Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2025-2026

Project Nº 23

Title: Antibiotic Discovery from Silent Genes in the Bacterium *Xenorhabdus nematophila*

Department/ Laboratory
Department/ Laboratory: Department of Microbiology and Parasitology-Edificio de Investigación

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Summary
Antibiotic resistance is one of the most pressing public health challenges of our time. By 2050, drug-resistant infections are projected to surpass cancer as a leading cause of death worldwide. Despite this urgent threat, the discovery of new antibiotics has slowed dramatically, with few novel compounds reaching clinical use in recent decades. Bridging this innovation gap requires exploring untapped microbial sources and activating dormant biosynthetic pathways hidden within bacterial genomes.

This project focuses on *Xenorhabdus nematophila*, a symbiotic bacterium renowned for its rich secondary metabolite profile. Many of its biosynthetic gene clusters (BGCs) are silent under standard lab conditions but may encode structurally diverse and potent antibiotics.

To unlock these hidden compounds, we generate a transposon mutant library by randomly inserting strong promoters across the *X. nematophila* genome, thereby activating underexpressed BGCs. Culture supernatants from these mutants are screened for antimicrobial activity using overlay assays against multi-drug resistant pathogens such as *Acinetobacter baumannii* and *Klebsiella pneumoniae*. Colonies showing inhibitory activity are isolated and characterized to identify promising antibiotic candidates.

By mining the cryptic biosynthetic potential of *Xenorhabdus*, this project supports the global search for new antimicrobials to counteract rising resistance. It also offers participating students an opportunity to engage with antibiotic discovery at the molecular and translational level — a critical frontier in modern microbiology and biomedical research.

yes	
no	**X**

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?