Microbiology

Environmental Biotechnology

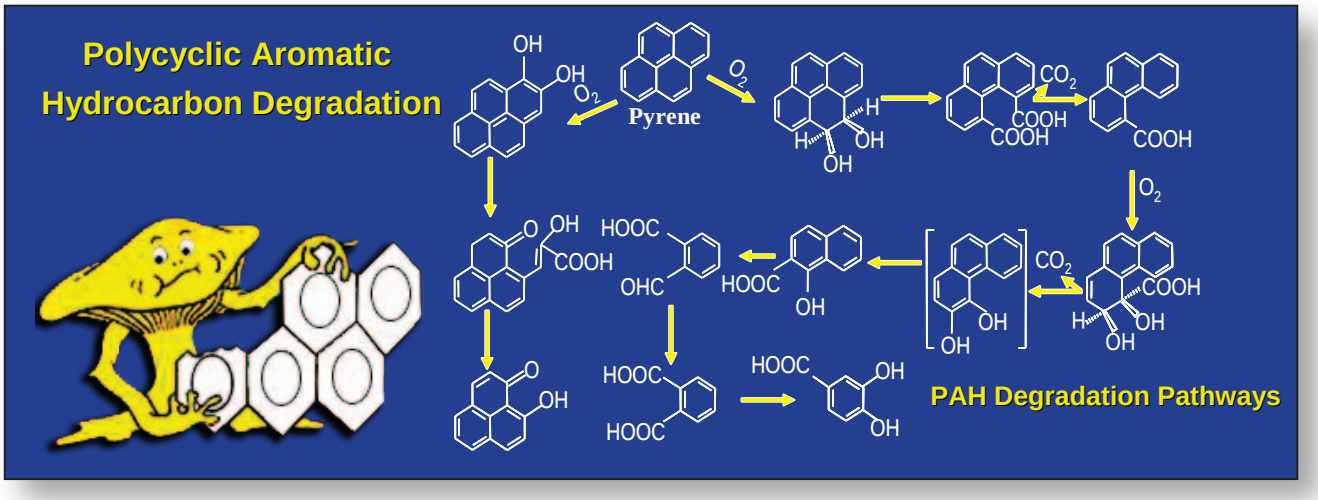
We have the capability:

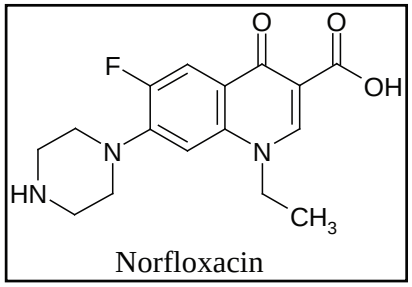
- to determine biochemical pathways for the degradation of toxic chemicals, using state-of-the-art analytical chemistry techniques
- to use microcosm test systems to determine pathways and increase detoxification rates for priority environmental pollutants
- to isolate microorganisms involved in the biodegradation of pollutants and related compounds
- to identify, by phenotypic and genotypic methods, the microorganisms involved in degradation of chemical wastes
- to characterize proteins and clone genes for the important enzymes from microorganisms that degrade toxic chemicals
- to use microorganisms as biocatalysts to degrade and mineralize toxic chemicals during bioremediation and to catalyze the synthesis of useful compounds, such as agrichemicals, pharmaceuticals, flavors, fragrances and other fine chemicals, by biotransformation

A major focus in the environmental biotechnology area in the Division of Microbiology has been to investigate the biodegradation of a wide range of pollutants with special emphasis on the ubiquitous carcinogens, polycyclic aromatic hydrocarbons (PAHs). Both fundamental and applied studies on the biodegradation pathways and the enzymatic and genetic basis for biodegradation of priority pollutants have been conducted. This pioneering research has led to the establishment of our laboratory as an internationally recognized biodegradation research facility. A team of scientists with expertise in analytical chemistry and molecular biology in the Microbiology Division has been involved in determining the feasibility of using microorganisms to remediate hazardous sites and in determining the enzymatic mechanisms involved in the biodegradation of priority pollutants.

Some examples of the expertise of the research team are listed below:

- **Polycyclic aromatic hydrocarbons (PAHs) constitute a class of organic compounds whose environmental fate is of concern because some PAHs have mutagenic, ecotoxic and carcinogenic potential.** We have elucidated PAH degradation pathways and developed proteomic and genomic techniques to characterize protein expression and the genes involved in the bacterial metabolism of PAHs.





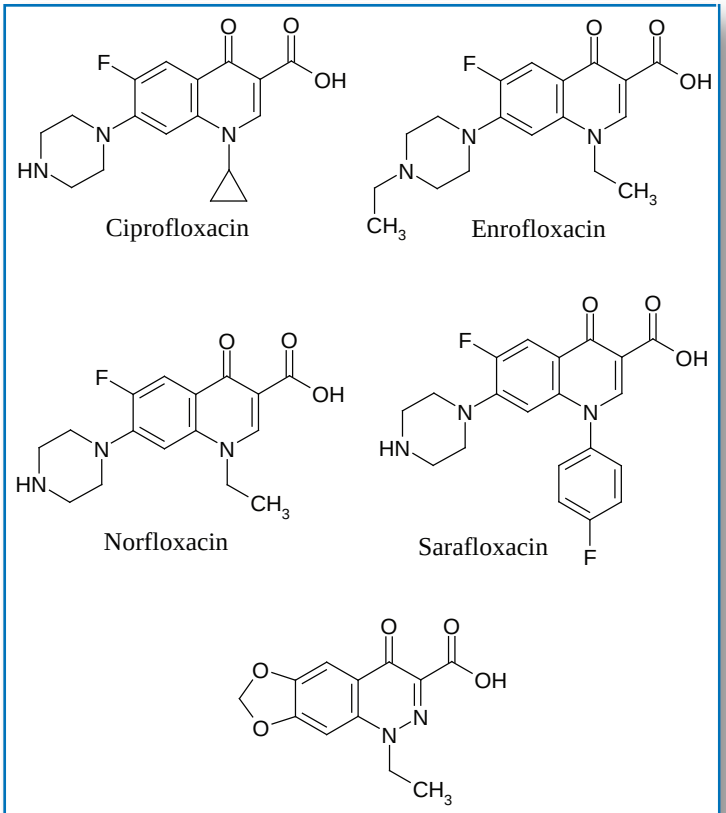
Biodegradation Of Antimicrobial Agents In Poultry Litter

When inoculated into rice-hull poultry litter, the nonpathogenic fungus *Pestalotiopsis guepini* degrades norfloxacin to four metabolites:

7-Amino-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinolone-3-carboxylic acid
N-Formylnorfloxacin
N-Acetylnorfloxacin
Desethylene-N-acetylnorfloxacin

When grown on ground corncobs, the fungus produces only the N-formyl and N-acetyl metabolites, and on pine shavings, it produces none at all.

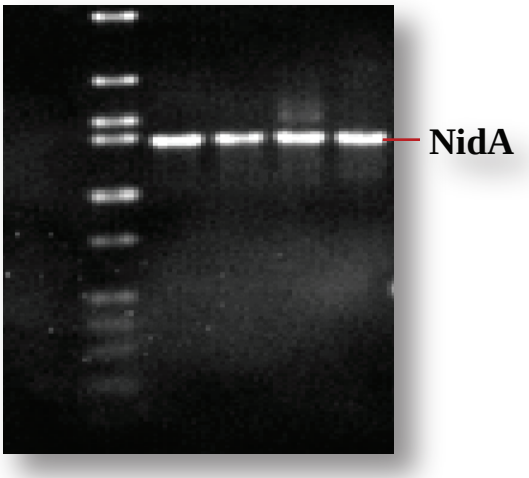
- **We are determining the pathways used by bacteria and fungi for the biodegradation of fluoroquinolone drugs in the environment.** These drugs may enter the environment in relatively large amounts, either as the unchanged parent compounds or as metabolites. Thus, it is important to determine the ability of environmental microorganisms either to degrade fluoroquinolones, thus rendering them harmless, or else to transform them to metabolites that have reduced antibacterial activity. For instance, appropriate microbial treatments of poultry litter may enhance the biodegradation of fluoroquinolone residues. We have shown that several fungi can metabolize flumequine, a fluoroquinolone used in aquaculture in some countries. Liquid chromatography, mass spectrometry, and nuclear magnetic resonance spectroscopy have been used to show that fungi oxidize the flumequine molecule to metabolites containing hydroxyl and keto groups.



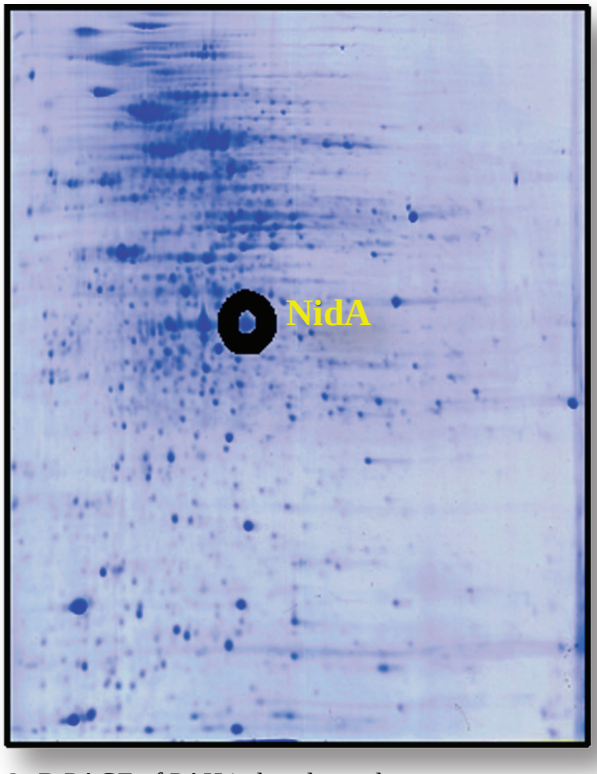
Fate Of Fluoroquinolones In The Environment

Fluoroquinolone drugs generally do not persist indefinitely in the environment, but are degraded by microorganisms.

The degradative microbes include fungi (such as *Umbelopsis*, *Pestalotiopsis*, *Trichoderma*, and *Beauveria*) and bacteria (such as *Mycobacterium*).



PCR Detection of nidA



2 - D PAGE of PAH induced sample

- **We have shown that the filamentous fungus *Cunninghamella elegans* simulates mammalian metabolism for numerous structurally diverse pharmaceutical compounds by phase I and phase II enzymes.** *C. elegans* biotransforms alkylamine, ethanolamine and ethylenediamine-type antihistamines, such as triprolidine, pheniramine, diphenhydramine, and thenyldiamine; tricyclic antidepressants, such as doxepin, cyclobenzaprine, amitriptyline, and protriptyline; and phenothiazines, such as chlorpromazine and methdilazine, to a range of different metabolites by aliphatic and aromatic hydroxylation, epoxidation, N- and O-dealkylation and N- and S- oxidation reactions. These studies demonstrate the usefulness of *C. elegans* to predict mammalian phase I drug metabolism and its potential for large-scale metabolite production for toxicological evaluation. The utilization of a microbial system for biotransformation studies provides several advantages over mammalian metabolism. One major attribute is the capability to increase metabolite production to give milligram, or sometimes gram, quantities for structure elucidation and biological evaluation. Furthermore, the metabolites produced in a microbial system can be used as reference standards to give insights for the characterization of mammalian metabolites.

www.fda.gov/nctr/science/divisions/micro.htm

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