# Description

## Background

Carbapenem-resistant Acinetobacter baumannii (CRAB), globally recognized as a “superbug”, has emerged as a leading cause of life-threatening nosocomial infections. Possessing extraordinary environmental adaptability, CRAB can survive on dry surfaces for weeks and resist most common disinfectants, making it highly prone to nosocomial transmission in ICUs and high-risk areas[1]. It invades hosts via damaged physical barriers or medical devices, requiring only a low inoculum ($10^3$~$10^5$ CFU) for stable colonization. Its infection spectrum covers pulmonary infections (VAP, 30-40%), bloodstream infections (CRBSI, 25-35%), and wound/soft tissue infections (15-20%), accompanied by staggering mortality rates—up to 50-70% for bloodstream infections and 70-80% for meningitis[2].

The clinical threat stems from the synergy of multidrug resistance mechanisms (e.g., OXA-type carbapenemase production, outer membrane porin loss) and biofilm formation, which increases bacterial drug resistance by 10-1000 times. Current antibiotic therapies are plagued by high costs (15,000-20,000 RMB per course), severe adverse effects (e.g., nephrotoxicity), and an inability to specifically target biofilms, leading to frequent recurrence.

While targeting the Quorum Sensing (QS) system is a promising strategy, existing methods face critical challenges in targeting efficiency, signal amplification, and therapeutic monitoring, limiting their clinical translation.

## Brief Introduction

### Diagnosis Module

We utilize a colloidal gold immunochromatography test strip combined with a visible light analysis device. The strip uses glass fiber pads to filter impurities[3], and the nitrocellulose membrane provides strong dipole interactions for protein immobilization[4]. By analyzing signal molecule ratios through grayscale

algorithms[5], the system enables rapid CRAB screening and distinguishes between “colonization” and “infection” states.

## Delivery Module

The core circuit implements a “sensing-amplification-execution” architecture to detect and disarm CRAB biofilms[6][7], specifically targeting 3-OH-C12-HSL[8], the primary quorum-sensing[9] signal, and utilizing PvdQ enzyme for efficient long-chain AHL degradation[10][11]. The system incorporates engineered chemotaxis receptors for active targeting and a positive feedback loop for sustained efficacy. Tailored strategies include: pH-sensitive liposomes encapsulating PvdQ for site-specific release in acidic pulmonary foci[12][13]; engineered OMVs with lipid raft structures[14] and dephosphorylated protamine targeting[15] for bloodstream delivery[16]; and a thermosensitive double-layer hydrogel system for wounds. The hydrogel utilizes Pluronic F127, QCS, and CMC for thermosensitive gelling and antimicrobial action[17][18][19][20][21][22][23], with core-shell micro-carriers[24][25][26] and a dual-chamber prefilled syringe[27] ensuring stability and biosafety.

## Visualization Module

Real-time efficacy monitoring is achieved through specific mechanisms: a genetic memory switch triggers BpsA to produce blue pigment in wound dressings[30]; an enzyme-probe competition mechanism generates water-soluble indigo carmine to indicate pulmonary therapeutic endpoints[29]; and PEG-shielded prodrug probes release red signals[30]upon specific protease CpaA cleavage[31] in bloodstream infections, excreted via urine.

## Kill Switch

A dual biocontainment system using the MazEF toxin-antitoxin module ensures safety. It features an arabinose-dependent “timed elimination” mechanism and a doxycycline-inducible “manual emergency kill” switch to guarantee complete clearance of the engineered bacteria after treatment.

# Reference

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