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金基纳米结构光热抗菌研究进展

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摘要 病原微生物会导致严重感染, 并且由于基因突变以及各种耐药机制的作用, 多重耐药菌的数量增长对人和动物的生存构成了极大的威胁, 引起了人们对抗菌替代解决方案的关注. 近年来, 由于金纳米结构良好的生物相容性、光热稳定性、高效的光热转化以及易于表面修饰等优点, 研究人员致力于设计由光辐射引发的具有可活化抗菌性能的金纳米结构. 本文综述了光活性金纳米结构及其在对抗病原菌尤其是耐药菌感染治疗中的应用, 揭示了当前技术的基本原理、重要发展、应用前景和局限性.

关键词 金纳米结构, 光热抗菌, 改性, 功能化

近年来, 由细菌引起的严重病原体感染的数量不断增加[1], 由于细菌的高适应性和高繁殖率, 给公共健康卫生带来了巨大的威胁[2,3]. 几十年来, 抗生素一直是治疗病原菌最有效的解决方案, 导致了抗生素在病原菌感染情况下的广泛应用. 然而, 随着抗生素的过度使用甚至滥用, 导致多重耐药菌, 如耐甲氧西林金黄色葡萄球菌、耐青霉素肺炎链球菌和耐甲氧西林表皮葡萄球菌数量的增长, 给治疗病原菌感染带来了巨大挑战. 目前, 抗生素对多重耐药菌感染的治疗效果较差, 甚至完全失效[4,5], 因此寻找新的细菌抑制和杀灭的替代解决方案非常重要.

由于细菌耐药性的出现和传播导致的抗生素失效, 目前, 已经有几种替代抗生素的灭菌方法被开发, 但大多数存在靶向选择性差、杀菌过程难以控制, 或者不适用于生物体内等缺点[6~12]. 光热抗菌因其具有高效、快速以及不易诱发细菌耐药性等优点, 得到了广泛的应用. 光热抗菌涉及光吸收剂与光的结合对细菌细胞的高温损伤, 因此也被称为光热细菌裂解(photothermal bacterial lysis, PTBL). 如图1所示, 在PTBL过程中, 光热剂首先被引入感染部位, 然后选择性地与细菌黏附, 最后用适当波长的光照射, 光热剂随后吸收光能, 并通过周围环境中的非辐射弛豫迅速将光能转化为热能, 产生的高温效应最终对细菌细胞造成不可修复的损伤, 导致细菌死亡. 在光热抗菌过程中, 光热剂起着至关重要的作用. 随着纳米技术的发展, 利用纳米材料作为光热抗菌剂成为可能, 这种光热剂可以通过紫外到近红外光谱的光辐射来激活. 在众多光热剂中, 由于金纳米结构具有高的光吸收系数、独特的尺寸和形状依赖的光学特性、易于合成、生物相容性好以及容纳多种功能配体的能力, 被认为是光热抗菌剂的首选之一, 近年来在光热抗菌领域受到了广泛的研究与应用[13~17]. 本文重点介绍了用于光热抗菌的金纳米结构材料的最新发展, 详细讨论了这些纳米材料在光热抗菌领域的应用.

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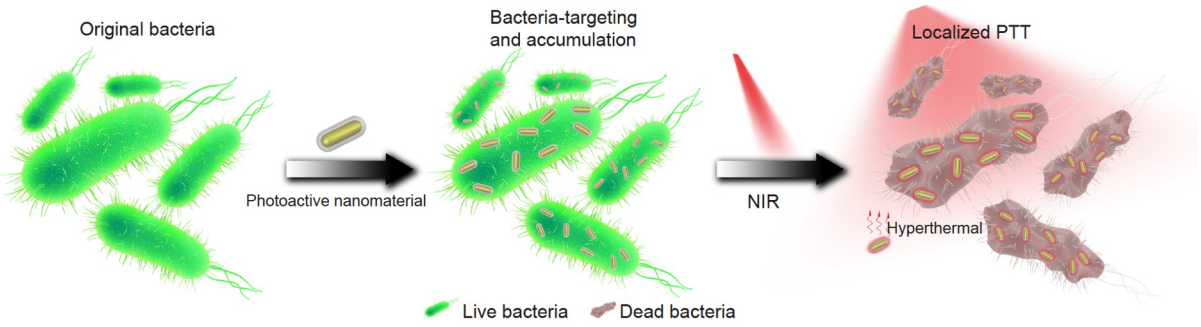

图 1 (网络版彩色)光热抗菌过程示意图
Figure 1 (Color online) Schematic diagram of photothermal antibacterial process

1 光热抗菌金纳米结构的种类

由于金纳米结构的局域表面等离激元共振(localized surface plasmon resonance, LSPR)效应和抗氧化性等许多优点, 已被广泛用作光热抗菌的光热剂, 特别是在非侵入性光热抗菌和治疗病原菌感染等方面受到了极大的关注. 金纳米颗粒、金纳米星、金纳米花、金纳米棒、金纳米笼和金纳米壳等具有不同的形貌结构, 且具有优异的光热抗菌潜力. 由于具有LSPR效应, 这些金纳米结构吸收的辐射被有效地转化为热量, 导致皮秒级的病原体破坏[18~21](图2). 并且由于组织对近红外辐射的微弱吸收, 近红外辐射能够穿透正常皮肤组织而不会造成太大损害, 因此被广泛用于局域的靶向抗菌治疗.

1.1 金纳米颗粒

金纳米颗粒(gold nanoparticles, GNPs)是一种常见的金纳米结构. 尺寸一般在1.5~180 nm, LSPR范围在520~650 nm, 其LSPR吸收峰可以通过改变GNPs粒径来调节, 主要利用种子介导生长法来获得. GNPs在520~650 nm的可见光波长范围内具有强烈的光热吸收[26~29], 但是生物组织对可见光的吸收和散射通常限制了GNPs在生物体层面的光热抗菌应用. 为了克服这一缺点, 研究人员利用GNPs的聚集诱导其LSPR峰红移, 从而改善GNPs的光热性能[30,31]. Wang等人[32]最近报道了一种基于细菌诱导的GNPs聚集的新型治疗策略. 其中GNPs可以聚集在细菌表面, 由于相邻GNPs之间的等离子体耦合, GNPs表现出很强的“热点”效应. 而在没有细菌菌株的情况下, GNPs是分散的, 表现出相对低的光热效应, 最大限度地减少了对周围健康组织的副作用.

1.2 金纳米星

金纳米星(gold nanostars, GNSs)尺寸一般在45~300 nm, LSPR范围在550~800 nm, 其LSPR可调性可以通过改变尺寸大小、分支密度、分支长度及其尖端锐度来实现. 目前GNSs的制备主要是利用种子介导法, 在金种子生长过程中使用合适的表面活性剂(如*N*, *N*-二甲基甲酰胺、聚乙烯吡咯烷酮、十六烷基三甲基溴化铵等)使其定向生长. 由核心和突出臂组成的分枝或星形金纳米结构由于具有独特的形态和光学性质, 近来引起了研究者特别的关注[33]. 由于存在多个尖锐的突起, GNSs表现出相对更高的光学灵敏度, 同时也具有更好的光热效率. Hasan等人[34]发现尖端的存在和高的比表面积使GNSs在光热转化和药物负载方面比具有光滑表面的GNPs更有效. Du等人[13]利用耐甲氧西林金黄色葡萄球菌可识别的特异性适配体以及酶响应荧光多肽修饰GNSs, 可以实现对耐甲氧西林金黄色葡萄球菌的靶向抗菌以及近红外荧光成像.

1.3 金纳米棒

金纳米棒(gold nanorods, GNRs)尺寸一般在20~1000 nm, LSPR范围在600~1800 nm, 可以通过改变直径以及纵横比来调节LSPR吸收峰, 主要通过种子介导的生长、电化学还原、微波辅助、溶剂热还原等方法制备. 由于GNRs在近红外区具有纵向LSPR的固有特征, 可以通过控制其尺寸和纵横比进行调整, 并且在可见光和近红外区具有很强的光学吸收, 可以通过简便的方法快速合成, 使其作为光热材料在光热杀菌领域获得了广泛的研究. 研究者通过将各种生物分子与GNRs结合, 增强其抗菌的靶向选择性和光热抗菌效率. 最近, Chen等人[35]利用抗菌肽、蟾蜍素2b和GNRs

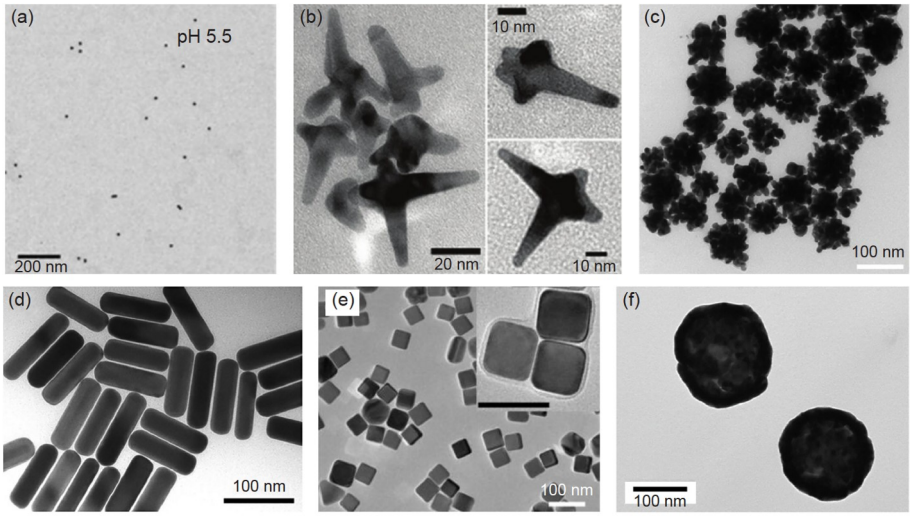

图 2 各种金纳米结构的透射电子显微镜(TEM)图像. (a) Au纳米颗粒[22]. Copyright © 2017, American Chemical Society. (b) Au纳米星[13]. Copyright © 2020, the Royal Society of Chemistry. (c) Au纳米花[15]. Copyright © 2020, Elsevier. (d) Au纳米棒[23]. Copyright © 2021, Elsevier. (e) Au纳米笼[24]. Copyright © 2019, American Chemical Society. (f) Au纳米壳[25]. Copyright © 2015, American Chemical Society

Figure 2 TEM images of various Au nanostructures. (a) Au nanoparticles[22]. Copyright © 2017, American Chemical Society. (b) Au nanostars[13]. Copyright © 2020, the Royal Society of Chemistry. (c) Au nanoflowers[15]. Copyright © 2020, Elsevier. (d) Au nanorods[23]. Copyright © 2021, Elsevier. (e) Au nanocages[24]. Copyright © 2019, American Chemical Society. (f) Au nanoshells[25]. Copyright © 2015, American Chemical Society

制备了一种特异性的抗菌复合材料，对耐甲氧西林金黄色葡萄球菌具有高效的灭菌效果. 同时, 蟾蜍素2b具有独特的抗菌性能，比传统抗生素更不易产生细菌耐药性. Norman等人[36]将GNRs与铜绿假单胞菌特异性抗体结合来构建纳米复合物，使其能选择性地与铜绿假单胞菌细胞结合，并且在近红外辐射下显示出优异的抗菌性能. 有研究发现，通过改变GNRs的长径比可以改变GNRs的光热吸收性能和周围电场，从而改变GNRs的光热杀菌效率. Mackey等人[37]发现长度和直径分别为28和8 nm的GNRs拥有光热吸收性能和光热转换效率的最佳组合. 使用密闭对流阵列技术制造的排列整齐的二维(2D)和三维(3D)GNRs阵列是另一种增强GNRs光热杀菌性能的有效途径，归因于GNRs的聚集可以增强近红外吸收[38]. 例如，Ramasamy研究组[39]设计并制备了一种可回收的抗菌聚苯乙烯球Janus颗粒，它由两种纳米结构包覆组成，颗粒的一半被GNRs阵列包覆, 另一半被磁性纳米粒子包覆. 该结构兼具金纳米棒和磁性纳米粒子的性质，可在近红外辐射下实现高效的细菌光热消融, 并且可通过磁性来回收.

1.4 金纳米笼

金纳米笼(gold nanocages, GNCs)尺寸一般在20~200 nm, LSPR范围在400~1200 nm, LSPR可调性是通过改变尺寸大小、化学组成(如金、银双金属)以及固体到多孔到中空的多层纳米结构来实现，主要通过种子介导的生长、电化学置换反应等方法制备. 由于GNCs具有高光热转换效率、中空的载药结构、可调的表面微孔和良好的生物相容性，已经成为一种有吸引力的药物传递平台和光热抗菌材料. 最近，Zhang等人[40]开发了一种基于GNCs的光激活纳米抗生素平台(TC-PCM@GNC-PND), 在近红外光照射下可以实现包封药物的精确可控释放，以及与光热抗菌的协同作用, 用于对牙周炎的精确协同光热抗菌治疗.

1.5 金纳米壳

金纳米壳(gold nanoshells, GNSs)结构由包围在介电核周围的薄金壳组成, 尺寸一般在20~200 nm, LSPR范围在400~1200 nm, 可通过改变壳层厚度以及壳、核直径比等来调节LSPR峰，主要通过模板导向合成法来制备. GNSs由于其LSPR峰位于近红外区，以及较强的LSPR效应而成为光热抗菌的高效试剂，在光热抗菌领域也得到了广泛的应用[41]. Fan等人[30]开发了爆米花状的铁磁芯-金壳(Fe@Au)，其在可见光区具有强吸收带(λ_{max} = 580 nm). 最近, Manivasagan等人[42]开发了巯基壳聚糖包裹的GNSs作为抗菌剂, 用于细菌的光热裂解, 并且利用万古霉素或抗体与之结合，实现对细菌高效

的捕获和杀灭. Khantamat等人[25]制备了二氧化硅@金核/壳纳米颗粒, 该纳米颗粒用羧酸酯封端的有机硫配体官能化, 并附着在导管表面, 在波长为810 nm的近红外激光下显示出对致病性粪肠球菌的高效黏附和杀灭.

1.6 其他金纳米结构

其他金纳米结构, 例如金纳米花、金纳米膜等, 在近红外光照射下也具有良好的光热抗菌性能. 最近, Wang等人[15]首次使用达托霉素胶束作为模板和还原剂, 在温和的条件下制备出稳定的达托霉素-金纳米花(Dap-Au$_n$NFs), 实现了对细菌的有效抑制. Gao等人[43]基于金纳米膜, 构建了多功能等离子体金芯片, 用于细菌的早期诊断和高效杀灭.

2 金基纳米材料的改性与应用

合成不同结构的金纳米材料并对其结构修饰改性, 近几年来得到了广泛的研究. 这一趋势在很大程度上是由于金纳米结构具有独特且可调的性质, 包括LSPR、生物相容性和易于表面改性. 因此, 研究者进一步拓展了金纳米材料在纳米医学中的应用. 例如, 金纳米颗粒可以将蛋白质分子吸附到表面, 导致金纳米颗粒的LSPR偏移[44]. 当用特异性抗体包被时, 这些免疫金纳米结构可用于探测细胞表面抗原的存在及位置, 并具有选择性递送药物的潜在能力.

为了提高金纳米结构对病原菌的靶向性, 以及进一步提高金纳米结构的光热抗菌效率, 实现对病原菌精确高效地杀灭并避免伤害健康细胞, 研究者探究了各种对金纳米结构进行修饰和改性的方法.

2.1 表面修饰增强病原菌靶向性

2.1.1 特异性抗体修饰

基于特异性抗体对细菌的靶向识别功能, 研究人员使用针对相应细菌的抗体与金纳米结构结合, 改善金纳米结构靶向性. 最近, Du等人[13]利用耐甲氧西林金黄色葡萄球菌特异性识别适配体功能化修饰金纳米星, 表现出对病原菌的高效杀灭. 同时, 由于其在耐甲氧西林金黄色葡萄球菌感染部位的靶向积累, 对周围健康组织的损伤可忽略不计, 保证了其优异的体内生物相容性. Norman等人[36]将金纳米棒与铜绿假单胞菌特异性抗体共价结合, 显示出对革兰氏阴性菌铜绿假单胞菌的选择性高效杀灭的能力. Wang等人[45]利用巨噬细胞膜上的细菌识别受体修饰金-银纳米笼(图3(a)),

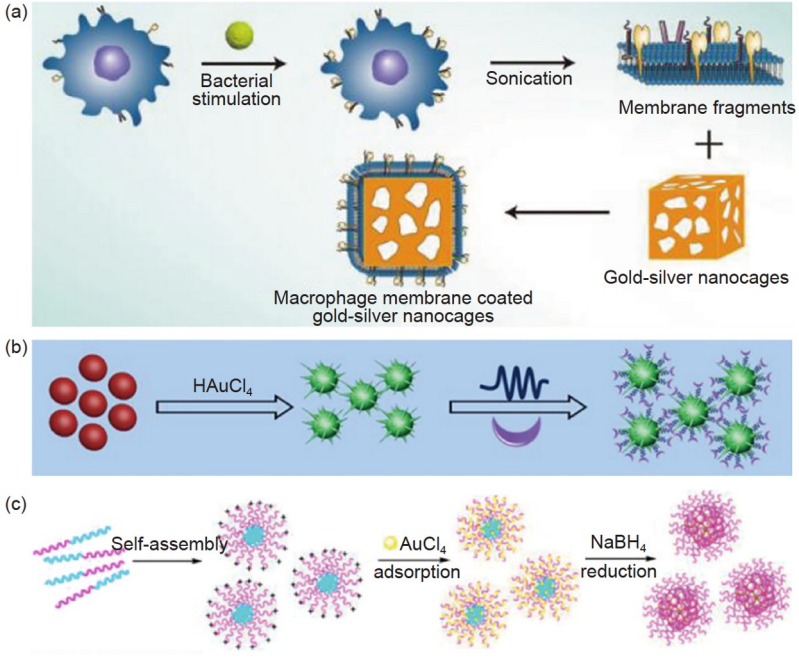

图 3 (网络版彩色)金纳米结构的改性示意图. (a) 金纳米结构的特异性抗体修饰[45]. Copyright © 2018, Wiley. (b) 万古霉素修饰[46]. Copyright © 2019, American Chemical Society. (c) 多肽修饰[47]. Copyright © 2021, Elsevier

Figure 3 (Color online) Schematic diagram of modification. (a) Schematic diagram of specific antibody modification[45]. Copyright © 2018, Wiley. (b) Vancomycin modification[46]. Copyright © 2019, American Chemical Society. (c) Polypeptide modification of gold nanostructures[47]. Copyright © 2021, Elsevier

有效改善了对细菌的靶向黏附与光热杀菌性能.

2.1.2 万古霉素修饰

一些研究者希望利用万古霉素的细菌结合亲和力可以与位于细菌细胞壁上的特定肽相互作用, 实现金基纳米结构的靶向性高效光热抗菌. Wang等人[46]开发了一种万古霉素修饰金纳米星的有效靶向和杀死革兰氏阳性菌的新策略(图3(b)). 在近红外光照射下, 在体内治疗细菌感染方面显示出令人满意的生物相容性和抗菌活性. Wang等人[32]报道了一种基于细菌诱导的金纳米颗粒聚集的新型治疗策略, 其中GNPs通过万古霉素的特异性靶向和生物正交环加成原位聚集在细菌表面. 更重要的是, GNPs的原位聚集显示出较强的近红外吸收和高光热转换, 从而增强了光热杀菌性能, 而在没有细菌菌株的情况下, GNPs是分散的, 表现出相对低的光热效应, 有效地减少了对周围健康组织的副作用.

2.1.3 多肽修饰

多肽纳米结构的使用可广泛应用于医疗器械和生物材料. 目前许多研究者利用多肽修饰金纳米结构, 制备出具有病原菌靶向性、高生物相容性的光热剂. 例如, Mu等人[48]将金纳米颗粒负载于牛血清白蛋白微纤维上, 开发了具有细菌过滤能力的新型蛋白质微纤维, 用于在近红外辐射下灭活细菌. 此外, 如图3(c)所示, Gui等人[47]利用超小的金纳米颗粒(ca. 4.0 nm)构建了一种新的核/壳结构金和淀粉样肽A$\beta_{25\text{-}35}$纳米复合材料(Au@Aβ NCs). 由于金纳米颗粒Aβ壳层的作用, Au@Aβ NCs可以强烈地黏附到细菌表面, 并通过淀粉样肽的固有自组装特性聚集在一起, 有助于细菌的局部光热消融.

2.1.4 其他改性修饰

噬菌体正越来越多地被用于治疗病原菌感染. 基于噬菌体对细菌宿主的多种靶向机制, 研究者将噬菌体与金纳米棒结合, 利用噬菌体对几种病原菌的特异性黏附, 将金纳米结构集中在细菌周围, 在近红外光的激发下, 金纳米结构产生局部高热, 利用光热消融选择性靶向杀死特定的细菌细胞. 最近, Peng等人[49]制备了一种噬菌体-金纳米棒生物偶联物, 能够通过光热效应特异性附着并杀死目标细菌. 值得注意的是, 光热裂解具有高度选择性, 可在几分钟内大量杀死目标细菌, 对非目标细菌和生物细胞的损伤率较低. 此外, 利用高生物相容性的分子或聚合物来选择性捕获细菌引起了很多关注. Gao等人[50]使用4-巯基苯硼酸作为细菌捕获单元, 构建了一种细菌捕获、检测和高效杀灭的抗菌平台.

2.2 多材料掺杂、负载增强抗菌性能

2.2.1 贵金属掺杂

为了应对多重耐药菌对抗生素表现出的强烈耐受性和不敏感性, 迫切需要开发高效的抗菌剂和策略. 研究者已经探索了各种抗菌剂来对抗细菌感染, 例如金、银、铂等贵金属纳米颗粒. 有研究者利用银、铂等贵金属负载修饰金纳米结构, 以增强金纳米结构的光热转换效率, 以及更长效、高效的光热抗菌性能. 如图4(a)所示, Hu等人[51]构建了一种由棒状核-壳-壳(金-银-金)纳米棒组成的新型杀菌材料, 外部金壳可在激光照射下熔化并导致内部银壳的暴露, 促进抗菌银离子的受控释放, 实现了金外壳的物理光热杀菌和银离子长效释放的多重抗菌效果. Hu等人[52]设计了一种新型三金属核壳纳米结构, 在金纳米棒上外延生长银铂合金纳米点作为潜在的抗菌剂. 该纳米结构的近红外光热效应显示出高度增强的抗菌活性. 此外, 由于近红外光谱区的LSPR可调, 有望利用光对抗菌活性进行额外的控制, 如光激发银离子释放. Wu等人[24]研究了一种SiO_2包覆的金银纳米笼作为抗菌材料, 它们的光热特性和银离子的缓释特性被用于近红外诱导的联合抗感染治疗, 并且在伤口感染大鼠模型中显示出优异的可持续抗菌治疗效果.

2.2.2 黑磷共轭负载

在光热抗菌领域, 黑磷由于其强大的近红外光吸收性能, 成为一种优秀的近红外光响应光热抗菌剂, 并且具有特定2D结构的黑磷纳米片能够穿透细菌膜[53]. 与其他2D纳米材料不同, 黑磷可以作为金属前体(如银和金)的支持物和还原剂[54,55], 黑磷的高表面积还有助于负载多种抗菌剂, 产生具有协同增强抗菌活性的组合分子纳米平台. 因此, 黑磷独特的理化性质使其成为生物医学应用(包括光热抗菌)的理想纳米平台候选材料. Aksoy等人[14]利用表面活性剂辅助的化学还原方法合成出单分散金纳米颗粒, 并将其组装在剥离的黑磷纳米片上制备出黑磷/金纳米复合材料(图4(b)), 显示出对细菌生物膜的有效抑制作用.

2.2.3 与其他抗菌材料联合

为了应对抗生素过度和持续使用导致的严重细菌耐药性问题, 研究者将金纳米结构与其他抗菌材料复合, 实现更长效的、优异的光热协同抗菌作用, 以此对抗多重耐药菌. Bermúdez-Jiménez等人[56]将金纳米棒嵌入壳聚糖水凝胶中, 作为PTT局部控制慢性感染的一种新型光热剂. Chen等人[35]利用抗菌肽、蟾蜍素2b和金纳米棒开发了一种特异性的药物输送系统(图4(c)), 用

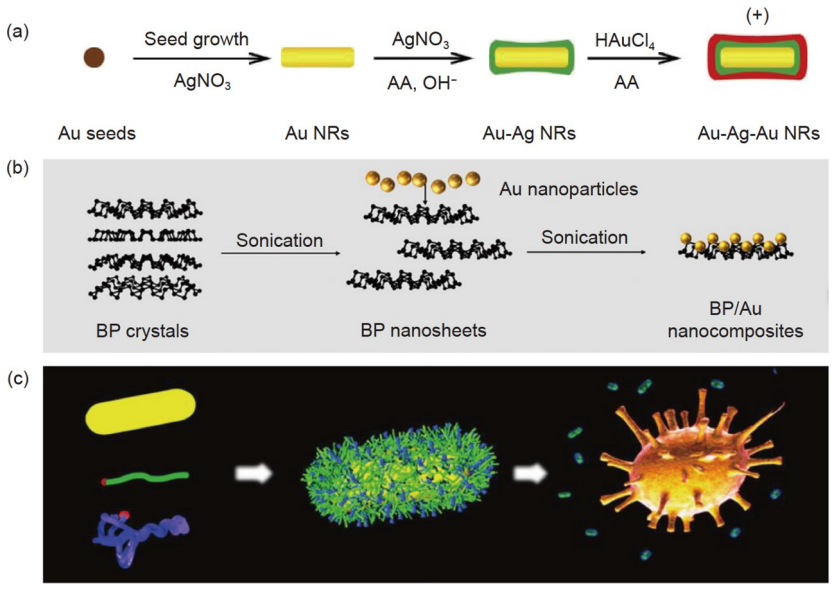

图 4 (网络版彩色)金纳米结构的改性示意图. (a) 贵金属掺杂[51]. Copyright © 2015, Elsevier. (b) 黑磷共轭负载[14]. Copyright © 2020, American Chemical Society. (c) 联合其他抗菌材料[35]. Copyright © 2020, the Royal Society of Chemistry

Figure 4 (Color online) Schematic diagram of modification. (a) Precious metal doping[51]. Copyright © 2015, Elsevier. (b) Black phosphorus conjugated load[14]. Copyright © 2020, American Chemical Society. (c) Synergistic effect of other antibacterial materials[35] . Copyright © 2020, the Royal Society of Chemistry

于杀灭耐甲氧西林金黄色葡萄球菌. 其中, 抗菌肽与金纳米棒起到协同杀菌作用, 蟾蜍素2b的高效细菌穿透能力使材料具有更好的杀菌性能.

3 总结与展望

本文系统总结了近年来利用金纳米结构在近红外光照射下进行光热抗菌的研究进展, 这是一种解决细菌对现有抗生素耐药性问题的有效策略. 金纳米结构被证明是一种有潜力的纳米光热剂, 可用于无抗生素的PTBL. 但是, 这些金纳米结构在临床应用方面仍然面临着许多挑战. 未来的发展很可能聚焦在基于可见光或近红外光触发的金纳米结构, 以及进一步提高这些金纳米结构的抗菌效率和降低其生物毒性的策略上. 除上述应用外, 由于金纳米结构的聚集会产生“热点”, 对信号分子具有信号增强的作用, 因此还可将其用作病原体检测传感器, 以指示病原体的存在. 金纳米结构在未来各种新领域应用中还具有广阔前景. 例如, 与光合细菌结合, 实现光热转换效率的进一步提高, 以及进一步细化对细菌的特异性识别功能, 实现高效、精准靶向、安全的杀菌效果.

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补充材料

表S1 不同金纳米结构的光热杀菌应用

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Summary for “金基纳米结构光热抗菌研究进展”

Frontier exploration for gold-based nanostructures for photothermal bacterial lysis

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Pathogenic microorganisms can lead to serious infection. The increased multi-drug-resistant bacteria poses a great threat to the survival of humans and animals due to gene mutations and various mechanisms of drug resistance, which attracts people’s attention to alternative solutions against bacteria. Developing new antibacterial nanomaterials is an effective way to solve this problem. Due to the excellent biocompatibility, photothermal stability, photothermal conversion efficiency, and easy modification of gold nanostructures, the research has focused on the design of gold nanostructures with activated antibacterial properties induced by light irradiation for use against drug-resistant bacteria. At present, a variety of gold nanostructures were used for photothermal bacterial lysis, and their antibacterial properties can be enhanced by adding components for specific targeting or modulating the structure and size for enhanced efficiency of photothermal conversion. The photoactive gold based nanostructure displayed the great advantages of killing pathogenic bacteria especially for the drug-resistance bacteria, due to the physical damage to the bacteria from the gold based nanostructure, which is totally different from the mechanism of disinfection of traditional antibiotics. They have a great and wide application for solving the problem faced now.

In this review, we introduced the photoactive gold nanostructures used to fight for pathogen diseases, especially for drug-resistant bacteria infection. The basic principles, important developments, promising applications and limitations of the current technology are revealed. Initially, the diversity of gold nanostructures was introduced (gold nanoparticles, gold nanostars, gold nanorods, gold nanocages, gold nanoshells, etc.), due to their amazing local surface plasmon resonance (LSPR) and oxidation resistance, which can present one advantage of antimicrobial activity by the hyperthermia to lysis the bacteria in a short time. Near-infrared irradiation (NIR) was widely used in these photoactive gold nanomaterials, with the ability to penetrate the skin tissue from 5 to 10 mm and low damage to tissue. It is another advantage compared to other antimicrobial materials. Subsequently, the surface modification of gold nanostructure was addressed in this review due to the significance of modulating the property of gold nanostructure to enhance the antimicrobial activity and the specificity to pathogens, as well as lowering the side effect of damaging the normal cell. For instance, one strategy is proposed to modify the antibody or specific peptide against bacteria on the surface of gold nanostructure to regulate both the LSPR of gold nanostructure and specificity of bacteria. Another one is the combination strategy which includes the doping of Ag and Pt on the surface of the gold nanostructure, 2D nanomaterial (graphene oxide nanosheet or black phosphorus nanosheet)/gold nanostructure, and gold nanostructure with antibiotics or antimicrobial peptides, etc. All the approaches summarized in this review could facilitate enhancing the efficiency of killing bacteria by the photoactive gold based nanostructures. Finally, the challenges and perspectives in this area were proposed. For instance, the construction of smart material based on gold nanostructure was emergent in further exploration, according to the microenvironment of infection sites. The biosafety of photoactive gold based nanomaterial is still the big issue in the next step, which is the key factor for further clinical application. In general, the gold based nanomaterial with a variety of nanostructures displays the designable structure in a controlled manner, the excellent photoactive properties, and amazing hyperthermia feature, which sheds light on further clinical applications, such as biosensor and biomedicine.

gold nanostructure, photothermal antibacterial, modification, functionalization

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