerebrospinal fluid, tyrosine hydroxylase, and ionized calcium binding adapter protein 1 to normal levels. Our work demonstrates the great potential of these robust biomimetic nanoparticles in the targeted treatment of PD and other central nervous degenerative diseases.



INTRODUCTION

Parkinson's disease (PD) is the second most common major central nervous degenerative disease, which is especially common in elderly people and has become a serious economic and social burden.[1] The current clinical treatment of PD is strongly reliant on chemical drugs (e.g., dopaminergic-type drugs, anticholinergics, glutamate antagonist). The chemotherapy of PD faces the challenge of effective targeted delivery of robust drugs to substantia nigra and striatum of the brain, however, due to the lack of targeting capability of drugs and the protection of the blood brain barrier (BBB). Moreover, the chemotherapy only relieves the patient's symptoms and cannot completely stop the progress of the disease or reverse the existing disabilities.[2] An alternative solution is surgical treatment, such as the neuronuclear destruction and deep brain stimulation (DBS).[3] The implantation of electrodes is invasive, however, with risks of inflammation and brain trauma.[4] It is of great importance to develop advanced noninvasive treatments for PD patients.

From a pathogenetic perspective, PD is usually characterized by the loss of dopaminergic neurons in the substantia nigra and striatum and the intracellular accumulation of α-synuclein,[5] both which involve multiple pathways and mechanisms, including oxidative stress, neuroinflammation, mitochondrial dysfunction, formation of Lewy bodies, and so on.[6−8] Under normal conditions, the homeostasis between oxidation and antioxidation and the resulting microenvironment of the brain are finely supervised and maintained by microglia.[9] Breaking such homeostasis in the brain could lead to an accumulation of excessive ROS to cause neuronal death and neural dysregulation.[10] Microglia usually participate in ROS generation, and ROS in turn can activate microglia to secrete proinflammatory factors and exacerbate inflammation, eventually leading to the apoptosis of neuronal cells.[11,12] In addition, excessive activation of microglia can cause astrocytes to convert to the pathological A1 morphology, which also results in various neurodegenerative diseases, including PD.[13]

The above statements demonstrate that microglia could be an important target for treating various neurodegenerative diseases. The interrelationship between microglia and ROS suggests that the elimination of excess ROS could significantly modulate the overactivation of microglia and alleviate the oxidative damage to neurons to improve the efficacy of PD treatment. There are two types of antioxidants for the elimination of ROS in the brain, i.e., enzymatic antioxidants, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), and nonenzymatic antioxidants, including vitamin C, vitamin E, reduced glutathione, carotenoids, trace elements, etc.[14] The amount and activity of endogenous antioxidant enzymes are decreased and

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Engineering Fe–N Doped Graphene to Mimic Biological Functions of NADPH Oxidase in Cells

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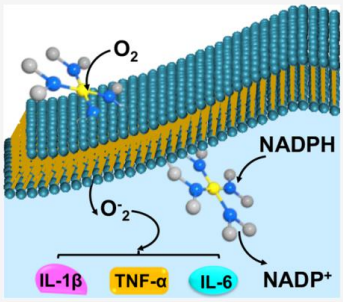
ABSTRACT: NADPH oxidase (NOX) as a transmembrane enzyme complex controls the generation of superoxide that plays important roles in immune signaling pathway. NOX inactivation may elicit immunodeficiency and cause chronic granulomatous disease (CGD). Biocompatible synthetic materials with NOX-like activities would therefore be interesting as curative and/or preventive approaches in case of NOX deficiency. Herein, we synthesized a Fe–N doped graphene (FeNGR) nanomaterial that could mimic the activity of NOX by efficiently catalyzing the conversion of NADPH into $NADP^+$ and triggering the generation of oxygen radicals. The resulting FeNGR nanozyme had similar cellular distribution to NOX and is able to mimic the enzyme function in NOX-deficient cells by catalyzing the generation of superoxide and retrieving the immune activity, evidenced by TNF-α, IL-1β, and IL-6 production in response to Alum exposure. Overall, our study discovered a synthetic material (FeNGR) to mimic NOX and demonstrated its biological function in immune activation of NOX-deficient cells.



INTRODUCTION

The membrane-bound oxidase enzyme called nicotinamide adenine dinucleotide phosphate (NADPH) oxidase is crucial to maintain a healthy level of reactive oxygen species (ROS) in phagocytic and vascular cells of mammals.[1,2] NADPH oxidase (NOX) is an enzyme complex consisting of six subunits: three cytosolic subunits ($p40^{phox}$, $p47^{phox}$ and $p67^{phox}$), a cytochrome b558 ($p22^{phox}$, $gp91^{phox}$), and a small G protein Rac.[3] Cytosolic subunits and $gp91^{phox}$ take part in the hydrogen abstraction of NADPH and one-electron reduction of molecular oxygen, respectively. Small G protein is a crucial switch to control the activation of the oxidase. While this enzyme is dormant under normal circumstances, it is activated during respiratory burst to generate superoxide and activate immune responses against foreign stimuli.[4] NOX deficiency may directly cause chronic granulomatous disease (CGD) in which the immune cells fail to generate essential oxygen radicals and burst immune responses for clearance of pathogenic bacteria and fungi.[5,6] Thus, CGD patients experience repeated infections and often develop severe granulomas leading to obstructive lesions in the stomach, urinary tract, and esophagus.[7] Although NOX is crucial to the normal functioning of the immune system of cells,[8,9] the purification and reconstruction of this enzyme is very challenging. In addition, while being attractive and logical, no attempts have been made hitherto to explore synthetic materials for mimicking the enzymatic activity of NOX.

Toward this goal, the rapid development of nanotechnologies has provided opportunities to engineer inorganic and/or organic nanocatalysts with enzyme-like activity, a.k.a. nanozymes[10−16] for tumor therapy,[17,18] antimicrobial,[19] and bioanalysis uses.[20−23] For instance, Fe_3O_4, nitrogen-doped carbon nanoparticles, and graphene oxide were found to display peroxidase-like activity;[24−26] carbon nitride and gold nanoparticles showed oxidase-like activity;[27,28] noble metal nanoparticles and SnSe nanosheets exhibited superoxide dismutase-[29] and dehydrogenase-like[30] activities, respectively. While most nanozymes could merely mimic simple enzymes to catalyze the degradation of H_2O_2, $O_2^{\bullet-}$, hydrogen transfer, etc, there is yet no identified nanozymes to mimic NOX, an enzyme complex, the activation of which requires the assembly of two or more proteins. NOX is able to catalyze the formation of superoxide radicals via selective hydrogen abstraction and one-electron transfer from NADPH to oxygen. Considering the decisive role of the heme core of NOX in electron transfer from NADPH, we hypothesized that Fe–N doped graphene (FeNGR) nanosheets with embedded single-metal atom catalytic sites similar to heme-like local coordination are able to mimic the biological functions of NOX in cells (Figure S1).

In this study, $Fe–N_x$ moieties covalently embedded in graphene (GR) sheets were prepared and characterized. We exploited liquid chromatography to examine the conversion of

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Communication

Electron Beam Irradiation as a General Approach for the Rapid Synthesis of Covalent Organic Frameworks under Ambient Conditions

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ABSTRACT: Crystalline porous materials such as covalent organic frameworks (COFs) are advanced materials to tackle challenges of catalysis and separation in industrial processes. Their synthetic routes often require elevated temperatures, closed systems with high pressure, and long reaction times, hampering their industrial applications. Here we use a traditionally unperceived strategy to assemble highly crystalline COFs by electron beam irradiation with controlled received dosage, contrasting sharply with the previous observation that radiation damages the crystallinity of solids. Such synthesis by electron beam irradiation can be achieved under ambient conditions within minutes, and the process is amendable for large-scale production. The intense and targeted energy input to the reactants leads to new reaction pathways that favor COF formation in nearly quantitative yield. This strategy is applicable not only to known COFs but also to new series of flexible COFs that are difficult to obtain using traditional methods.

State-of-the-art crystalline porous materials such as covalent organic frameworks (COFs) are being utilized in a number of research fields, e.g., gas purification, catalysis, biomedicine, and energy storage,[1] because of the structural tunability of their organic linkages and the structural robustness of covalent bonds.[2] COFs have been predominantly synthesized by solvothermal/hydrothermal reactions, with thermal energy as the exclusive input for the activation of reactions. However, thermal treatment is an inefficient process, as most of the energy is deposited in thermal motion of the reagents and solvents instead of activation of the chemical bonds. In general, the formation and crystallization of COFs require long reaction times on the order of hours or days and continuous heating above 100 °C. Besides, these syntheses often have to be conducted in a closed environment to maintain the solvent level and autogenous pressure, which is difficult to translate to industrial production.[3]

Research to find more green and high-throughput synthetic strategies has focused on the development of new types of energy sources. For instance, microwave energy and low-energy photons such as UV light have been utilized to accelerate the synthesis, as well as, more recently, electrochemistry.[4] Still, closed systems, elevated temperatures, and special apparatus constraints are often required, and there is no general method applicable to these porous materials. Over the past few decades, sources of high-energy ionizing radiation such as γ rays and electron beams have been adopted as unique energy sources for the synthesis and modification of a variety of functional materials, including organic polymers and inorganic nanoparticles.[5] These high-energy particles not only directly deposit energy into the reagents to overcome the reaction activation barrier but also ionize the whole reaction system, including the solvent, to produce a series of highly reactive species that can significantly accelerate the reaction. This unique activation mode allows for more mild reaction conditions and simpler operation and can give rise to rapid and quantitative formation of the products. However, previous studies produced only amorphous structures, probably because of the degradation effect of excessive radiation.[6] Here we successfully balance radiation-induced activation for product formation and radiation-induced structural degradation to produce porous crystalline materials of high quality. By controlling the absorbed dose, we obtained a variety of products in ultrashort periods of time (within several minutes) under ambient temperature. Only a radiation source and simple apparatus are required, and the setup is amendable for high-throughput industrial production. This synthetic route can be generalized for different COFs, including series of new structures that cannot be obtained by traditional methods.

The radiation-induced synthesis of COFs was carried out using high-energy (1.5 MeV) electron beam irradiation provided by an electron accelerator. The initial material target

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RESEARCH HIGHLIGHT OPEN

Asynchronous actions of immune responses in COVID-19 patients

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Various components of the immune system are fine-tuned and coordinated for the protection and maintenance of tissue homeostasis in various organs. Evolution has ensured the precise activation and synchronization of specific immune components at a given time to provide proper defense and regeneration environment to tissues of our body. Any disorders may lead to imperfect protection and uncontrolled tissue damages. A new study from the Sette and Crotty group just reported in Cell demonstrated that COVID-19 patients, especially at elder ages, suffered the most when the immune components were asynchronous.[1]

Like most viral infections, SARS-CoV-2 elicits strong inflammatory responses. It has been proposed that the immune responses induced by SARS-CoV-2 infection are two-phased. Specific adaptive immune responses are critical for the elimination of the virus during the incubation and non-severe stages and for stopping disease progression to severe stages. When the protective immune responses are insufficient, due to genetic predisposition or preexisting medical conditions, the virus will propagate and massive destruction of the affected tissues, such as lungs, will occur.[2] Most studies are focused on the inflammation and tissue damages at severe stages. However, recent investigations on non-severe or convalescent patients have provided clues to the understanding of protective immune responses.

In an effort to understand human $CD4^+$ and $CD8^+$ T cell responses to SARS-CoV-2 infection, the same research group employed human leukocyte antigen (HLA) class I and II predicted peptide "megapools"[3] and $CD8^+$ and $CD4^+$ T cells from convalescent patients and found that 87% and 93% of these recovered patients possessed SARS-CoV-2-specific $CD8^+$ and $CD4^+$ T cells, respectively.[1] Remarkably, when antibodies (Abs) made from B cell clones derived from convalescent patients were tested for their ability to neutralize SARS-CoV-2 virus in vitro in plastic and in vivo in hamsters, it was found that the receptor binding domain (RBD) specific Ab provided strong protection.[4]

Upon until now, the most comprehensive study on SARS-CoV-2 virus-specific adaptive immunity in humans is by the Sette and Crotty group just published in *Cell*, which is the subject highlighted herein. It not only involved a larger number of convalescent and acutely infected patients, but also divided adaptive immune responses into viral protein-specific $CD4^+$ T cells, $CD8^+$ T cells, and Abs, the three most critical components of the adaptive immune responses. Although each component can work separately, together, the three components bring best protection. In the vaccinia virus system, based on the pooled viral peptides, it was shown that $CD8^+$ T cell, $CD4^+$ T cell, and Ab responses tend to recognize different antigens with distinct characteristics, $CD8^+$ T cells recognize early antigens, and $CD4^+$ T cells and Abs recognize later antigens.[5] This same pattern is also demonstrated by Moderbacher et al. in SARS-CoV-2 infection, during which all three arms work together to bring the best protection and if these adaptive immune responses are not synchronized COVID-19 patients are in trouble.[1] In this coordinated process, B cell-produced Abs are able to attach to and neutralize extracellular SARS-CoV-2 virus. For various reasons, if the Abs are unable to stop the virus from entering cells, $CD8^+$ T cells are called in to destroy the infected cells. Regarding $CD4^+$ T cells, the third arm, they are helpers and coordinators for production of Abs and the activation of $CD8^+$ killer T cells (Fig. 1).

Moderbacher et al. analyzed the blood of COVID-19 patients suffering from mild to ultimately fatal infection. Their immune responses were compared to those of convalescents and unexposed control individuals. The Ab levels alone did not correlate with COVID-19 severity. Those worst cases of COVID-19 had low levels of $CD8^+$ killer T cells and $CD4^+$ T helper cells. It is highly possible that T cells play a more important role than Abs in combating ongoing COVID-19 infections. In fact, the authors identified one case that had no detectable neutralizing antibodies and resolved infection without hospitalization. In addition, some infected children recovered before developing an Ab response, again arguing for the importance of T cells.

When blood samples from the older participants (≥65 years old) with acute infections were analyzed, it was found that they were far more likely to have asynchronous immune responses among $CD4^+$ T cells, $CD8^+$ T cells, and Abs than younger infected patients. In older patients, high levels of Abs could be seen, while one of the T cell responses remained weak. Interestingly, older COVID-19 patients tended to also have smaller populations of the "naive" T cells, which could recognize the new SARS-CoV-2 virus and then develop into mature $CD8^+$ killer T cells and $CD4^+$ T helpers, which otherwise mounts a coordinated attack against SARS-CoV-2.

There is much talk about the cytokine storm in COVID-19 patients. It should be recognized that due to the lymphopenia in severe patients, the cytokine storm in these patients should not be expected

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CANCER

Bacteria-triggered tumor-specific thrombosis to enable potent photothermal immunotherapy of cancer

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We discovered that attenuated *Salmonella* after intravenous injection would proliferate within various types of solid tumors but show rapid clearance in normal organs, without rendering notable toxicity. Bacteria-induced inflammation would trigger thrombosis in the infected tumors by destroying tumor blood vessels. Six types of tested tumors would all turn into darkened color with strong near-infrared absorbance, as observed by photoacoustic imaging. Under laser irradiation, those bacterial-infected tumors would be effectively ablated. Because of the immune-stimulation function, such bacteria-based photothermal therapy (PTT) would subsequently trigger antitumor immune responses, which could be further enhanced by immune checkpoint blockade to effectively suppress the growth of abscopal tumors. A robust immune memory effect to reject rechallenged tumors is also observed after bacteria-based PTT. Our work demonstrates that bacteria by themselves could act as a tumor-specific PTT agent to enable photoimmunotherapy cancer therapy to inhibit tumor metastasis and recurrence.

INTRODUCTION

To conquer the threat of cancer, a large variety of treatment strategies based on different mechanisms have been applied or tested in the clinic (*1*). However, conventional cancer therapies such as chemotherapy and radiotherapy have limitations in severe side effects, therapeutic resistance, and limited specificity (*2*). Light-triggered phototherapies, including photothermal therapy (PTT) and photodynamic therapy, are known to be less invasive with higher specificity but are normally applied for treatment of local tumors instead of distant metastatic ones (*3*, *4*). In 2019, Rastinehad *et al.* (*4*) reported the first clinical trial of PTT based on gold-shelled silica nanoparticles to treat patients with prostate cancer with the help of stereotactic trocar/laser fiber. Thirteen of 15 treated patients had no signs of cancer in 1 year after treatment, demonstrating the promises of laser-based PTT for clinical use (*4*). On the other side, cancer immunotherapy, by using the host's immune systems to attack tumor cells, has presented tremendous promises in recent years (*5*). For instance, immune checkpoint blockade (ICB) therapy using antibodies to block immune checkpoint receptors such as programmed cell death protein 1/programmed cell death ligand 1 (PD1/PD-L1) and cytotoxic T lymphocyte–associated protein-4 (CTLA-4) have been clinically used for treatment of various types of tumors (*6*). However, the overall clinical response rate of ICB therapy alone, which is not a tumor-specific therapy, is known to be relatively low (*7*, *8*). Therefore, the combination of ICB therapy with other types of therapeutic methods, including chemotherapy, radiotherapy, and phototherapy, has attracted a great deal of attention in recent years (*9*–*11*). For instance, the combination of PTT based on immune-adjuvant nanoparticles with ICB therapy could trigger antitumor immune responses to suppress tumor metastasis and recurrence after local tumor ablation (*11*). However, in those systems, the immune-adjuvant nanoparticles with limited tumor-homing specificity are normally locally injected into tumors to avoid side effects (e.g., cytokine storms).

Recently, live tumor-targeting microorganisms, such as bacillus Calmette-Guérin, anaerobic bacteria, and even oncolytic virus, have emerged as tumor-specific drug delivery carriers or as therapeutic agents by themselves (*12*–*15*). In particular, because of the hypoxic, immunosuppressive, and biochemically unique microenvironment within solid tumors, *Salmonella typhimurium* can selectively colonize in tumor tissues (*16*, *17*). Moreover, bacterial infection may induce innate and adaptive immune responses against both tumor-colonizing bacteria and the tumor cells, resulting in nonspecific killing of heterogeneous tumor cells (*18*, *19*). For safety reasons, *S. typhimurium* should be attenuated by different approaches to reduce their systemic toxicity (*20*–*22*). However, as shown in phase 1 clinical trials, attenuated *S. typhimurium* treatment alone usually could not effectively eliminate the tumor (*23*, *24*). To augment the antitumor efficacy of bacterial therapy, transport of therapeutic agents such as various cytotoxic agents, prodrug-converting enzymes, or immunomodulators by tumor-homing bacteria has been proposed to be an alternative strategy in cancer treatment (*25*–*27*). Recently, it has been reported that certain types of bacteria could delivery near-infrared (NIR) absorbing agents such as gold nanorods or polydopamine into tumors for photothermal tumor ablation (*28*, *29*). Nevertheless, using bacteria alone without loading of additional therapeutic agents or nanoparticles to achieve phototherapy or photoimmunotherapy has not yet been reported to our best knowledge.

In our work, a bacteria-based photoimmunotherapy is proposed using intact microbes without any chemical modification or loading of additional payloads. We accidently found that different types of solid tumors on mice with intravenous injection of low doses of the attenuated *Salmonella* ΔppGpp strain, which is defective in guanosine 5′-diphosphate-3′-diphosphate synthesis (ΔppGpp *S. typhimurium*), would show obviously darkened colors a few hours after injection. Further investigation verified that ΔppGpp *S. typhimurium* after intravenous injection could specifically colonized in the tumor, with little infection in other normal organs, owing to the facultative anaerobic habit of those bacteria and the unique hypoxic tumor microenvironment. The bacterial proliferation within tumors would trigger activation of innate immunocytes, release of proinflammatory factors,

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IMMUNOLOGY

IGF2R-initiated proton rechanneling dictates an anti-inflammatory property in macrophages

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Metabolic traits of macrophages can be rewired by insulin-like growth factor 2 (IGF2); however, how IGF2 modulates macrophage cellular dynamics and functionality remains unclear. We demonstrate that IGF2 exhibits dual and opposing roles in controlling inflammatory phenotypes in macrophages by regulating glucose metabolism, relying on the dominant activation of the IGF2 receptor (IGF2R) by low-dose IGF2 (L-IGF2) and IGF1R by high-dose IGF2. IGF2R activation leads to proton rechanneling to the mitochondrial intermembrane space and enables sustained oxidative phosphorylation. Mechanistically, L-IGF2 induces nucleus translocation of IGF2R that promotes Dnmt3a-mediated DNA methylation by activating GSK3α/β and subsequently impairs expression of vacuolar-type H^+-ATPase (v-ATPase). This sequestrated assembly of v-ATPase inhibits the channeling of protons to lysosomes and leads to their rechanneling to mitochondria. An IGF2R-specific IGF2 mutant induces only the anti-inflammatory response and inhibits colitis progression. Together, our findings highlight a previously unidentified role of IGF2R activation in dictating anti-inflammatory macrophages.

INTRODUCTION

Monocytes patrolling the bloodstream emigrate into adjacent tissues where they mature into macrophages and acquire either a pro-inflammatory or anti-inflammatory phenotype (*1*, *2*). Emerging evidence has demonstrated that these divergent immune phenotypes in macrophages can persist for a prolonged period, a phenomenon termed "innate immune memory" (*3*–*5*). Epigenetic modifications and metabolic rewiring are critical for building this innate immune memory (*6*, *7*). It has been established that pro-inflammatory macrophages use mainly aerobic glycolysis for their energy needs (*4*), while mitochondria-driven oxidative phosphorylation (OXPHOS) predominates in anti-inflammatory macrophages (*8*). Although mitochondrial metabolism and dynamics are known to be closely linked to monocyte homeostasis and macrophage maturation (*9*), little is known about how external stimulation affects the outcome of macrophage maturation by modulating mitochondria activities.

Recently, it was demonstrated that stimulation through insulin-like growth factor 1 receptor (IGF1R) endows macrophages with a persistent pro-inflammatory phenotype (*6*, *10*). This pro-inflammatory phenotype can be induced by many IGF1R ligands and factors, such as insulin-like growth factor 1 (IGF1), mevalonate, and apoptotic bodies (*6*, *11*, *12*). In contrast, IGF2, a mitogenic polypeptide, can bind to either IGF1R or IGF2R (*11*). While ligation of IGF1R is believed to mediate many of effects of IGF2 in regulating somatic growth, development, and tissue repair (*13*, *14*), the mechanism of IGF2R function is largely unknown, beyond its role as a decoy receptor or carrier protein (*11*).

Here, we show that IGF2 ligation of IGF2R during macrophage maturation induces the rechanneling of protons from cytosol to mitochondria initiating the reprogramming of cellular metabolism toward OXPHOS, and thus resulting in an anti-inflammatory phenotype. At the same time, however, very robust activation of IGF1R by IGF2 imposes a strong bias toward aerobic glycolysis, thus countering any anti-inflammatory–inducing effect of IGF2R. These findings reveal an unappreciated biological function of the IGF2-IGF2R axis in regulating the fate of maturing macrophages to acquire either a pro- or anti-inflammatory phenotype. Therefore, targeting IGF2R activation can potentially be used to reduce inflammation in the treatment of inflammatory disease.

RESULTS

IGF2 exhibits dual opposing roles in determining macrophage phenotype

Our recent study demonstrated that IGF2 alleviates both experimental autoimmune encephalomyelitis (EAE) and dextran sulfate sodium (DSS)–induced colitis by programing macrophages to acquire an anti-inflammatory phenotype (*15*). When IGF2 was applied to treat colitis, we found that its anti-inflammatory effect occurred only in a specific dose range. Administration of L-IGF2 (≤50 ng per mouse; L-IGF2) reduced the severity of DSS-induced colitis, as revealed by significant improvement in body weight, survival rate, stool score, bleeding score, colon length, as well as inhibition of mononuclear cell infiltration into the colon (Fig. 1, A to D, and fig. S1A). Histopathological analysis showed obvious inhibition of DSS-induced colon damage by L-IGF2 (Fig. 1C). Consistent with our previous results, L-IGF2 administration inhibited immune cell infiltration into colonic lamina propria, with a significant reduction in interleukin-1β (IL-1β)–expressing $CD11b^+F4/80^+$ macrophages (Fig. 1E). In contrast, H-IGF2 (1000 ng per mouse; H-IGF2) failed to ameliorate colitis and instead exacerbated its progression and

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Imaging Agents Hot Paper

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An Activatable Polymeric Reporter for Near-Infrared Fluorescent and Photoacoustic Imaging of Invasive Cancer

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Abstract: *Discriminative detection of invasive and noninvasive breast cancers is crucial for their effective treatment and prognosis. However, activatable probes able to do so in vivo are rare. Herein, we report an activatable polymeric reporter (P-Dex) that specifically turns on near-infrared (NIR) fluorescent and photoacoustic (PA) signals in response to the urokinase-type plasminogen activator (uPA) overexpressed in invasive breast cancer. P-Dex has a renal-clearable dextran backbone that is linked with a NIR dye caged with an uPA-cleavable peptide substrate. Such a molecular design allows P-Dex to passively target tumors, activate NIR fluorescence and PA signals to effectively distinguish invasive MDA-MB-231 breast cancer from noninvasive MCF-7 breast cancer, and ultimately undergo renal clearance to minimize the toxicity potential. Thus, this polymeric reporter holds great promise for the early detection of malignant breast cancer.*

Introduction

Early detection of tumors is crucial for their effective treatment and prognosis.[1] Among many type of tumors, breast cancer is the leading cause of cancer-related death in women worldwide.[2] Breast cancer has subtypes, such as luminal type, human epidermal growth factor receptor 2 (HER2) type, and triple-negative breast cancer (TNBC) type, with distinct differences in therapeutic treatment, invasiveness, and prognosis.[3] Compared with other subtypes, TNBC is a highly aggressive subtype with poor prognosis and is generally inert to endocrine and HER2-directed therapy; this necessitates its early diagnosis and the in-depth understanding of the heterogenetic pathological processes.[4] Current diagnosis of breast cancer in the clinic commonly relies on X-ray mammography, which has limited sensitivity and difficulty in differentiating benign from malignant lesions.[5] To accurately identify a suspicious lesion, an excisional biopsy is required.[6] This process is invasive and less capable of providing real-time information for treatment guidance and prognosis.

Optical imaging probes enable the visualization and monitoring of subtle molecular alterations occurring at early stages of disease with superb sensitivity and high specificity.[7] Many fluorescent probes on the basis of protease,[8] pH,[9] or microRNA[10] detection have been explored for breast tumor imaging, but they are less competent for in vivo deep-tissue imaging due to the shallow penetration depth of fluorescence.[11] By contrast, photoacoustic (PA) imaging as a hybrid imaging modality detects sound instead of photons after light excitation, which has minimal attenuation due to negligible sound scattering in biological tissues, and thus provides deeper penetration depth (7–10 cm) and higher spatial resolution (submillimeter) for whole-body imaging.[12] Many absorbing agents have been tested for PA imaging, and advances have shifted towards the development of activatable PA imaging probes capable of correlating signals with the concentration or activities of biomarkers. Activatable PA probes have been explored for deep-tissue imaging, such as for tumor,[13] bacteria,[14] vulnerable plaque,[15] and acute edema imaging.[16] However, existing PA probes have not been exploited for specific discrimination between invasive breast cancer and noninvasive breast cancer.[12b,16,17] Besides, current PA agents are often not rapidly cleared from living organisms, causing potential toxicity and preventing them from clinical translation.[18]

Herein, we report the development of an activatable polymeric reporter (termed P-Dex) for dual-modal imaging of malignant breast cancer. The probe can specifically turn on its near-infrared (NIR) fluorescence and photoacoustic (PA) signals in the presence of urokinase-type plasminogen activator (uPA), which is overexpressed in invasive breast cancer and associated with tumor invasion and metastasis.[19] Up to now, only a few uPA-responsive probes have been reported, and they can only emit fluorescence and have not been utilized for the detection of breast tumors in vivo.[20]

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Mouse models have been approved. Supporting information, including materials, instruments, synthetic procedures, and supporting Figures (Figures S1–S22) and Tables (Tables S1 and S2), and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.202000035.

Biocatalysis

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Two-Dimensional Tin Selenide (SnSe) Nanosheets Capable of Mimicking Key Dehydrogenases in Cellular Metabolism

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Abstract: *While dehydrogenases play crucial roles in tricarboxylic acid (TCA) cycle of cell metabolism, which are extensively explored for biomedical and chemical engineering uses, it is a big challenge to overcome the shortcomings (low stability and high costs) of recombinant dehydrogenases. Herein, it is shown that two-dimensional (2D) SnSe is capable of mimicking native dehydrogenases to efficiently catalyze hydrogen transfer from 1-(R)-2-(R′)-ethanol groups. In contrary to susceptible native dehydrogenases, lactic dehydrogenase (LDH) for instance, SnSe is extremely tolerant to reaction condition changes (pH, temperature, and organic solvents) and displays extraordinary reusable capability. Structure–activity analysis indicates that the single-atom structure, Sn vacancy, and hydrogen binding affinity of SnSe may be responsible for their catalytic activity. Overall, this is the first report of a 2D SnSe nanozyme to mimic key dehydrogenases in cell metabolism.*

Introduction

Dehydrogenases as an indispensable part of tricarboxylic acid (TCA) cycle in all aerobic organisms could facilitate the release of stored energy in carbohydrates, fats, and proteins. This subclass of enzymes could catalyze the transferring of hydrogen atoms from substrate to an electron acceptor, commonly nicotinamide adenine dinucleotide (NAD^+) or flavin adenine dinucleotide (FAD) in the TCA cycle, and is crucial to immune responses and carcinogenesis.[1] For instance, succinate dehydrogenase was found to drive inflammatory macrophages by bursting mitochondrial reactive oxygen species (ROS).[2] While recombinant dehydrogenases have been extensively investigated in energy science, biomedicine, and genetic engineering,[3] it is a big challenge to overcome the shortcomings of protein enzymes, such as low yields, high costs, and poor stability.

As inorganic nanoparticles are relatively stable and some of them have been reported to exhibit high catalytic efficiencies in diverse chemical reactions,[4] the rapid developments of nanotechnologies provide opportunities to engineer nanocatalysts with enzyme-like activities, namely nanozymes. Recently, a few engineered nanomaterials (ENMs) were found to display enzyme activities in physiological conditions. For instance, Fe_3O_4 is the first reported nanozyme to show peroxidase-like activity;[5] CuO,[6] V_2O_5,[7] Co_3O_4,[8] Au,[9] Pt,[10] carbon nanotubes (CNTs),[11] and graphene oxide (GO)[12] have been reported to show superoxide dismutase-, peroxidase-, oxidase-, or catalase-like activities. However, these nanozymes could only catalyze the degradation of H_2O_2, oxygen and $O_2^{\cdot-}$. Beside of these inorganic oxygen species, it is unclear whether the burgeoning nanocatalysts can mimic dehydrogenases to catalyze the hydrogen transfer in organic substrates, which are the major components of all living organisms.

Herein we made an intriguing finding that two-dimensional (2D) SnSe nanosheets (Supporting Information, Figure S1) are able to catalyze the dehydrogenation of organic molecules and they exhibit dehydrogenase-like activities. Indeed, this discovery had unexpectedly arisen in assessments of TCA cycle activity in cells. We found that although SnSe nanosheets induce cell death along with inactivation of TCA cycles as well as deficient dehydrogenases, SnSe is able to serve as an alternate of dehydrogenases to efficiently catalyze the conversion of a dehydrogenase substrate, 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2*H*-tetrazolium (MTS)[13] (Supporting Information,

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Fluorescent Probes

Engineering the Protein Corona Structure on Gold Nanoclusters Enables Red-Shifted Emissions in the Second Near-infrared Window for Gastrointestinal Imaging

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Abstract: *The application of NIR-II emitters for gastrointestinal (GI) tract imaging remains challenging due to fluorescence quenching in the digestive microenvironment. Herein, we report that red-shifting of the fluorescence emission of Au nanoclusters (AuNCs) into NIR-II region with improved quantum yields (QY) could be achieved by engineering a protein corona structure consisting of a ribonuclease-A (RNase-A) on the particle surfaces. RNase-A-encapsulated AuNCs (RNase-A@AuNCs) displayed emissions at 1050 nm with a 1.9% QY. Compared to rare earth and silver-based NIR-II emitters, RNase-A@AuNCs had excellent biocompatibility, showing >50-fold higher sensitivity in GI tract, and migrated homogenously during gastrointestinal peristalsis to allow visualization of the detailed structures of the GI tract. RNase-A@AuNCs could successfully examine intestinal tumor mice from healthy mice, indicating a potential utility for early diagnosis of intestinal tumors.*

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Introduction

Barium swallow and endoscopic techniques are the mainstream techniques for gastrointestinal (GI) imaging.[1] However, barium swallow is an X-ray based diagnosis technique with limited spatial resolution and notable radiation risk; endoscopy is an invasive diagnostic technique contraindicated in patients with suspected bowel stricture or obstruction. Therefore, non-invasive and X-ray-free imaging technologies are highly desired for early diagnosis of some severe GI diseases, especially tumors.[2]

Fluorescence emissions in the second near infrared window (NIR-II, 1000–1400 nm) have attracted substantial research enthusiasms for bio-imaging.[3] Since the excitation and emission wavelengths involved in obtaining NIR-II emissions already allow deep tissue penetration as display a strongly reduced autofluorescence and photon scattering, one-photon excitation was often used as laser source in NIR-II imaging. Compared to small molecular NIR-II emitters (e.g. IR1061,[4] CH1055[5] and BTC1070[6]), nano-sized NIR-II emitters including quantum dots (QDs),[7] rare earth nanoparticle (RENP),[8] and single wall carbon nanotube (SWNT),[9] show relatively higher quantum yields (QYs), and lower susceptibility to photobleaching. They have been exploited for liver,[10] kidney,[11] brain[5] and lung[12] imaging. However, few reports focus on NIR-II imaging of GI tract. As the acidic and enzymatic bio-contexts of GI tract may lead to fluorescence quenching of most nano-sized emitters, we proposed to synthesize inert metal (e.g. Au, Pt) based emitters for NIR-II imaging of GI tract.[13]

In this study, we exploited a theory of ligand-metal-metal charge transfer (LMMCT)[14] to synthesize Au-based nanoclusters (AuNCs) with emissions in NIR-II region. Ribonuclease-A (RNase-A) were therefore selected to encapsulate gold nanocluster (RNase-A@AuNC) for red-shifted emissions as it consists of a desired cocktail of thiol group (cysteine) and aromatic amino acids (histidine and tyrosine). The resulting RNase-A@AuNCs were exposed to GI tract simulated fluids and mammalian cells for stability and biosafety assessments. The in vivo imaging capability of RNase-A@AuNC in GI tract was examined in mice by oral administration. Finally, we employed an intestinal cancer model to justify the potential utility of AuNCs as an imaging agent for tumor diagnosis.

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Smart Oral Administration of Polydopamine-Coated Nanodrugs for Efficient Attenuation of Radiation-Induced Gastrointestinal Syndrome

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High-dose ionizing radiation can lead to death from the unrecoverable damage of the gastrointestinal tract, especially the small intestine. Until now, the lack of predilection for the small intestine and rapid clearance by digestive fluids limit the effects of conventional radioprotective formulations. Herein, an innovative radioprotective strategy is developed for attenuating gastrointestinal syndrome by smart oral administration nanodrugs. The nanodrug is first engineered by encapsulating thalidomide into chitosan-based nanoparticles, and then coated with polydopamine. The behaviors of gastric acid-resistance, and pH-switchable controlled release in the small intestine enhance the oral bioavailability of the pyroptosis inhibitor thalidomide. In a mouse model, nanodrugs demonstrate prolonged small intestinal residence time and accessibility to the crypt region deep in the mucus. Furthermore, the nanodrugs ameliorate survival rates of C57BL/6J mice irradiated by 14 Gy of subtotal body irradiation and also maintain their epithelial integrity. This work may provide a promising new approach for efficiently attenuating lethal radiation-induced gastrointestinal syndrome and add insights into developing nanodrug-based therapies with improved efficacy and minimum side effects.

1. Introduction

Small intestinal epithelium is one of the most vulnerable sites to high doses of irradiation.[1] Human beings exposed to above 10 Gy irradiation would suffer from considerable gastrointestinal syndrome (GIS), which is characterized with severe diarrhea, electrolyte disturbances, hematochezia, and even subacute death.[2] However, there is still no practicable countermeasure for attenuating GIS induced by either accidental or deliberate radiation exposure.[3]

Radioprotective agents given by intravenous injection are candidates for attenuating GIS, such as antioxidants[4] and thiols compounds[5] for eliminating reactive oxygen species (ROS), small molecular-[6] and protein-based[7] pharmaceuticals for inhibiting apoptosis, and cytokine therapy agents[8] and bone marrow cell-derived extracellular vesicles[9] for accelerating the restitution of intestinal stem cells. However, these radioprotective agents exhibit a body-wide distribution with varying predilection for tissues[10] such as spleen and liver, but not intestine. Higher doses of agents must be given to achieve optimal radioprotective efficacy for small intestine, thereby leading to serious side effects. For countermeasures via oral route, such as fecal microbiota transplantation,[11] amifostine microcapsules,[12] and Ex-RAD,[13] the radioprotectants have to reside in intestinal lumen or cross the intestinal epithelium to reach systemic circulation. Unfortunately, invalidation of these agents may occur due to harsh environment (especially in the highly acidic stomach) during gastrointestinal tract passage.[14] Even if the radioprotectants successfully reach the region of small intestine, they may not withstand the rapid trapping and clearance of the mucus layer and intestinal fluid,[15] limiting their exposure to intestinal tissues. Consequently, oral administration of radioprotectants in conventional formulations could be inefficient.

In previous studies, we can find the low toxicity, stable encapsulation of radioprotective agents,[16] and adjustable physicochemical properties[17] of chitosan-based nanodrugs intended for parenteral administration. However, the possibility of this system as orally administered radioprotectant formulation has rarely been explored. Recently, we noticed that the deficiency of double-stranded DNA sensor Absent-In-Melanoma 2 (AIM2) could protect small intestinal stem cells from radiation-induced pyroptosis.[3] Thalidomide (THA), a potential AIM2 inhibitor,[18] may be a good choice of radioprotective agents. It should be noted that THA is not suitable for pregnant women due to embryotoxicity.[19] In order to efficiently protect the radiosensitive intestinal stem cells, THA should overcome back diffusion[20] and stay

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X-rays-optimized delivery of radiolabeled albumin for cancer theranostics

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ABSTRACT

Exploiting the specific biological behaviors of the metabolizable nano-drugs assisted by X-rays exposure will be benefit for the optimization of radiotherapy-based combination therapy. Herein, Human serum albumin (HSA) nanoparticle, a familiar and metabolizable nanomaterial, is selected to investigate the changes of tumor accumulation and retention under X-rays exposure. Caveolin-1, an important protein which has positive correlation with cell uptake of nanomaterials, is expressed increasingly under X-rays exposure, resulting the enhanced cell uptake and prolonged tumor retention of HSA nanoparticles. After being labeled by radioactive iodine-125, HSA could be used for SPECT/CT imaging of mice. Moreover, it discovered that ^{125}I-HSA nanoparticles possess much longer-time retention time in pre-irradiated tumor than that of controlled tumor. Using this strategy, the therapeutic efficiency of ^{131}I-HSA injected mice after irradiating their tumors by X-rays is better than that of opposite sequence treated mice. In order to further improve the targeting ability of HSA, GNQEQVSPLTLLKXC peptide (A15) is conjugated to HSA nanoparticles for targeting the thrombosis in the tumor tissue triggered by X-rays exposure, realizing the high tumor accumulation of ^{131}I-HSA assisted by X-rays exposure. Therefore, taking advantage of the increased expression of Caveolin-1 and the induced thrombosis under X-rays exposure, we optimized the delivery of radiolabeled HSA via enhancing the cell uptake and prolonging tumor retention of HSA for cancer combination therapy. Our work make contribution to guide the clinical albumin based combination therapy.

1. Introduction

External beam radiotherapy (EBRT) has been widely applied in clinical treatment of cancer owing to its controlled irradiation field and limited side effects [1,2]. In a conventional process, the cancer discovered by a variety of imaging methods would be irradiated by external radiation sources including X-rays, electron beam and heavy ion beam in a designated area [3]. Therefore, the effective imaging of tumor region and the complete elimination of tumor under external radiation sources were of great concerned in EBRT [4]. At the present stage, however, the therapeutic effect of EBRT is not satisfactory enough because of the existence of radiation resistance [5,6]. In order to enhance curative potential of cancer under X-rays exposure, a series of radiation sensitizers such as nitroimidazoles, chinese herbs and nanomaterials assisted by different tumor treatment modality including chemotherapy, phototherapy as well as immunotherapy has been carried out, aiming to achieve synergistic antitumor effect [7–10].

According to the literature, X-rays exposure could induce tumor vascular disruption with the help of vascular-targeted gold nanoparticles, resulting enhanced tumor perfusion of nano-drug delivery system (NDDS) [11–13]. The tumor microenvironment including vascular morphology, interstitial fluid pressure and tumor-infiltrating immune cells has been changed for enhancing the delivery and permeation of partial NDDS [14–17]. Additionally, radiotherapy (RT) could trigger the rapid expression of some cell adhesion molecules in tumor vessels and numerous stress proteins on the tumor cellular membrane, both of which could make the specific peptide modified nanomaterials target to the irradiated tumor [18–20]. In our recent work, cancer cells exposed by X-rays could enhance the cell uptake of various nanoparticles via up-regulating the expression of Caveolin-1 and arresting the cell cycle at G2/M, realizing the excellent radio-chemotherapy effect [21]. Therefore, the drug delivery efficiency based on NDDS could be optimized under X-rays exposure for more effective combination therapy.

At the present stage, the metabolizable nanomaterials have been extensively investigated in biomedical application owing to their rapid

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Cell Death & Differentiation

EDITORIAL

COVID-19 infection: the perspectives on immune responses

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More than 100 years since the outbreak of the 1918 influenza pandemic, we now seem to face another pandemic. The outbreak of the new coronavirus (SARS-CoV-2) infection is spreading to every continent, forcing us to live with this virus for perhaps a long time. Scientists and clinicians have learned much of coronavirus disease 2019, COVID-19, and its pathogenesis [1]: not all people exposed to SARS-CoV-2 are infected and not all infected patients develop severe respiratory illness. Accordingly, SARS-CoV-2 infection can be roughly divided into three stages: stage I, an asymptomatic incubation period with or without detectable virus; stage II, non-severe symptomatic period with the presence of virus; stage III, severe respiratory symptomatic stage with high viral load [2]. From the point of view of prevention, individuals at stage I, the stealth carriers, are the least manageable because, at least on some occasions, they spread the virus unknowingly: indeed, the first asymptomatic transmission has been reported in Germany [3]. The role of asymptomatic SARS-CoV-2 infected individuals in disseminating the infection remains to be defined.

Among over 1000 patients analyzed in Wuhan, except occasionally in children and adolescence, it infects all the other age groups evenly. About 15% of the confirmed cases progress to the severe phase, although there is a higher chance for patients over 65 to progress into the severe phase [1]. One of the biggest unanswered questions is why some develop severe disease, whilst others do not. Clearly, the conventional wisdom based on overall immunity of the infected patients cannot explain this broad spectrum in disease presentation.

Two-phase immune responses induced by COVID-19 infection

Clinically, the immune responses induced by SARS-CoV-2 infection are two phased. During the incubation and non-severe stages, a specific adaptive immune response is required to eliminate the virus and to preclude disease progression to severe stages. Therefore, strategies to boost immune responses (anti-sera or pegylated IFNα) at this stage are certainly important. For the development of an endogenous protective immune response at the incubation and non-severe stages, the host should be in good general health and an appropriate genetic background (e.g. HLA) that elicits specific antiviral immunity. Genetic differences are well-known to contribute to individual variations in the immune response to pathogens. However, when a protective immune response is impaired, virus will propagate and massive destruction of the affected tissues will occur, especially in organs that have high ACE2 expression, such as intestine and kidney. The damaged cells induce innate inflammation in the lungs that is largely mediated by pro-inflammatory macrophages and granulocytes. Lung inflammation is the main cause of life-threatening respiratory disorders at the severe stage [4]. Therefore, good general health may not be advantageous for patients who have advanced to the severe stage: once severe lung damage

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Polyoxomolybdate (POM) nanoclusters with radiosensitizing and scintillating properties for low dose X-ray inducible radiation-radiodynamic therapy†

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In order to overcome the weak penetration of near infrared (NIR) light in photodynamic therapy (PDT), X-ray radiation (X-RT) with high deep tissue penetration could be used as a therapeutic option to completely destroy tumors. Herein, polyoxomolybdate nanoclusters (POMo NCs) with rose Bengal (RB) loading, are functionalized with chitosan (CS) and polyethylene glycol (PEG) for X-ray inducible radiation and radiodynamic therapy (X-RRDT). Our obtained POMo NCs demonstrate a strawberry shape containing 163 Mo (Mo)3 units of three edge sharing MoO_6 octahedra and connecting to the central PO_4 octahedron. Under low dose X-ray radiation, the communal effect of radiosensitization and scintillation of POMo NCs along with RB, can decrease the side effects of RT and enhance both RT and PDT efficiency. This is because the POMo NCs can not only augment RT efficacy by producing auger electrons which directly provoke DNA damage, but also enhance PDT efficacy by converting high energy X-rays into light to stimulate RB to generate singlet oxygen ($^1O_2$). *In vivo* results show that X-RRDT using POMo NCs significantly inhibits tumor growth under low dose X-ray radiation. More importantly, the as-made PEGylated POMo NCs cause no obvious side-effects to the major normal organs through histological examination. This work describes a simple strategy to design effective X-RRDT agents with multiple properties including X-ray radiosensitization, X-ray scintillation and photosensitization for X-RRDT under low dose X-ray irradiation. Our developed strategy will further promote the cancer therapeutic efficiency under low dose X-ray radiation, and bring hope for clinical cancer treatment.

New concepts

X-rays with high deep tissue penetration could be used as an excellent excited light source for enhanced photodynamic therapy (PDT), avoiding the weak penetration of near-infrared light and further improving the therapeutic efficiency of PDT. Herein, our developed polyoxomolybdate nanoclusters (POMo NCs) with the largest strawberry shape possess dual-function including X-ray triggered PDT (X-RPDT) and X-ray inducible radiation (X-RT). Under X-ray irradiation, POMo NCs could transfer high energy of X-rays into light to stimulate RB and then generate singlet oxygen for killing cancer cells. Meanwhile, the POMo NCs could also augment RT efficacy by producing auger electrons to induce DNA damage, further improving the therapeutic efficiency. We believe that the designed POMo NCs could significantly improve the therapeutic efficiency of cancer under low dose X-rays, binging hope for further cancer clinical treatment.

Compared to chemotherapy and surgery, radiotherapy (RT) using X-rays, gamma rays or an electron beam is still broadly applied for cancer treatment in clinical applications.[1] Numerous RT clinical trials have revealed that using high dose X-rays could kill most of the cancer cells, but also cause side effects to the patients.[2] Optical therapy including photodynamic therapy (PDT)[3,4] and photothermal therapy (PTT)[5,6] have been developed for the last two decades to decrease the side effects. However, the weak penetration of light limits the therapeutic efficiency of optical therapy of tumors in deeper tissue.[7] Therefore, X-rays with high deep penetration are widely used compared with NIR light. However, the side effects of RT are unavoidable. Certainly, they have been partially alleviated by advanced nano-biotechnology. During X-ray radiation therapy (X-RT), radio-sensitizers produce Compton or photoelectrons which strike adjacent water or biomolecules to generate reactive oxygen species (ROS), breaking indirectly DNA strands.[8] Owning to insufficient biomolecules near to the radiosensitizers, loss of Compton or photoelectrons is another drawback of X-RT along

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十、获奖情况

序号	奖励编号	奖励名称	奖励类型	获奖单位	获奖等级	获奖人员（固定人员）
1		中国科学院杰出科技成就奖（突出贡献者）	其他国家奖励	个人奖	其他	柴之芳
2		吴阶平医学奖	其他国家奖励	苏州大学附属第一医院、苏州大学	其他	阮长耿
3		中华医学会血液学分会终身成就专家奖	其他国家奖励	苏州大学附属第一医院、苏州大学	其他	阮长耿
4		何梁何利基金科学与技术创新奖	其他国家奖励	苏州大学	其他	路建美
5		何梁何利基金科学与技术进步奖	其他国家奖励	苏州大学	其他	吴德沛
6		第十六届中国青年科技奖	其他省部级奖励	苏州大学	其他	王殳凹
7	DL2020005	中国毒理学会优秀青年科技奖	其他省部级奖励	苏州大学放射医学与防护学院	其他	张乐帅
8	DL2020002	中国毒理学会优秀青年科技奖	其他省部级奖励	苏州大学放射医学与防护学院	其他	尚增甫
9	2019-2-33	认知功能辐射损伤机制和防治关键技术研究	其他省部级奖励	核工业总医院	二等奖	田野,杨红英
10		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	科技进步奖	苏州大学附属第一医院、苏州大学	一等奖	戴克胜,周泉生,阮长耿
11		2020 年第一届核应急管理国际论坛	其他省部级奖励	核工业总医院	一等奖	刘玉龙
12		智能医学影像分析及其临床诊断应用	其他省部级奖励	苏州大学,汕头大学,苏州比格威医疗科技有限公司	一等奖	陈新建

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	GZN1202001	王殳凹	教授	基于新型纳米孔道材料的军民两用氡污染控制技术应用基础研究	150	2020.06-2022.12
2	GZN1202002	何玉龙	教授	电离辐射致淋巴管损伤与重塑的机制研究	150	2020.06-2022.12

十二、开放课题

序号	课题名称	课题负责人	专业技术职务（职称名称）	工作单位	课题开始时间	课题结束时间	总经费(万元)
1	二甲双胍通过抑制衰老改善放射诱导的人冠脉内皮损伤	王海鹏	副主任医师	苏州大学附属第一医院	2020-06	2021-12	5
2	FEN1 靶向治疗中的功能研究 在电离辐射诱导 DNA 双链断裂损伤修复通路及肿瘤	李金利	副主任医师	苏州大学附属第一医院	2020-06	2021-12	5
3	TnC/TPM4 信号通路在氚水诱发心脏发育毒性中的作用及机制研究	宦　坚	主任医师	南京医科大学附属苏州科技城医院	2020-06	2021-12	5
4	共刺激分子 B7-H3 在胃癌放疗中的作用及其机制探究	邹汉青	副主任医师	苏州大学附属第二医院	2020-06	2021-12	5
5	ROS 伤的治响应型聚合物胶束负载四氢生物蝶呤用于放射性肺损疗及机制	贺　丹	副主任医师	核工业四一六医院	2020-06	2021-12	5
6	外照射致皮肤损伤的分子病理机理研究	徐龙江	副主任医师	苏州大学附属第二医院	2020-06	2021-12	5
7	巨噬细胞内质网应激作用及免疫机制-前列腺素通路在放射损伤性疼痛中的	张玉松	主任医师	苏州大学附属第二医院	2020-06	2021-12	5
8	间充质干细胞促进小鼠放射性皮肤损伤创面愈合机制的研究	马　磊	主任医师	南阳第一人民医院	2020-06	2021-12	5
9	基于多种生物标记监测管电压对 学效应的影响 CT 图像质量和 CT 辐射生物	张　博	副主任医师	苏州大学附属第二医院	2020-06	2021-12	5
10	MSLN GPIA MR/CD206 对大肠癌细胞放射敏感性的影响 信号途径调控 M2 型巨噬细胞功能	邢春根	教授	苏州大学附属第二医院	2020-06	2021-12	5
11	177Lu 的作用标记的西妥昔单抗复合物在脊索瘤靶向诊断及放疗中	邹　俊	副主任医师	苏州大学附属第一医院	2020-06	2021-12	3

序号	课题名称	课题负责人	专业技术职务（职称名称）	工作单位	课题开始时间	课题结束时间	总经费(万元)
12	多模态诊疗一体化纳米探针用于肝癌早期诊断和内外放疗的研究	原　强	主治医师	苏州大学附属第二医院	2020-06	2021-12	3
13	肺恶性小结节精准活检快速现场病理诊断同步距离放疗的临床转化研究 125I 粒子近	喻岳超	副主任医师	徐州医科大学第二附属医院	2020-06	2021-12	3
14	放疗、前研究 PD 1 抗体和 GM CSF 联合治疗对食管鳞癌疗效的临床	张力元	主任医师	苏州大学附属第二医院	2020-06	2021-12	3
15	HDAC3/miR 研究 -451/c-Myc 信号轴调控肺腺癌放疗抵抗的机制	王　蓉	主任医师	苏州大学附属第一医院	2020-06	2021-12	3
16	靶向 研究 TGFβ1 基因的特定 miRNA 对放射性肺损伤的作用机制	张建东	主治医师	南阳市第一人民医院	2020-06	2021-12	3
17	基于 疗联合内分泌治疗研究 PSMA 靶向放射性分子探针的前列腺癌多模态成像及放	周　峰	副主任医师	苏州大学附属第 一医院	2020-06	2021-12	3
18	11C-尿素标记及 PET/CT 影像确认 HP 呼气原理研究	张晓懿	副主任医师	常熟市第二人民医院	2020-06	2021-12	3
19	医用电子加速器光中子污染的防护关键问题研究	邓　磊	副研究员	江西省职业病防治研究院	2020-06	2021-12	3
20	胰腺肿瘤手术导航分子探针的基础研究	李　伟	副主任医师	苏州大学附属第二医院	2020-06	2021-12	3
21	m 抵抗中的作用及机制研究 iR 210/MAGL 通路调控前列腺素 E2 生成在直肠癌放射	朱雅群	主任医师	苏州大学附属第二医院	2020-06	2021-12	自筹
22	miRNA 性的影响及机制研究 -233 途径介导的自噬及外泌体分泌对胃癌放射敏感	朱宝松	副主任医师	苏州大学附属第二医院	2020-06	2021-12	自筹
23	激素非依赖型前列腺癌微环境响应性 辑纳米载体的构建及体内 MRI 导航诊疗研究 CRISPR/Cas9 基因编	魏超刚	主任医师	苏州大学附属第二医院	2020-06	2021-12	自筹

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24	血浆游离 DNA 作为早期快速辐射生物剂量计的研究	蒲汪旸	副主任医师	苏州大学附属第二医院	2020-06	2021-12	自筹
25	Tim4+T 细胞在 1 型糖尿病发病中作用的核素示踪研究	方　晨	副主任医师	苏州大学附属第二医院	2020-06	2021-12	自筹
26	C XCL10 理研究 通过 Smac 调控胰腺癌细胞辐射敏感性的分子机	张永胜	副主任医师	苏州大学附属第二医院	2020-06	2021-12	自筹

十三、2020 大事记

1 月 14 日，苏州市曹后灵副市长一行率队到实验室视察安全工作

5 月 12 日，实验室中能多粒子超导医学研究加速器论证会成功举行

8 月 4 日，国重实验室临床中心联合工作会议成功举行

9 月 2 日，苏州姑苏实验室杨辉主任一行访问实验室

10 月 10 日，江苏省委书记娄勤俭一行调研苏州大学并考察实验室

11 月 19 日，质子重离子学术论坛（2020）

暨苏州大学质子重离子医学研究中心成立大会成功召开

11 月 20 日，国重实验室召开第一届学术委员会第三次会议

11 月 30 日，中国科协科普部钱岩副部长一行调研实验室

十四、科普活动

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

2020 年，结合国家新冠疫情防控和提升全民科学素养具体要求和号召，国重室科普基地开展了“重”志成城　放医战“疫”、辐射安全文化宣传月、暑期社会实践和夏令营、“核+X”等全国核科普相关作品竞赛、“以核济世护健康”—全国科技创新周、健康核卫士系列开放日等活动，受到省市科协的支持和广泛参与，直接累计参与人数达 3 万人。此外，国重室柴之芳院士及时玉舫院士等专家借助网络平台给予毕业生寄语及科普讲座，反响热烈，累计参与人数达 10 万余人。苏州市项目资助的《辐射与健康》科普系列丛书（8 个分册）的编撰已进入最后校样阶段，国重室科普吉祥物“辐娃”家族及科普主题曲《放医 DISCO》已融入到各项活动中，增强了活动的趣味性及影响力。由放射医学专业大学生自发成立“苏州大学辐射与健康科普协会”，志愿者团队不断壮大，以创作科普作品为建设重点，正为创新性科普作品和活动孵育的摇篮。





科普活动（左上：“以核济世护健康”—校园科普宣传；左中：辐射安全文化宣传月—放射性核素 131I 事故应急演练；左下：“核+X”初赛作品校内颁奖；右上：国重室时玉舫院士《免疫学与再生医学》线上线下科普讲座；右中：碳 14 的人体之旅开放日—探索辐射与人体的消化系统的奥秘；右下：国重室科普志愿者团队建设—苏州大学辐射与健康科普协会成立）

国重室始终坚持以核技术广泛应用及放射医学为科普基石，坚持“与核同行”普及科学知识，化“深奥”为“浅显”，为全面提升国民的核科学素养助力，并不断开拓科普工作新局面，力争努力建成一个有影响力核特色鲜明的“放射医学”科普教育基地。

十五、助力企业　共渡难关

为了贯彻落实中央和省委省政府关于做好疫情防控，统筹推进经济社会发展的决策部署，深入落实科技部《关于科技创新支撑复工复产和经济平稳运行的若干措施》。苏州大学放射医学与辐射防护国家重点实验室积极响应号召，在苏州市科技局、苏州大学及重点实验室各级领导高度重视下，立即安排落实帮助企业加快复工复产，有效应对疫情、共渡发展难关。

2020 年初起，苏大放医国重室主动作为开展“助力企业，共渡难关”系列活动，共助力全国企业 20 余家，参加服务企业人员 100 余人次，国重实验平台为企业提供样品检测服务近 1300 个，累计开放仪器 66 台，组织了科技成果转化发布会，9 月平台为企业免费提供检测服务 1 个月，全年累计参加活动近 7000 人次。典型案例如下：

案例 1.助力苏州嘉乐威开展新型介入辐射防护手套标准化生产应用推广

国重室许玉杰和王敬东科研团队带介入辐射防护手套专利项目到苏州嘉乐威企业发展有限公司，利用放射医学的专业知识为企业生产的新型介入防护手套的质控检测进行了方法学研究，在新型介入辐射防护手套的成果转化、质量控制和市场推广等关键环节提供了大力支持。

案例 2.助力山东大华医特方舱 CT 研发与应用推广

涂彧、孙亮老师带领研究生立即与大华医特设计人员组成方舱医院 CT 屏蔽设计团队，通过微信群开展工作，并展开 CT 辐射屏蔽计算和优化，进行网上远程快速蒙特卡洛建模运算，为项目的开展争取了大量的时间，第一时间将优化计算结果反馈企业，对不同规格的 CT 方舱给出了“最优化”的防护当量设计，确保了防护性能符合国家现行标准要求的方舱 CT 尽快投产使用。

案例 3.助力苏州欣影生物公司纳米造影剂产业化

高明远教授等多次通过电话、视频会议、现场走访等方式与其企业团队频繁开展交流。针对项目推进过程中存在的问题，建言献策，提出解决方案。国重室实验平台还为企业免费提供透射电子显微镜、动态光散射检测仪、核磁共振造影剂弛豫率分析仪等仪器使用，让公司所研发出的样品性能得到及时的反馈，准确地确定下一步的研发方向，力争帮助企业将疫情对的项目影响降至最小，确保合作项目“新型纳米氧化铁磁共振造影剂”的研发进度。

案例 4.助力江苏华益科技有限公司共同打造同位素药物研发

自疫情发生以来，国重室王殳凹教授、王敬东老师、刘汉洲老师等通过网络视频、电话会议、现场走访等方式与企业共同推动合作项目的进展，确保研发进度。

十六、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。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。目前开放式的放射性实验楼蕴藏着极大风险。

2、重点实验室科研成果原创性和成果转化有待加强。基础研究应加强与国家重大需求的结合，成果转化应按照国家和学校的有关规定进行，加大转化力度。

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

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

5、实验室重器欠缺。目前中能粒子加速器装置处于关键时刻，这不仅关系到未来的战略发展规划、更关系到实验室未来的地位。中能粒子加速器装置既是当前国际放射医学的前沿，也是重点实验室的重器，可使实验室立于全国之巅。