# 口服工程化益生菌以实现有效的铀暴露防护

## 摘要

在紧急核事故中，人为核活动带来放射性核素向环境泄漏的风险 [1–3]。特别是铀作为核燃料循环中最重要的元素，在其开采、加工、燃料废料处理和贫化铀武器的使用过程中可能会释放到环境中。这些放射性污染物一旦进入水循环和生态食物链 [4]，主要通过肠道吸收在人体内积累，威胁公众健康 [5]。研究发现，被吸收的铀会长期沉积在肾脏和骨骼中，造成严重的慢性毒性。二乙烯三胺五乙酸水合三钠钙盐（Ca-DTPA）和三钠锌盐（Zn-DTPA）是美国食品和药物管理局（FDA）批准的唯一用于从体内排出锕系放射性核素的整合剂，其他一些整合剂仍在开发中。[6] 然而，除非在铀暴露后立即使用，否则 Ca/Zn-DTPA 的铀去除效果非常有限。因此需要一种能够适应人体的预防长期暴露生物保护剂。本研究开发了一种经基因工程改造、表达铀酰结合蛋白的益生性大肠杆菌 Nissle 1917（EcN-U），用于预防铀经口暴露引发的健康损害。该工程菌通过口服给药后，利用其固有的肠道定植特性，可在动物肠道内形成生物屏障，特异性结合饮用水中的铀酰离子，阻断其进入血液循环并加速粪便排泄。

## 关键词

工程化细菌、铀酰暴露、铀酰结合蛋白

## Abstract

As a critical radionuclide in the nuclear fuel cycle, uranium if released to the environment during its mining, processing, and fuel disposal, or from depleted uranium weapons left in former war-zones, could accumulate in human bodies through oral uptake, posing high risks to the public health. In this study, probiotic Escherichia coli Nissle 1917 (EcN) genetically engineered to express a uranyl-binding protein (EcN-U) is developed to protect animals from oral uranium exposure. Leveraging its inherent intestinal colonizing ability, engineered EcN-U after oral administration could colonize in the animals'intestinal tracts and bind with uranyl in the drinking water, preventing uranyl from entering blood circulation and accelerating its clearance via feces. As the results, mice with acute oral exposure of high dose of uranyl if pretreated with EcN-U would survive from uranyl-induced death. As further demonstrated in mouse, rat and beagle dog models, animals with long-term oral exposure of uranyl if pretreated with EcN-U would show significantly reduced uranyl deposit in main organs, alleviated intestinal oxidative stress, normalized intestinal flora, as well as reduced tissue damages in other organs. Our work presents a general prevention strategy to efficiently and continuously protect the public against radioactive containments during nuclear accidents using orally fed natural probiotics.

## Keywords

engineered bacteria, uranyl exposure, uranyl-binding protein,

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