Cover sheet
Title: Integrated Approaches to Combat Bacterial Antibiotic Resistance
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Summary
A highly interdisciplinary team to discover new antibiotics, to monitor patterns and elucidate mechanisms of resistance in Indiana, and to establish best practices for antibiotic use and infection prevention.

Abstract
The world is at the precipice of a post-antibiotic era, in which routine medical procedures, minor injuries, and food consumption can result in bacterial infections that can no longer be effectively treated by antibiotics. Improved stewardship of existing antibiotics and the development of new antibiotics are top priorities for the United States and countries around the world in the 21st century. This Grand Challenge (GC) will meld interdisciplinary teams into two paths to combat infection by antibiotic-resistant bacteria. The first path will establish coordinated antibiotic drug-hunting teams and infrastructure and work to discover unique, validated antibiotic lead compounds. The second path will study the complex ways bacteria become resistant to antibiotics in healthcare centers and through agricultural practices, and seek to better inform practices and policies to decrease the development and spread of resistance. Indiana University is uniquely placed with faculty with requisite expertise and experience and with outstanding research facilities to meet the goals of this GC, which by its multidisciplinary nature is not possible to accomplish through conventional university organizational and funding paradigms. Success in this challenge will lead to new strategies to discover antibacterial agents, potentiate the efficacy of existing antibiotics and to identify, track, and manage antibiotic-resistant bacteria in Indiana and elsewhere. This GC will have profound repercussions for human health and contribute solutions to an urgent worldwide medical need. Finally, this GC will establish Indiana University as a major research and student training center for combating antibiotic resistance in the future.
1. THE GRAND CHALLENGE, SIGNIFICANCE

The United States and entire world face a crisis due to the emergence and rapid spread of antibiotic-resistant human pathogenic bacteria. This serious threat to human health is well documented in recent reports from the Center for Disease Control and Prevention of the United States, the World Health Organization, and the Department of Health of the United Kingdom (1-3). The consensus conclusion from these reports is that the world is rapidly returning to a “pre-antibiotic” era that will lead to ever increasing loss of human life to once treatable bacterial infections and staggering economic loss. Combating antibiotic resistance is a grand challenge of the highest priority to the State of Indiana, the United States, and the rest of the world. The White House issued a National Action Plan (NAP) to combat antibiotic-resistant bacteria in March 2015 (4). In this proposal, we marshal the extraordinary scientific talent and depth of expertise of faculty at the Bloomington and Medical School campuses and healthcare centers to address major goals in the NAP. One path in the proposal seeks to discover and characterize new antibiotic lead compounds for future development. The second path in the proposal seeks to determine mechanisms of antibiotic resistance in bacteria isolated from patients, healthcare centers and agriculture settings in Indiana to enable improved diagnosis, antibiotic development, stewardship, and public policies. These two paths of the GC proposal are integrated and interconnected. Together, results and information from both paths of this proposal will offer tangible milestones important to the health of Indiana and the country and establish Indiana University as a center for overcoming bacterial antibiotic resistance long term.

2. GOALS

PATH 1

a. Establish a new paradigm for sustainable antibiotic drug discovery in an academic setting. Numerous financial and organizational constraints severely limit pharmaceutical and biotech company efforts to discover new antibiotics. Many of these constraints are not present in academia. Indiana University has outstanding microbiology, chemistry, and bioinformatic faculty and facilities needed for antibiotic discovery. Moreover, at least four faculty members have worked during their careers on antimicrobial discovery in industry. We will establish a sustainable antibiotic discovery program. This academic discovery paradigm will also provide a robust training environment for students interested in learning drug discovery.

b. Optimize antibiotic properties of four current chemical compounds with antibacterial activity and evaluate lead compound status. Four compounds with antibiotic activities are already being studied in IUB laboratories (5-9). We will use microbiology, enzymology, molecular modeling, and initial drug testing groups established by the GC to optimize the compounds and push them toward either lead compound status or elimination as candidates.

c. Target recently discovered extracellular protein surface targets for discovery of new classes of antibiotic lead compounds. A recent $3.4 mil NIH grant on bacterial cell wall synthesis to IUB investigators in Biology and Chemistry was to discover new targets for antibiotic discovery. Three cell wall biosynthesis proteins have been identified and will be targeted to find new classes of antibacterial molecules. Starting
molecular platforms will be chosen based on molecular modeling, previous inhibitor classes, and screening and optimized as described in section 2.1.b.

d. **Interface with Path 2 to identify genes that potentiate resistance to current antibiotics and indicate new antibiotic targets.** Expertise from Path 2 will determine possible functions of accessory genes that contribute to or enhance antibiotic resistance identified by Path 2 (see 2.2.b and 2.2.c, below). Potential new antibiotic targets that emerge from these analyses will feed into the antibiotic discovery pipeline.

e. **Move validated lead antibiotic compounds into development partnerships.** Tangible milestones of Path 1 will be validated lead antibiotic compounds with optimized efficacy against pathogenic bacteria, known targets in select or a broad range of bacteria, minimal resistance development, minimal mammalian cell toxicity, and good efficacy and pharmacological distribution in animal models of infection. Our goal will be to identify lead antibiotic compounds for future development through industrial, foundation, and government collaborations. This success will make the antibiotic discovery pipeline we establish highly competitive for external funding to develop antibiotics and continue discovery of new classes of lead antibiotic compounds.

**PATH 2**

a. **Establish detailed epidemiology of carbapenem-resistant Enterobacteriaceae (CREs) in extended care facilities and acute-care hospitals.** CREs are resistant to nearly all available antibiotics and kill up to 50% of infected people (10). Initially identified in 1996, CREs have been reported globally, especially throughout the United States. Molecular characterization of CREs from patients from Indiana health care centers (HCC) has identified the major beta-lactamases associated with CREs since 2009 (11). Epidemiological data from multiple Indiana HCCs will be collected to determine the frequency of CRE-infected patients in each institution, the incidence of CRE as related to other antibiotic resistances and susceptibility of CREs to other antibiotics. These studies will enable better healthcare practices against CRE infection.

b. **Identify mechanisms for resistance to multiple antibiotic classes in CRE clinical isolates.** Bacteria become resistant to antibiotics multiple ways. Identifying the mechanism(s) for resistance will guide the development of more effective antibiotics as well as implementation of best practices in healthcare settings to minimize the spread of pathogenic bacteria. We will identify traditional and novel resistance mechanisms to known antibiotics, including beta-lactams, aminoglycosides, tetracyclines, and quinolones in CREs using microbiological and biochemical approaches, whole genome sequencing and transcriptome analyses to direct appropriate therapy. Identification of novel resistance determinants will potentially reveal new targets for antibiotic discovery by Path 1.

c. **Predict emerging antibiotic resistance that will inform discovery of antibiotics.** Genome-wide sequencing of antibiotic-resistance bacteria will identify changes that occurred to confer and potentiate resistance. Genomic analysis will also reveal patterns of mutations indicative of mechanisms that enhance antibiotic resistance and will identify clonal outbreaks of epidemic strains of bacteria. Genes that enhance resistance will be characterized and verified by microbiologists from Path 1 and putative new targets will be fed into the Path 1 antibiotic discovery pipeline (Section 2.1.b). The
annotated information from genomic analysis and mechanism of resistance to antibiotics will be processed and made available in databases that can be accessed by HCCs and medical diagnostic labs to enable rapid identification of pathogens. Efforts will also be made to establish a national database for this information.

d. Assess human and environmental pathways of antibiotic resistance in rural Indiana agricultural communities. Human antibiotic-resistant pathogens can have their origin in the agricultural uses of antibiotics (12). We will elucidate the prevalence of antibiotic-resistant species belonging to the *Enterobacteriaceae* family of bacteria in rural Indiana agricultural communities. We will examine the presence of resistant bacteria in human household and the effects of occupational behaviors, environmental factors and their interaction that promote antibiotic resistance.

e. Identify ways to improve the transmission of knowledge from the bench to practice. Advances in medicine must still be evaluated by policymakers and implemented by healthcare practitioners. We seek to evaluate the effectiveness of current practices in the prevention and treatment of infections caused by antibiotic-resistant bacteria and will develop ways to transmit best practices to practitioners.

3. PROPOSED RESEARCH AND ITS IMPACT.

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<thead>
<tr>
<th>Organization Chart and Resources for Integrated Approaches to Combat Antibiotic Resistance</th>
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<th><strong>Antibiotics Discovery</strong></th>
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<tr>
<td>Existing molecules</td>
<td>Healthcare and agricultural settings</td>
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<td>Identify novel compounds</td>
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Biology, Biotech, Chemistry

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<tr>
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<th><strong>Bioinformatics</strong></th>
<th><strong>Elucidate Resistance mechanism</strong></th>
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Biology, Chemistry, Biotech, IUMS, CGB, Informatics

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Biology, Chemistry, IUMS

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<th><strong>Sociology, SPH Cent. Survey Research</strong></th>
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<th><strong>Potential Resources</strong></th>
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<td>Grand challenge</td>
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<td>Federal funding</td>
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<td>NIH, HHS, DOE, NSF,</td>
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<td>Foundations</td>
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<td>Federal funding (see above)</td>
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<td>Foundations (see above)</td>
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<td>Industry collaborations</td>
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<td>CTSI</td>
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Grand Challenge
Federal funding (above) and:
SBIRS/STTRs
DARPA
Indiana H5 initiative
Foundations (see above)
Industry collaborations
Industry licenses
CTSI

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Path 1. We will establish coordinated antibiotic drug-hunting teams and infrastructure and work to discover unique, validated antibiotic lead compounds that will go into development and further testing by outside partners. Antibiotic drug discovery is highly
interdisciplinary and interactive and requires groups of microbiologists, microbial enzymologists, synthetic organic medicinal chemists, structural biochemists, molecular modelers, and pharmacological testers (see summary figure). A major reason that industry has not been successful in antibiotic drug discovery in the past decades is their high personnel costs viewed against the higher profit margins associated with drugs to treat chronic diseases (13). The abandonment of antibiotic drug discovery for commercial reasons by large pharmaceutical companies has led to the current crisis of a lack of new drugs to treat antibiotic-resistant infections. These issues do not exist in academia, where there is great scientific talent. However, academic organizational structures often impede the formation of broadly interdisciplinary teams required for antibiotic discovery. We will change this paradigm in this GC.

The key to antibiotic discovery is subjecting compounds with antibiotic properties to an iterative process to optimize bacterial killing, minimize mammalian cell toxicity, minimize resistance development, and optimize biodistribution. This process must be done rapidly and efficiently to drive compounds forward toward optimization or failure. The team leaders and participating faculty will assemble, train, and oversee the highly coordinated interdisciplinary teams to carry out antibiotic discovery. The teams will consist of microbiologists (compound screening and resistance testing and characterization), enzymologists (target assay set up and screening), medicinal organic synthetic chemists (compound synthesis and optimization to find “structure activity relationships” [SARs]), structural biochemists (target determination with compounds), molecular modelers (in silico compound optimization to drive SAR), and pharmacological testers (mammalian cytotoxicity assays and testing in animal infection models).

We will start by optimizing sets of antibiotic compounds already being developed in laboratories at IUB. These compounds will establish the discovery pipeline and include: D-amino acid derivatives specific for bacterial growth (VanNieuwenhze [5]); an inhibitor of the bacterial regulatory protein critical for translation and flagella assembly (Kearns [6]); and derivatives of antimicrobial peptides (Kao, 7) and chemokines (Winkler, 8, 9). The discovery pipeline will rapidly advance these compounds to a decision point about their future as antibiotics. In parallel, recently discovered, highly conserved proteins that mediate bacterial cell wall biosynthesis will be used as targets to discover entirely new classes of antibiotic compounds. These targets were found in NIH-funded basic work and have never been targeted before. We will start with two classes of cell wall hydrolases, which are compelling new targets with compound scaffolds as starting places for inhibitors (8). Additional promising targets will be added later. Last, novel targets will emerge from Path 2 studies of the mechanisms of resistance to currently used antibiotics. These targets will be characterized and fed into the discovery pipeline. This research plan will deliver several novel, lead antibiotic compounds validated in animal disease models to partners for next stages of development.

Path 2. We will establish coordinated teams and infrastructure to identify mechanisms that confer antibiotic resistance in bacteria that infect patients, to explore the effect of antibiotic use in agriculture on resistance in humans, and to establish best practices in healthcare settings for antibiotics use and preventing and treating infections.
Understanding resistance and the causes of new antibiotic-resistant bacteria also enables us to identify new target for antibiotic discovery by scientists in Path 1.

Identifying mechanisms for resistance is critical to understanding transmission and will enable the selection of effective therapies against drug-resistant bacteria (14). The initial effort will focus on CREs collected by Indiana clinical microbiology laboratories. It is important to focus on CREs, as they are resistant even to last-resort antibiotics and they are rapidly spreading worldwide. An initial, low-throughput analysis of CREs has already been established (15). The new pipeline for analysis will use next generation sequencing and bioinformatic analysis to identify changes in the bacterial genome and transcriptome, and the locations of the resistant genes on either plasmids or in the bacterial chromosomes. Genes suspected to confer antibiotic resistance would be transferred to laboratory strains of bacteria to evaluate their contribution to antibiotic resistance. The results will be made available in databases searchable by healthcare professionals to improve the assessment of treatments and to trace the sources of pathogens. The genetic and biochemical properties of novel molecules that confer resistance will be assessed, as will susceptibility of pathogens to novel antibiotics. In future years, we will establish the analysis of other classes of antibiotic-resistant bacteria in addition to CREs.

More antibiotics are used in agricultural practices than to treat patients (12). Food animals can generate resistant pathogens and potentially be reservoirs for diseases that could infect humans (12,16). The contribution of antibiotic use to animal health and to zoonotic human infections must be better characterized. We will collect information from farm owners, farm employees and meat and poultry processing plant workers about type, timing and quantity of antibiotic products used in animal production. We will also examine samples collected from both animals and humans for microbiological characterization, including resistance and susceptibility to antibiotics. Biomedically significant pathogens will be investigated for mechanisms of antibiotic resistance as described above. Information on infection outbreaks will also be determined, as will the impact of the environment on the production of antibiotic-resistant bacteria.

We seek to translate academic knowledge into clinical practice. We will conduct a survey of biomedical scientists and academic physicians to establish what experts see as the best current practices for preventing and treating infections related to antibiotic-resistant organisms. Interviews with infection control personnel and other healthcare professionals will be performed to understand their current practices in the prevention and treatment of infections caused by antibiotic-resistant organisms. Finally, we will conduct an experiment with several Indiana hospitals to explore policies and interventions to improve the transmission of knowledge from “the bench” into practice. Environmental sampling of possible sources of contamination will be performed. We will develop criteria to identify “leaders” or “champions” within the hospitals, invite them to a seminar on best practices, and then conduct follow-up interviews to assess whether the practices had a measurable impact.

**Summary.** Efforts from Paths 1 and 2 of this GC will contribute solutions to combat antibiotic resistance within the state of Indiana and beyond. Execution of the two paths will also establish Indiana University as a major center for combating antibiotic resistance.
4. RESOURCES

The most valuable resource for this GC is the existing researchers from the multiple departments, campuses, and disciplines who have individually excelled in antibiotic resistance research and antimicrobial discovery. The GC will mobilize these experienced, successful researchers into the multidisciplinary team required to meet the goals of this project.

IU has equipped laboratory spaces, core facilities, and computer resources for most of the proposed work. The facilities include one for microbiological work with pathogenic bacteria, chemistry and structural biology laboratories, screening facilities, Centers for genomics and bioinformatics, proteomics, and multiple forms of microscopy.

**Hiring.** The proposed paths require bench scientists, primarily postdocs and students to carry out the work. We will establish programs to train them. With new faculty hires, we seek to be strategic and emphasize hiring faculty of exceptional quality to meet needs in the project. This strategy is made viable by the already strong cadre of IU researchers whose expertise is relevant to antimicrobials and antibiotic resistance.

**Postdocs and students.** We estimate that we will need **four postdoctoral scientists and eight graduate students per path.** The majority of the students will be trained in at least two disciplines, rather than by only one laboratory. The research will be jumpstarted by the hiring of research associates who will be responsible for daily operations while we recruit students and postdocs.

**Professor of Practice.** By the end of year 1, we will hire **two** highly experienced, accomplished scientists from the private sector on antibiotic discovery and antibiotic resistance as non-tenure track Professors of Practice. The positions will be renewable on a biannual basis. A pool exists of highly successful industrial scientists who have been downsized or retired from industry as antibiotic discovery and development efforts have contracted in industry. The scientists will contribute to research but will also serve as advisors to projects, teach, and help attract resources from the private sector.

**Strategic Hires.** Tenure-track faculty searches will initiate in year 2 of the project. By that time, we will have a strong pipeline of antibiotic lead compounds, smooth functioning of the units researching antibiotic resistance, and initial staffing of the projects. These factors will improve our competitiveness for hiring outstanding faculty. We propose making **eight hires** in the following areas: microbiology and drug discovery (2; Biology); medicinal organic chemistry (2; Chemistry); molecular modeling and computational biology (1; Biochemistry/Bioinformatics); biological engineering (1; Biology/Engineering), Environmental Health (1, School of PH); biomedical policies (1; Sociology).

**Equipment.** The GC will largely use equipment and laboratory space already in place on IU campuses. However, at the start of the project, we will purchase equipment currently lacking on the IUB campus: (1) VITEK-MS instrument for the rapid detection and identification of different bacterial species (~$272,115); (2) VITEK2 to assess antibiotic susceptibility (~$126,920); (3) Shimadzu ultra-high-performance liquid chromatography system with MS detectors to analyze bacterial cell walls (~$265,000); and (4) BioTek Cytation imaging reader for compound screens (~$154,000). The equipment will be made available to other researcher in the University.
5. TEAM

1. Contact: Path 1: Malcolm Winkler; Path 2: Cheng Kao.

2. Team leaders

Malcolm Winkler will lead the Antibiotic discovery project. Malcolm is a Professor and Section Associate Chair of Microbiology in the Biology Department. He was a Research Director in antibacterial research at Eli Lilly for four years before joining the faculty at IUB. He is a Fellow of the American Academy of Microbiology and the American Association for the Advancement of Science (AAAS).

Michael VanNieuwenzhe will co-lead the antibiotic discovery program. Michael is an Associate Professor of Chemistry. He has discovered novel antibiotics and developed diagnostics for bacteria and interdisciplinary research at both industry and academia.

Cheng Kao will lead the antibiotic resistance program. Cheng is the Director of the Biotechnology Program and a Professor of Mol. & Cell. Biochemistry. He has 20 years of experience working with academic scientists to study antimicrobial resistance and worked with industrial scientists to develop four antiviral and anti-inflammatory therapies that have entered clinical trials.

Karen Bush will co-lead the antibiotic resistance program. Karen is a Professor of Practice in the Biotechnology Program. She has 35 years of experience in discovering and developing antibiotics in Fortune 500 companies, where she led or participated on teams that introduced nine antimicrobial drugs into clinical trials. She is a Fellow of the American Academy of Microbiology.

Shawn Gibbs will lead studies of antibiotic resistance in rural Indiana agricultural communities. Shawn is the Associate Executive Dean, School of Public Health and Professor of Environmental Health. He served as a Director for the Central States Center for Agricultural Safety and Health and the Nebraska Biocontainment Unit that addressed the needs of the 2014 Ebola outbreak in Africa.
6. SUSTAINABILITY

The scope of our projects on antibiotic resistance requires significant resources in addition to those provided by the GC. Indeed, we perceive funding by the GC to serve as catalyst to organize and initiate the building of self-sustaining platforms. Our efforts are timely and in line with national and worldwide priorities, as infection by antibiotic-resistant bacteria is one of the most pressing problems of our times, with impact on human health, food production, and national security. Diseases resulting from antibiotic-resistant bacteria are also the focus of organizations formed to address specific diseases and social issues. Thus, resources to develop solutions to antibiotic resistance are available through a large number of public and private institutions.

Agencies that fund projects on antibiotic discovery and antibiotic resistance are listed in the schematic to our organization (p. 4). In addition to the traditional federal agencies, such as the NIH, NSF, and the USDA, potential funding agencies include the CDC, Department of Defense, the Biomedical Advanced Research and Development Authority, and the World Health Organization. Private organizations soliciting proposals in this area include the Cystic Fibrosis Foundation, the TB Alliance, the Gates Foundation, and the Pew Charitable Trust. The effort to discover antibiotics will also lead to funding research for small businesses, industrial grants, and potential revenue from licenses.

7. PARTNERS

Partners will include additional IU academic researchers and Infectious Disease prevention experts at Indiana health care centers. The National Center for Genomic Analysis Support will partner with us on managing complex biological datasets. We will partner with scientists at other universities to develop antibiotics or study resistance mechanisms. Finally, we will partner with companies that develop drugs, medical devices and diagnostics. Current collaborations with industry developing antibiotics or studying antibiotic resistance or medical devices include Achaogen, Actavis, Tetraphase Pharmaceuticals, and Cook Biotech.
8. METRICS

Year 1
- Execute evidence-based triage of investigational antimicrobials already identified at IUB.
- Develop SAR for antimicrobial compounds that pass triage process.
- Evaluate and identify novel bacterial targets, set up screens to identify hits.
- Whole-cell screening of natural products synthesized at IUB and elsewhere.
- Collect and analyze CREs from clinical samples collected in 2015.
- Establish database of Indiana CRE bacteria, their mechanism for resistance.
- Identify and classify antibiotic-resistant bacteria from agricultural practices.
- Initiate examination of antibiotic use in IN health care centers.
- Hire Professors of Practice (2).
- Establish contacts with key scientists outside of IU with relevant experience.
- Establish training curriculum for graduate students on antibiotics and antibiotic resistance.
- Initiate annual symposium on antibiotics discovery and resistance.
- Peer-reviewed publications (every year of this GC).
- Establish a scientific advisory board.

Year 2
- Continue SAR for molecules already identified on campus, including structure-based modeling approaches.
- Identify hit compounds against novel targets and begin SAR.
- Start structural studies of targets bound to compounds to drive modeling approaches.
- Continue analysis of antibiotic-resistant CREs from clinical samples.
- Expand pipeline to collect and analyze a second group of antibiotic-resistant bacteria.
- Report on antibiotic use in Indiana agriculture and its impact on human infection in rural Indiana communities.
- Establish best practices for antibiotic use and organize workshops on best practices.
- Submit proposals to fund research in antibiotic discovery and antibiotic resistance.
- Recruit students and scientists and establish an improved training curriculum.
- Strategic hires (3).

Year 3
- Continue productive directions listed above.
- Continue SAR of potential lead compounds, including resistance and preclinical testing.
- Obtain intellectual property rights on potential antibiotics and diagnostics.
- Initiate discovery of new antibiotics based on resistance profiles from clinical samples.
- Continue analysis of antibiotic-resistant bacteria and expand collection and analysis of a third group of antibiotic-resistant bacteria based on analyses of resistance profiles.
- Follow-up evaluation of the impact of best practices workshops on hospital practices.
- Establish a summer outreach program for high school students and teachers.
- Obtain postdoctoral fellowships.
- Submit multiple PI grants.
- Submit proposals to fund a center for integrated management of antibiotic-resistant bacteria.
- Strategic hires (3).

Year 4
- Continue productive directions listed above.
- License first compounds for shared development with industry.
- Submit graduate student training grants.
- Strategic hires (2).

Year 5
- Continue productive directions listed above.
- Become financially independent from the GC through extramural funding.
- Graduate new PhDs and independent investigators.
References cited


## Appendix

### Table 1. Investigators, Grand Challenge on Integrated Approaches to Combat Bacterial Antibiotic Resistance.

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<thead>
<tr>
<th>Investigators</th>
<th>Title, Department, School, Campus</th>
<th>Relevant expertise</th>
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<tbody>
<tr>
<td>Path 1</td>
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<tr>
<td>Yves Brun</td>
<td>PhD, Prof., Biology, COAS, IUB</td>
<td>Microbiology, high-throughput screening</td>
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<tr>
<td>Karen Bush*</td>
<td>PhD, Prof. of Practice, Biotechnology, COAS, IUB</td>
<td>Antibiotic resistance; antibiotic development</td>
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<td>Charles Dann</td>
<td>PhD, Assoc. Prof. Chemistry, COAS, IUB</td>
<td>Structural biology; biochemistry</td>
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<td>Clay Fuqua</td>
<td>PhD, Chair &amp; Prof. Biology, COAS, IUB</td>
<td>Bacterial physiology and metabolism</td>
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<tr>
<td>David Giedroc</td>
<td>PhD, Prof., Chemistry</td>
<td>Biochemistry; structural biology</td>
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<tr>
<td>Cheng Kao*</td>
<td>PhD, Prof., MC Biochemistry, COAS, IUB</td>
<td>Antimicrobial discovery</td>
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<td>Dan Kearns</td>
<td>PhD, Assoc. Prof., Biology, COAS, IUB</td>
<td>Bacterial genetics and physiology</td>
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<td>Samy Meroueh</td>
<td>PhD, Assoc. Prof., IUMS, IUPUI</td>
<td>Computational biology; drug development</td>
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<td>Richard Nass</td>
<td>PhD, Assoc. Prof., Pharmacology, toxicology, IUPUI</td>
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<td>David Williams</td>
<td>PhD, Prof. Chemistry, COAS, IUB</td>
<td>Medicinal organic chemistry</td>
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<td>Malcolm Winkler*</td>
<td>PhD, Prof. Biology, COAS, IUB</td>
<td>Bacterial physiology and pathogenesis</td>
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<td>Jeff Zalesky</td>
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<td>Bioinorganic chemistry; antimicrobials</td>
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<td>Mike VanNieuwenhze</td>
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<td>Occupational health; TB prevention/control</td>
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<td>Farrah Bashey-Visser</td>
<td>PhD, Asst. Scientist, Biology COAS, IUB</td>
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<td>Volker Brendel</td>
<td>PhD, Prof. Biology and Computer Science, COAS, IUB</td>
<td>Genomics and bioinformatics</td>
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<td>Karen Bush*</td>
<td>PhD, Prof. of Practice, Biotechnology, COAS IUB</td>
<td>Antibiotic resistance; antibiotic development</td>
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<td>Gerald Denys</td>
<td>PhD, Visiting Professor, IUMS, IUPUI</td>
<td>High throughput diagnosis, microbiology</td>
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<td>Shawn Gibbs*</td>
<td>PhD, MBA, Prof. Environmental Health, SPH, IUB</td>
<td>Infectious disease management</td>
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<td>Khalid Khan</td>
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<td>Agriculture; rural health, epidemiology</td>
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<td>Cheng Kao*</td>
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<td>Host-pathogen interaction; antimicrobial discovery</td>
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<td>Emily Meanwell</td>
<td>PhD, Director, Social Science Res., COAS, IUB</td>
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<td>Scott Michaels</td>
<td>PhD, Professor, Biology, COAS, IUB</td>
<td>Gene expression; genomics</td>
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<td>Fabio Rojas</td>
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<td>Organizational analysis; health policy research</td>
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<tr>
<td>Scott Stiebner</td>
<td>MD, Parkview Hospital, Fort Wayne IN</td>
<td>Infectious disease specialist, epidemiology</td>
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<td>Lilian Yahng</td>
<td>Director, Center for Survey Research, IUB</td>
<td>Scientific surveys</td>
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<td>Margaret Weigel</td>
<td>PhD, Prof. Environmental Health, SPH, IUB</td>
<td>Disease epidemiology, prevention</td>
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*Team leaders*