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Bridging Oncology and Infectious Disease: AI-Driven Biotechnological Strategies Against Antimicrobial Resistance

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ABSTRACT: Antibiotic resistance is a pressing global health crisis, driven by multidrug-resistant pathogens such as *A. baumannii* that render last-resort antibiotics less effective. Despite advances in antibiotic discovery, drug development pipelines remain slow, costly, and vulnerable to the emergence of cross-resistance. This paper explores the integration of AI into antimicrobial drug research and delves into an interdisciplinary approach that leverages tools from other fields, especially oncology, to expedite antimicrobial research. Zosurabalpin is a novel drug with high specificity for *A. baumannii* that disrupts the lipopolysaccharide transport (LPT) system, thereby undermining the bacteria's structural integrity. Halicin was repurposed as an antibiotic after AI screening of existing compounds identified it as having promising antimicrobial properties. The parallel between oncology and antimicrobial resistance offers a rich collection of knowledge transferable into antimicrobial research. Using oncology tools, such as DNA microarrays, monoclonal antibodies, and predictive modeling, provides a broader scope, enabling an integrative and comparative approach to accelerate innovation while reducing costs and redundancy.

KEYWORDS: Antimicrobial and Antibiotics, Immunology, Zosurabalpin, Oncology, AI.

Introduction

Since the discovery of penicillin in 1928, bacteria have rapidly developed resistance to a wide range of antibiotics, including last-resort drugs such as carbapenems and polymyxins. Multidrug-resistant (MDR) bacteria are outpacing pharmaceutical innovation. In 2019, 1.27 million deaths were attributed to antibiotic resistance worldwide.[1] Even when new antibiotics are developed, they are slightly modifi ed versions of existing drugs, making them susceptible to cross-resistance. In this phenomenon, bacteria already resistant to one drug in a class are likely to be resistant to drugs with similar mechanisms of action. Medical professionals are discouraged from increasing antibiotic doses because resistant mutants survive the higher dose and replicate, contributing to greater resistance in that strain. These issues have slowed the development of eff ective drugs against highly resistant bacteria, as growing bacterial cultures can take days, which critical patients do not have, let alone the time it'll take to test the effi cacy of a new drug against the bacteria. AMR currently causes an estimated annual death of 700,000, projected to reach 10 million by 2050, with potential $100 trillion global economic losses. Patients with drug-resistant infections often remain hospitalized for over 13 days, costing $29,000 per case.[2] Beyond these economic costs, pharmaceutical companies face little incentive to invest in new antibiotics, which are used for short-term treatment compared to chronic disease treatments. These statistics underscore the need for antimicrobial stewardship and the growing use of AI to screen existing compounds for antimicrobial potential, accelerating drug discovery.

Classifi ed by the World Health Organization as "Priority 1: Critical Pathogen," *Acinetobacter baumannii* is resistant to carbapenem—a type of beta-lactam antibiotic that is a last-resort drug to treat multidrug-resistant bacteria—decreasing the effi cacy of current treatments while also contributing to antibiotic overuse, a driving factor of antibiotic resistance. Intensive Care Unit (ICU) patients are especially vulnerable to *A. baumannii* infections due to the bacterium's biofilm–complex bacterial microcolonies, which reduce cell membrane permeability, allowing it to adhere to and survive on catheters, surgical instruments, and ventilators for long periods. People in low-and middle-income countries are also vulnerable to antibiotic-resistant bacterial infections due to the misuse of antibiotics.[3] Thus, expediting the development and testing of novel drugs is an urgent priority. Cancer patients also suff er from a higher risk of bacterial infection, so exploring oncology data provides a vast perspective in fi ghting hospital-acquired infections. Bacteria and cancer cells share mechanisms to counteract treatment eff ects, such as drug effl ux and mutations, which we will explore in more detail later. Of course, infectious diseases diff er from cancers in their etiologies, responses, and environmental factors, but the shared complexity of biological resistance warrants a logical exploration of innovations. It should still be acknowledged that Zosurabalpin is in the nascent stages, so its performance in real-world settings remains to be determined.

Extensive cancer research has identifi ed antimicrobial properties in human monoclonal antibodies. Additionally, antimicrobial peptides (AMPs) have been used to treat a variety of infections, including cancer and fungal infections. Using an interdisciplinary approach to cancer research to combat antibiotic resistance is feasible and enables the development of faster, novel treatments for resistant bacterial infections. Given the growing issue of antibiotic resistance, driven by factors such as unnecessary antibiotic prescribing, poor infection control, and the fi nancial burden of pharmaceuticals, a multidisciplinary

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approach off ers a new perspective for combating this global health crisis.

Moreover, exploring alternative strategies to combat antibiotic resistance beyond traditional antimicrobial development is increasingly important. In fi elds such as oncology and HIV research, predictive AI and machine learning models have already been extensively developed to identify resistance mutations and guide treatment decisions. Leveraging substantial funding off ers a practical and effi cient pathway to repurpose treatments for AMR. This paper fi rst explores novel drugs and the application of AI tools from other fi elds to antibiotic drug discovery, offering deeper insights and providing a holistic overview of existing research as a preface to repurposing oncology tools for AMR. This paper argues that oncology-derived AI tools and therapeutic frameworks off er a scalable, underutilized pathway for accelerating AMR innovation. By drawing parallels between emerging antibiotics like Zosurabalpin and how other fi elds have integrated AI, bioinformatics, and predictive modeling into drug development, we can identify overlooked strategies and potential shortcuts. In the following subsections, we'll review the existing literature and innovations that use AI to combat antibiotic resistance. Then, we'll proceed to expand on the idea of repurposing drugs and resources from other medical fi elds in subsection two.

■ Overview of Novel Compounds and Existing Applications of AI in Antibiotic Resistance Research

This section will cover bacterial biofilms and the genetic mechanisms of transformation, conjugation, and transduction. Outlining key resistance strategies—drug modifi cation, target modifi cation, effl ux pumps, and altered membrane permeability—and highlighting parallels between bacterial resistance and cancer drug resistance. First, we'll delve into the physical properties of bacteria. More specifically, bacterial biofilms, formed by both Gram-positive and Gram-negative bacteria, are structured communities embedded in a self-produced polymer matrix composed of polysaccharides, DNA, and proteins. Then, we will cover how Zosurabalpin works through the mechanisms of action that degrade bacteria and other compounds, as well as the applications of AI tools in drug discovery. These similarities motivate the use of predictive models originally developed in oncology.

Along with biofilm-buff ered support, bacteria can acquire resistance through various mechanisms, including transformation, conjugation, and transduction. Transformation occurs when bacteria incorporate DNA fragments from the environment; conjugation is the active exchange of genetic material between two bacteria via plasmids; and transduction is the acquisition of resistance genes via phages that inject new DNA. Driving factors of antibiotic resistance include antibiotic misuse, which increases mutation rates and the likelihood of resistance, releases DNA from dead cells, and ensures the survival of the fi ttest bacteria. Bacterial resistance mechanisms include spatial exclusion, drug modifi cation, target modifi cation, bypass mechanisms, effl ux pumps, and alterations in membrane permeability. Spatial exclusion is the prevention of antibiotics from reaching their targets by barriers such as bacterial cell walls and biofilms. This is especially challenging for treating gram-negative bacteria, which form cell walls and biofilms, whereas gram-positive bacteria do not. Bacteria may acquire or naturally possess genes encoding enzymes that modify antibiotic molecules by adding functional groups, thereby hindering their binding to target sites or simply deactivating the drug. Such resistance strategies parallel how cancer cells alter therapeutic binding sites, underscoring why oncology models help predict patterns of resistance. Some bacteria may also produce enzymes such as β-lactamases, which break down β-lactam antibiotics like penicillin, and aminoglycoside-modifying enzymes that add chemical groups to aminoglycosides, inactivating them. Target modifi cation refers to the antibiotic's target protein in bacteria, whose structure or function can be altered by mutations in ribosomes, DNA gyrase, and other proteins. Even if the antibiotic reaches the target site, reduced binding affi nity prevents it from interacting properly with the substrate. Bacteria can also bypass antibiotic-disrupted processes, such as folic acid synthesis, by obtaining folic acid from the environment. Effl ux pumps are membrane proteins that actively transport antibiotics that enter the cell. For example, the AcrAB-TolC system, powered by the proton gradient, is integrated into the inner, periplasmic, and outer membranes of Gram-negative bacteria. Reduced membrane permeability, achieved by downregulating porins or other protein channels, prevents drugs from entering the cell effi ciently. The variety of resistance mechanisms, along with the improper use of antibiotics, underscores the urgency of exploring and rapidly developing eff ective treatments.

Antimicrobial Stewardship:

This subsection evaluates Antimicrobial Stewardship (AMS), a set of practices that ensure antibiotics are used only when necessary and appropriately, as a frontline strategy to mitigate antibiotic resistance through optimized antibiotic use. Issues such as prophylaxis and overreliance on broad-spectrum antibiotics constrain the use of AMS as a long-term solution. Thus, these gaps underscore the need for complementary innovation. A systematic meta-analysis of 26 studies found that hospital-based ASP implementation reduced overall antibiotic consumption by ~19.1%, restricted antibiotic use (e.g., carbapenems, glycopeptides) by ~26.6%, ICU use by ~39.5%, and antimicrobial spending by ~33.9%.[2] In hospitalized cancer patients with febrile neutropenia, adherence to stewardship-guided antibiotic protocols has been associated with significantly lower mortality, indicating that optimized antibiotic selection and duration can improve outcomes even in immunocompromised populations.[4]

However, since AMS focuses on optimizing existing drugs rather than developing new therapeutic options, its impact is inherently limited as resistance continues to evolve. Moreover, stewardship principles are already practiced in other fi elds such as oncology, where treatment decisions routinely balance effi cacy, toxicity, and long-term outcomes. The general appli-

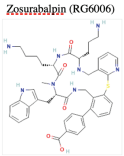
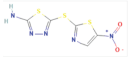
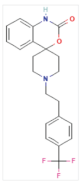
cations of AMS highlight its role as foundational rather than as a strategy that can be used alone. More importantly, what oncology stewardship that AMS currently lacks are adaptive protocols that adjust in real time to biomarker data, personalized dosing guided by pharmacokinetic/pharmacodynamic (PK/PD) modeling, and AI-assisted monitoring of treatment response. These well-established oncology tools represent a new frontier for AMS to incorporate.

The following section explores novel compounds to complement existing treatments and sustain eff ective antimicrobial therapy.

Novel Compounds:

One of the primary reasons AMR persists is the formation of biofilms by Gram-negative bacteria, which block antibiotic penetration and disrupt essential cellular processes. Addressing this structural defense has become a central focus of AI-driven drug discovery, leading to the identification of novel compounds such as Zosurabalpin. The biofilm creates a barrier to antibiotic penetration and disrupts biological processes. Zosurabalpin is a macrocyclic peptide that exhibits selective activity against carbapenem-resistant *A. baumannii*. It requires LPS to maintain the LptB2FGC complex in a substrate-bound conformation, thereby inhibiting LPS transport and damaging membrane integrity. The accumulation of LPS in the inner membrane becomes toxic to the cell, triggering cell death. Zosurabalpin, a macrocyclic peptide discovered through AI screening by Roche and Harvard, targets the outer membrane biogenesis of Gram-negative bacteria by inhibiting the LptB2FGC complex, blocking LPS transport to the outer membrane. It has shown potent activity against multidrug-resistant pathogens, especially *Acinetobacter baumannii* and *Klebsiella pneumoniae*.[5] Critically, it demonstrated no resistance emergence in *in vitro* testing, develops easily *in vitro*, and exhibits a mechanism of action not seen in previous antibiotics, making it especially promising and novel. Roche has announced plans to initiate Phase 3 trials, expected to enroll approximately 400 patients with carbapenem-resistant *A. baumannii* infections. While Zosurabalpin has been promising, it does not remain in the bloodstream for long and is cleared quickly from the body, so higher or more frequent dosages are necessary. It should still be acknowledged that Zosurabalpin is in the nascent stages, so its performance in real-world settings remains to be determined.[6] Such limitations emphasize the need for oncology-style optimization frameworks, such as PK/PD modeling from cancer trials, to adjust dosing and adapt to short half-life.

Table 1: Summary of Key AI-Discovered Antibiotic Candidates.

Compound	Drug Class	Mechanism	AI Method	Spectrum	Stage/Limitation
Zosurabalpin (RG6006) 	Tethered macrocyclic peptide	Inhibits LptB2FGC complex; blocks LPS transport to the outer membrane	AI compound screening (Roche/ Harvard)	Narrow: *A. baumannii*, *K. pneumoniae*	Phase 3 planned; short half-life requires dosing optimization
Halicin (SU3327) 	Thiadiazoles	Disrupts proton motive force; impairs ATP synthesis and iron regulation	Deep learning screen of ZINC15/Drug Repurposing Hub (MIT)	Broad: Gram-positive and Gram-negative	Preclinical; stability concern after storage; reduced efficacy vs *P. aeruginosa*
Abaucin (RS102895) 	Benzoxazine	Inhibits LolE (lipoprotein trafficking/ ABC transporter)	Deep learning trained on *A. baumannii* inhibition	Narrow: *A. baumannii* (MIC 2 μg/ mL, 41 strains)	Preclinical; narrow spectrum limits generalizability

Halicin was initially developed as an anti-diabetic drug. In 2020, MIT researchers built a deep learning model to screen the ZINC15 database for compounds with antimicrobial properties that were structurally distinct from current medications, enabling their repurposing as antibiotics. Unlike traditional antibiotics, Halicin disrupts the electrochemical gradient across bacterial membranes, interfering with their ability to produce energy (ATP synthesis), eff ectively killing them. Table 2 summarizes Halicin's novel mechanism of action and AI method of discovery.

Another promising strategy for using AI to synthesize and refi ne antimicrobial compounds is to leverage antimicrobial peptides (AMPs). AMPs are 2–50-amino-acid peptides produced by multicellular organisms as a defense mechanism against pathogenic microbes. AMPS have hydrophobic and hydrophilic regions and cationic properties, which allow them to disrupt bacterial membranes. They interact with the bacterial membrane, causing membrane perturbation and disrupting membrane-associated physiological processes, including cell wall synthesis, cell division, and translocation. AMPs also exhibit anti-biofilm activity while enhancing phagocytosis, wound healing, and angiogenesis. Platforms such as Deep-AmPEP30, IAMPE, and DeepACP have greatly facilitated the discovery and synthesis of novel peptides. There are well-maintained databases of AMPs derived from genetic sequences, and eff orts to design and synthesize protein epitope mimetics (PEMs) often lead to novel AMPs.

In parallel, bacteriophages—viruses that infect and replicate within bacteria—are being explored as promising AMR treatments because they share similarities with oncology viral vector-based therapies, in which engineered viruses are used to target and destroy malignant cells selectively. Bacteriophages have a tail-like structure that helps them attach to and inject their genetic material into bacterial cells. These viruses evolve rapidly to counter bacterial resistance and are highly specific, minimizing disturbances to the microbiota and preventing antibiotic-induced AMR. However, discovering novel bacteriophages can be tedious, and AI models can expedite the process. Two useful tools are PhageBoost and VirSorter2.

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PhageBoost is a novel ML method based on a feature space, designed for fast, generalizable prophage discovery and to significantly enhance bacteriophage identification. Another AI model, VirSorter2, substantially improves the accuracy and breadth of virus sequence detection in metagenomic datasets by leveraging multiple classifiers to identify a wide range of viruses with high precision.[7]

Collectively, these AI-enabled approaches encourage more targeted and adaptable treatments for antimicrobial resistance. Novel compounds such as Zosurabalpin and the repurposing of Halicin demonstrate how AI can uncover antibiotics with entirely new mechanisms of action that can bypass traditional resistance pathways and biofilm defenses. AI-driven design of AMPs and bacteriophages expands therapies, offering concrete, mechanism-diverse alternatives. Despite their promise, each approach faces practical limitations, such as narrow activity and dosing challenges, reinforcing the idea that no single solution is sufficient. Together, these advances highlight the value of combining AI-guided discovery with insights from complementary fi elds such as oncology. In the following subsection, the paper will delve further into the benefi ts of using AI tools in drug discovery and other therapeutic areas.

AI Tools: Expediting Connection from Oncology:

AI has substantially accelerated drug discovery to specific resistance problems, using support vector machines (SVMs), neural networks, and Hidden Markov Models (HMMs). SVMs classify novel genomic sequences as resistant or non-resistant by learning structural patterns from a curated database such as CARD. HMMs model the mutation pathway in a bacterial population under antibiotic pressure. Moreover, neural networks have been used to forecast cross-resistance. As these models are trained on large, comprehensive oncology datasets, they can be reused for antimicrobial resistance drug discovery.

Table 2: Summary of Key AI-Discovered Antibiotic Candidates.

Model Type	Core Functions	Oncology Example	AMR Applications
Predictive ***(SVMs, HMMs, Random Forest)***	Forecast resistance mutations from existing genomic data; classify susceptibility phenotypes.	Predicts which cancer patients will develop resistance to a targeted therapy (e.g., EGFR inhibitors in lung cancer) based on tumor genomic data	Deep-Arg (predicts ARGs); DASP (susceptibility phenotyping in 30 minutes)
Generative ***(GANs, VAEs, transformer-based)***	Synthesize novel molecular structures with desired biological properties	PETrans, ChemSpaceAL (de novo cancer drug design from cancer protein-ligand interaction data). ChemSpaceAL uses active learning, meaning it refines outputs based on experimental feedback.	Stanford's SyntheMol is a generative model trained on 13,000 *A. baumanii* compounds; 6/58 synthesized candidates showed potent activity against multiple resistant strains.
Screening/Classification ***(CNNs, deep learning)***	Screen large compound libraries for antimicrobial or anti-cancer activity, narrowing the database of chemical compounds to the most promising candidates for lab testing.	Oncology compound library screening (ZINC, ChEMBL to identify molecules that bind to cancer-relevant proteins)	MIT used deep learning to screen ~107 million compounds and identified Halicin (ZINC15); APRA-H TARGET project (107M molecule screen)

Abbreviations: AMR = antimicrobial resistance (when bacteria no longer respond to antibiotics); SVM = Support Vector Machine; HMM = Hidden Markov Model; GAN = Generative Adversarial Network; VAE = Variational Autoencoder; CNN = Convolutional Neural Network; ARG = antimicrobial resistance gene (a gene that allows bacteria to survive antibiotic treatment); MIC = minimum inhibitory concentration (the lowest drug dose that stops bacterial growth); PK/PD = pharmacokinetics/pharmacodynamics (how a drug moves through and acts on the body)

Models such as PETrans and ChemSpaceAL, originally trained on cancer proteome datasets, use transfer learning to generate de novo molecules for specific protein targets, making them well-suited to complex biological systems. These tools can be fine-tuned on bacterial genomic and structural datasets. The shared molecular properties—operating in protein-ligand binding interactions—enable knowledge transfer of generalized binding affi nities and structures between AMR and oncology.

Another transferable method from oncology is PK/PD optimization, a proven framework for individualized dosing that relies on real-time pharmacokinetic monitoring, biomarker-guided response assessment, and adaptive trials. This is especially applicable to Zosurabalpin, which has a short half-life and requires frequent redosing. Applying cancer-derived dosing optimization frameworks to antimicrobial agents with similar pharmacokinetic constraints would accelerate clinical translation.

In Table 2, you can see the various types of AI models and their diff erences, including ChemSpaceAL, Deep-ARG, and Synthemol. ChemSpaceAL is an AI model trained on four sources, combining SMILE strings from ChEMBL, GuacaMol, MOSES (~1.8 million molecules selected from ZINC15), and BindingDB. ChemSpaceAL uses active learning to create new molecules targeted to a particular protein, and part of its training data includes cancer-relevant compounds and general drug-like compounds. It fine-tunes a generative model to learn to produce compounds with desired biological properties.[8] This model has not been trained on bacterial proteins, which is where this tool can be transferable. The AMR application would require fine-tuning the model on bacterial protein-ligand datasets such as those for LptB2FGC or LolE.

AI-facilitated small-molecule antibiotic discovery can be used to identify biosynthetic gene clusters (BGCs), screen compound libraries, and repurpose drugs. For example, DeepARG, a DL-based model trained on a dissimilarity matrix derived from all known categories of antimicrobial resistance genes, achieves high precision and recall. DeepARG has two versions: SS and LS, tailored to handle short- and long-read sequences from metagenomic libraries. Another way AI has aided drug discovery is Synthemol, a generative AI model developed by Stanford Medicine to synthesize potential antibiotic compounds. It was trained explicitly on 13,000 compounds used to treat *A. baumannii*. Of the 58 synthesized candidates, six structurally novel molecules showed potent antibacterial activity against multiple strains, including resistant *A. baumannii*.[9]

A novel method, Deep Antimicrobial Susceptible Phenotyping (DASP), uses deep learning to analyze single-cell morphological phenotypes. It provides results in as little as 30 minutes, compared with antimicrobial susceptibility testing, which takes 18-24 hours. It examines individual bacterial cells and analyzes how their cell structures (DNA & membranes) change when treated with antibiotics. The method combines microscopy, which captures images of internal structures such as DNA and membranes, with the ability to observe individual cells in real time and track how they change when exposed to antibiotics.[10] Models, such as DASP, demonstrate how

phenotypic AI can reduce the time required to test bacterial responses to antibiotics delayed by biofi lms, thereby helping expedite antibiotic selection for critical care patients in ICUs.

Furthermore, AI models trained on datasets against specifi c bacteria, such as *A. baumannii*, have proven effective and efficient in discovering Abaucin and Zosurabalpin. Abaucin is a benzoxazine compound that kills cells by interfering with lipoprotein trafficking, the process cells use to transport proteins from the cell interior to the cell envelope. It inhibits LolE, a protein part of an ATP-binding cassette (ABC) transporter complex in Gram-negative microorganisms. While Zosurabalpin targets the membrane of Gram-negative bacteria by binding to the LptB2FGC complex in the periplasm, both drugs are specific for *A. baumannii*. They are most eff ective against *A. baumannii* and its close relatives compared to other bacterial classes.[11]

AI has played a crucial role in combating antibiotic resistance, from predicting ARGs to designing new compounds, but it faces limitations. Some AI-generated molecules cannot yet be synthesized, and many promising candidates remain in preclinical stages. Despite the urgent demand for new treatments eff ective against MDR pathogens, the pharmaceutical industry shows little inclination to support and invest in R&D&I in this area. The journey from discovery to commercialization averages between $161 million and $4.54 billion, not to mention the considerable time investment required.[12] Antimicrobial drug development receives substantially less funding and market priority than fields such as oncology, where higher commercial incentives and perceived urgency drive research investment. As a result, progress in AMR must be contextualized within this imbalance, requiring strategies that coexist with, rather than compete against, dominant cancer research pipelines.

While novel compounds, such as antimicrobial peptides (AMPs), show promise, they also pose challenges, including toxicity and proteolytic degradation. Because of AMPs' cationic nature, they interact with negatively charged human and bacterial cell membranes, increasing the risk of cytotoxicity. Both AMPs and bacteriophages face challenges with delivery and stability: bacteriophages, in particular, and agents like Zosurabalpin balance resistance avoidance with limited adaptability and a narrow therapeutic scope. Future research should focus on enhancing compound stability, delivery mechanisms, and the generalizability of promising AI-discovered drugs. Pairing AMPs and other particular drugs with oncology-derived delivery systems, such as nanoparticles, can improve stability and target accuracy. Consequently, repurposing cancer-derived tools and compounds offers a compelling interdisciplinary approach to overcoming persistent barriers in the fight against antimicrobial resistance. The following section explores how oncology strategies can be adapted to advance AMR therapeutics.

■ Insights on the Intersection of Oncology and AMR

Cancer Patient Vulnerability to AMR:

Cancer therapies like chemotherapy, radiation, and surgical procedures can weaken immune defenses. Chemotherapy is designed to target and eliminate rapidly replicating cells without much specificity, killing healthy body cells in the process. Specifically, bone marrow is reduced, where B cells mature and produce antibodies upon encountering antigens on pathogens, playing a critical role in human adaptive immune defenses.[13] Moreover, chemotherapy can directly affect immune cells, leading to cytotoxic effects, cell differentiation and function alterations, and disruptions in cell communication and signaling pathways. Such immune suppression can weaken the anti-tumor immune response and increase the risk of immune-related toxicities.[14] Chemotherapy disrupts the gut lining, allowing bacteria to enter the body more easily and compromising the immune system, which can lead to other health issues and increase susceptibility to infections. Antibiotic-resistant microbes are more likely to survive in hospital settings, including on equipment such as catheters and surgical tools, as well as on surfaces. Surgical procedures can create entry points for bacteria, leading to infections, and urinary catheters can introduce bacteria into the urinary tract. Therefore, cancer patients in weak conditions and those who must be hospitalized for long periods of time have a higher risk of severe infections compared to those without cancer. Drug-resistant bacteria can cause persistent infections, raising concerns among oncologists about the effectiveness of chemotherapy. Extended use of broad-spectrum antibiotics contributes to the emergence of resistance.

90% of cancer deaths when initial treatments fail, it is directly attributed to cancer drug resistance, not necessarily to early-stage or untreated cancers. Like bacteria, cancer exhibits resistance mechanisms, including mutating the drug target, pumping the drug out, repairing the damage it causes, and isolating in parts of the body where the drug cannot reach. Cancer and bacterial cells constantly mutate, creating diversity that may lead to the emergence of resistant genes. Drug efflux in both cancer and bacterial cells allows them to pump drugs out or break them down before they can work. Mutations in drug targets usually affect specific proteins, altering their shape or amount, so the drug no longer works. Cancer cell phenotypic plasticity means "shape-shifting" into more aggressive or drug-resistant forms, such as epithelial-to-mesenchymal transition (EMT), which enables cells to move more easily and better resist therapy.

Given the many commonalities between the two fi elds, existing oncology resources can be repurposed for AMR, reducing costs compared to developing new drugs and off ering a novel perspective on drug use. Potentially repurposing tools in AMR could also aff ect oncology, given the signifi cant impact of bacterial infections on cancer patients. To delve further into bacterial infections in oncology, prophylactic treatments are used to prevent them in cancer patients. Essentially, patients are treated with antibiotics before an infection occurs to lower the risk of serious Gram-negative infections in cancer

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patients, especially those undergoing chemotherapy. Patients with acute leukemia, neutropenia, or moderate-to-low infections are advised to use fluoroquinolones such as ciprofl oxacin or levofloxacin. Using this method also increases the risk of harmful side effects, such as *C.difficile* infection, which can cause dangerous diarrhea due to bacterial overgrowth from a gut microbial imbalance. Along with an increased risk of *C. difficile* infection, this method also promotes the growth of antibiotic-resistant bacteria, potentially hindering treatment of future infections.[15]

An example of a repurposed drug for its antimicrobial properties is human monoclonal antibodies, produced *in vitro* by B cells.[16] They have been used to treat cancer and autoimmune disease, with proven success in the treatment of COVID-19 of late. Subsequently, palivizumab, the first human monoclonal antibody, was approved in 1998 to prevent respiratory syncytial virus infection in high-risk infants, and obiltoxaximab was approved in 2016 to treat inhalational anthrax in combination with antibiotics. Monoclonal antibodies can block receptors or signaling pathways, such as anti-EGFR in cancer; tag cells for destruction by immune cells, such as through Antibody-Dependent Cell-Mediated Cytotoxicity; deliver toxic payloads, such as radioisotopes, toxins, or chemotherapy drugs; and neutralize viruses, such as anti-HIV or anti-COVID antibodies. Human monoclonal antibodies exert rapid and sustained antimicrobial activity through several mechanisms, including enhanced opsonization for phagocytosis, direct bactericidal activity, complement deposition, anti-virulence activity, and toxin neutralization. The high specificity of human monoclonal antibodies preserves the host's natural microbiota and minimizes the selective pressure for cross-resistance.

DNA Microarray Analysis:

In oncology, different gene expression patterns correlate with tumor aggressiveness, relapse likelihood, and treatment response. DNA microarrays are used to examine thousands of genes simultaneously in cancer cells, and have been a foundational oncology tool for predicting recurrence, guiding chemotherapy, and analyzing cancer gene expression. Despite early accuracy limitations—primarily due to small study sizes—microarray utility has improved through cross-validation and larger cohort designs. The benefit of DNA microarrays is that they offer a faster, cheaper alternative to whole-genome sequencing and are higher-throughput than PCR. PCR tests only a few genes at a time, whereas whole-genome sequencing (WGS) provides complete data but is more expensive and time-consuming. Given the overlapping resistance mechanisms—efflux pumps, mutations, and phenotypic plasticity—between cancer and AMR, DNA microarrays can detect known ARGs. Arrays can include probes for hundreds of known resistance genes, such as blaCTX-M, mecA, and vanA.[17]

Monoclonal Antibodies:

Extensive cancer research has led to the development of human monoclonal antibodies (mAbs) as precision therapeutics that can block receptors or signaling pathways (e.g., anti-EGFR in cancer), tag cells for immune destruction via antibody-dependent cell-mediated cytotoxicity, deliver toxic payloads, and neutralize viruses. Their high target specificity preserves the host microbiome and minimizes selective pressure for cross-resistance. Currently, 14 human mAb products are in development for ESKAPEE pathogens and *C. difficile* infections.[15]

Bispecific antibodies bind two targets to reduce the likelihood of resistance. Still, they have not yet been widely explored for antibiotic resistance. Bispecific antibodies are engineered to bind two distinct epitopes, such as two different antigens (e.g., CD3 and a tumor antigen) or two distinct sites on the same antigen, to block or cross-link. This dual binding enables unique therapeutic mechanisms that are not possible with standard antibodies. The involvement of additional target sites for bispecific monoclonal antibodies adds an extra layer of complexity and novelty, hindering the effi cacy of the various resistance mechanisms exhibited by MRSA bacteria or pan-resistant *A. baumannii*.[18] The overlap between oncology and AMR broadens the scope of research, advancing a deeper conceptual understanding and methodologies against these challenges. To apply monoclonal antibodies in AMR, they can be engineered to target bacterial virulence factors or toxins.

A Decision Framework for Cross-Domain Transfer:

Table 3: Oncology-to-AMR Transfer Mapping.

Resistance Mechanism	Example in Bacteria	Analog in Cancer	Oncology AI Tool	AMR Translation (Status)
Drug Efflux	AcrAB-TolC (Gram-negative efflux pump)	P-glycoprotein (MDR1) overexpression	ML models predicting MDR1 substrate binding	Predictive models for efflux pump inhibitor design (proposed)
Target Mutation	Ribosomal mutations (aminoglycoside resistance)	Kinase domain mutations (TKI resistance)	PeTrans / ChemSpaceAL (de novo inhibitor design)	Transfer learning for resistance mutation prediction (proposed)
Phenotypic Plasticity	Biofilm formation; persister switching	Epithelial-to-mesenchymal transition (EMT)	RNA-seq/ microarray gene expression profiling	Microarray-based AMR gene expression profiling (proposed)
Compound screen/ repurposing	Multi-drug resistance in ESKAPEE pathogens	Cancer polypharmacology/ combination screens	Deep learning (MIT Stokes et al.); ARPA-H TARGET	Halicin (validated); Abaucin (validated); ARPA-H 107M screen (in progress)
Immune evasion/ virulence	Toxin secretion; immune suppression	Immune checkpoint upregulation	Bispecific antibodies; mAb engineering	14 mAbs in development for ESKAPEE / C. difficile (active)
PK/PD Optimization	Short half-life (Zosurabalpin)	Narrow therapeutic window in targeted cancer therapy	Oncology PK/PD adaptive dosing models	CURATE.AI (validated in oncology; adapted for CRE/AMR in Singapore trials)

Furthermore, we can combine antibodies with antibiotics to neutralize bacterial defenses and design bispecific antibodies recognizing bacterial proteins and host immune receptors. The value of this perspective lies in acknowledging the alternative introduction and laying the groundwork for future research. Additionally, the Drug Repurposing Hub, ZINC15, and ChEMBL database contain millions of structurally characterized compounds screened in oncology contexts. Deep learning models trained on oncology activity data can be reused to screen the same libraries for antimicrobial agents against specific pathogens. This methodology was exactly how Halicin was discovered, and the synthesis of modifi ed monoclonal an-

tibodies can be advanced using models such as SyntheMol to treat hospital-acquired infections in cancer patients.

Ethical and Translational Constraints

Despite the promise of repurposing oncology-derived AI tools for antimicrobial resistance, this approach raises essential ethical and translational challenges that warrant careful consideration. AI-driven drug discovery models are susceptible to hallucinations—predicting compounds or interactions that cannot be synthesized or validated experimentally—posing risks of resource misallocation and delayed clinical translation. Moreover, while adaptive trial designs are well-established in oncology, their application to AMR is constrained by smaller patient cohorts, shorter infection durations, and ethical concerns regarding experimental therapies for acute infections. These concerns are real, as patients hospitalized with multi-organ failure or unconscious are often unable to provide informed consent, yet they're the most likely candidates for experimental antibiotic therapies.[20] These limitations underscore the need for rigorous human oversight, transparent model validation, and conservative deployment of AI predictions in clinical decision-making. Addressing these ethical challenges is essential to ensuring that oncology-inspired AI frameworks are not only innovative but also safe, equitable, and clinically responsible when applied to AMR.

Conclusion

This review establishes three strong arguments. First, oncology and AMR share fundamental resistance mechanisms—drug efflux, target mutation, phenotypic plasticity—which provide a basis for transferring existing tools for AMR drug discovery. To bridge the research between oncology and AMR, we can train oncology AI models on bacterial genomic datasets to predict emerging resistance mutations, or deploy AI screening systems such as AlphaFold or the DeepChem pipeline to discover new antibiotics or AMPs. Second, we already see this transfer being validated, with models screening antibiotic databases, leading to the discovery of Halicin and Abaucin. By adopting adaptive clinical trial designs for antibiotic testing, we can use real-time AI monitoring of patient responses to guide dosing and combination therapy and build AMR patient registries similar to oncology cohorts. Third, drug repurposing reduces time to approval by approximately 50% and can save more than $1 billion per compound compared to de novo discovery pipelines, averaging 10–12 years and $2+ billion per approved drug.[21]

According to the WHO, global statistics show that approximately 1 in 5 people develop cancer in their lifetime, and ~1 in 9 men and 1 in 12 women die from it.[22] Cancer is a universal and diverse disease, affecting populations across all demographics and geographies, which has positioned it as one of the most heavily researched biomedical fields. The intensity and breadth of cancer research have yielded cutting-edge techniques—from AI-driven predictive modeling to personalized therapeutic targeting—that remain underexplored in AMR contexts. The United States, in particular, stands at the forefront of cancer research and innovation, offering a rich repository of tools, data, and methodologies that can be adapted for AMR. The National Cancer Institute (NCI), a division of NIH, is the world's largest funder of cancer research, with an annual budget of approximately $6.9 billion.[23] By reimagining these assets for bacterial resistance, we stand to accelerate solutions for a problem that threatens to undermine decades of medical progress. Monoclonal antibodies, which have transformed oncology through targeted therapies and immune modulation, are now emerging as promising tools in AMR, and the adaptation against resistant bacteria represents a powerful comparative strategy. Their high specificity neutralizes bacterial toxins, blocks virulence factors, and precisely clears the pathogen without disturbing the human microbiome. To implement these actionable steps, we can establish interoperability between AMR genomic databases and oncology AI frameworks by funding interdisciplinary training programs through the Centers for Antimicrobial Precision Medicine that bridge microbiology, bioinformatics, and cancer biology.

This research primarily draws on existing literature and experimental data, but its value lies in providing a broader, clearer picture of current conditions and challenges related to antimicrobial resistance. This paper presents an interdisciplinary perspective on the use of existing oncology tools to explore AMR, opening new avenues for future research and inspiration within the scientific community. Although this paper primarily considers datasets from a Western setting and uses them to comment on a general geographical arc, it is still vital to acknowledge geographical variation. The datasets have transferable value and incorporate adaptations to local geographic factors, providing an overarching argument and supporting global AMR solutions. This offers a flexible foundation and data to use rather than a fixed framework that cannot be widely applied. The novelty of this approach lies in reframing established cancer research methodologies as tools for AMR innovation, thereby linking two high-impact global health challenges within a single research strategy. Furthermore, combination therapy is more promising given the added complexity of combating bacterial resistance.

Despite the promise of several novel antimicrobials, these agents face limitations in toxicity, stability, delivery, and specificity. AMPs can damage bacterial membranes, leading to cytotoxicity and proteolytic degradation. Similarly, both AMPs and bacteriophages provide delivery, but bacteriophages' high specifi city—while effective at preventing resistance—limits adaptability because bacterial targets rapidly mutate. Compounds like Zosurabalpin also pose this challenge, demonstrating strong efficacy against *A. baumannii* but restricted broader applicability. These constraints highlight the need for advanced delivery systems, stability enhancement, and target-expansion strategies, areas in which oncology has developed mature, clinically validated solutions that can be repurposed to advance antimicrobial resistance therapies.

Bridging insights from oncology into AMR accelerates drug discovery and underscores the value of leveraging well-developed cancer research platforms to tackle one of the most urgent infectious threats worldwide. Regarding future studies, the implications of this research are expansive. Future work could

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focus on developing AI-powered AMR predictive models, informed by cancer prognostic tools, to enable earlier detection and tailored interventions for infections resistant to antibiotics. The highlights of this research are the exploration and combat of AMR through the lens of cancer research, enabling future innovation.

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References

1. World Health Organization. *Antimicrobial resistance*. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance.
2. Majumder, M. A. A.; Rahman, S.; Cohall, D.; Bharatha, A.; Singh, K.; Haque, M.; Gittens-St Hilaire, M. Antimicrobial Stewardship: Fighting Antimicrobial Resistance and Protecting Global Public Health. *Infection and Drug Resistance* **2020**, *13* (1), 4713–4738. https://doi.org/10.2147/idr.s290835 (accessed 2025-08-27).
3. Gautron, J. M. C.; Tu Thanh, G.; Barasa, V.; Voltolina, G. Using Intersectionality to Study Gender and Antimicrobial Resistance in Low- and Middle-Income Countries. *Health Policy Plan*. **2023**, *38* (9), 1017–1032. https://doi.org/10.1093/heapol/czad054.
4. Rosa, R. G.; Goldani, L. Z.; dos Santos, R. P. Association between Adherence to an Antimicrobial Stewardship Program and Mortality among Hospitalized Cancer Patients with Febrile Neutropaenia: A Prospective Cohort Study. *BMC Infect. Dis*. **2014**, *14* (1), 286. https://doi.org/10.1186/1471-2334-14-286.
5. Manning, A. *Paving the Way for a New Class of Antibiotics | Harvard Medical School*. hms.harvard.edu. https://hms.harvard.edu/news/paving-way-new-class-antibiotics (accessed 2025-11-07).
6. Zampaloni, C.; Mattei, P.; Bleicher, K.; Winther, L.; Thäte, C.; Bucher, C.; Adam, J.-M.; Alanine, A.; Amrein, K. E.; Baidin, V.; Bieniossek, C.; Bissantz, C.; Boess, F.; Cantrill, C.; Clairfeuille, T.; Dey, F.; Di Giorgio, P.; du Castel, P.; Dylus, D.; Dzygiel, P.; Felici, A.; García-Alcalde, F.; Haldimann, A.; Leipner, M.; Leyn, S.; Louvel, S.; Misson, P.; Osterman, A.; Pahil, K.; Rigo, S.; Schäublin, A.; Scharf, S.; Schmitz, P.; Stoll, T.; Trauner, A.; Zoff mann, S.; Kahne, D.; Young, J. A. T.; Lobritz, M. A.; Bradley, K. A. A Novel Antibiotic Class Targeting the Lipopolysaccharide Transporter. *Nature* **2024**, *625* (7995), 566–571. https://doi.org/10.1038/s41586-023-06873-0.
7. Liu, G.-Y.; Yu, D.; Fan, M.-M.; Zhang, X.; Jin, Z.-Y.; Tang, C.; Liu, X.-F. Antimicrobial Resistance Crisis: Could Artifi cial Intelligence Be the Solution? *Mil. Med. Res*. **2024**, *11* (1), 7. https://doi.org/10.1186/s40779-024-00510-1.
8. Herráiz-Gil, S.; Nygren-Jiménez, E.; Acosta-Alonso, D. N.; León, C.; Guerrero-Aspizua, S. Artifi cial Intelligence-Based Methods for Drug Repurposing and Development in Cancer. *Appl. Sci.* **2025**, *15* (5). https://doi.org/10.3390/app15052798.
9. Swanson, K.; Liu, G.; Catacutan, D. B.; Arnold, A.; Zou, J.; Stokes, J. M. Generative AI for Designing and Validating Easily Synthesizable and Structurally Novel Antibiotics. *Nat. Mach. Intell*. **2024**, *6* (3), 338–353. https://doi.org/10.1038/s42256-024-00809-7.
10. Zagajewski, A.; Turner, P.; Feehily, C.; El Sayyed, H.; Andersson, M.; Barrett, L.; Oakley, S.; Stracy, M.; Crook, D.; Nellåker, C.; Stoesser, N.; Kapanidis, A. N. Deep Learning and Single-Cell Phenotyping for Rapid Antimicrobial Susceptibility Detection in Escherichia Coli. *Commun. Biol*. **2023**, *6* (1), 1164. https://doi.org/10.1038/s42003-023-05524-4.
11. Liu, G.; Catacutan, D. B.; Rathod, K.; Swanson, K.; Jin, W.; Mohammed, J. C.; Chiappino-Pepe, A.; Syed, S. A.; Fragis, M.; Rachwalski, K.; Magolan, J.; Surette, M. G.; Coombes, B. K.; Jaakkola, T.; Barzilay, R.; Collins, J. J.; Stokes, J. M. Deep Learning-Guided Discovery of an Antibiotic Targeting Acinetobacter Baumannii. *Nat. Chem. Biol*. **2023**, *19* (11), 1342–1350. https://doi.org/10.1038/s41589-023-01349-8.
12. Schlander, M.; Hernandez-Villafuerte, K.; Cheng, C.-Y.; Mestre-Ferrandiz, J.; Baumann, M. How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *PharmacoEconomics* **2021**, *39* (11), 1243–1269. https://doi.org/10.1007/s40273-021-01065-y.
13. Safdar, A.; Bodey, G.; Armstrong, D. Infections in Patients with Cancer: Overview. *Princ. Pract. Cancer Infect. Dis*. **2011**, 3–15. https://doi.org/10.1007/978-1-60761-644-3_1.
14. Sharma, A.; Jasrotia, S.; Kumar, A. Eff ects of Chemotherapy on the Immune System: Implications for Cancer Treatment and Patient Outcomes. *Naunyn. Schmiedebergs Arch. Pharmacol*. **2024**, *397* (5), 2551–2566. https://doi.org/10.1007/s00210-023-02781-2.
15. Ho, C. S.; Wong, C. T. H.; Aung, T. T.; Lakshminarayanan, R.; Mehta, J. S.; Rauz, S.; McNally, A.; Kintses, B.; Peacock, S. J.; de la Fuente-Nunez, C.; Hancock, R. E. W.; Ting, D. S. J. Antimicrobial Resistance: A Concise Update. *Lancet Microbe* **2025**, *6* (1), 100947. https://doi.org/10.1016/j.lanmic.2024.07.010.
16. Kothari, M.; Wanjari, A.; Acharya, S.; Karwa, V.; Chavhan, R.; Kumar, S.; Kadu, A.; Patil, R. A Comprehensive Review of Monoclonal Antibodies in Modern Medicine: Tracing the Evolution of a Revolutionary Therapeutic Approach. *Cureus 16* (6), e61983. https://doi.org/10.7759/cureus.61983.
17. Ntzani, E. E.; Ioannidis, J. P. Predictive Ability of DNA Microarrays for Cancer Outcomes and Correlates: An Empirical Assessment. *The Lancet* **2003**, *362* (9394), 1439–1444. https://doi.org/10.1016/S0140-6736(03)14686-7.
18. Ingham, J.; Ruan, J.-L.; Coelho, M. A. Breaking Barriers: We Need a Multidisciplinary Approach to Tackle Cancer Drug Resistance. *BJC Reports* **2025**, *3* (1). https://doi.org/10.1038/s44276-025-00129-2.
19. Li, M.; You, K.; Wang, P.; Hooi, L.; Chen, Y.; Siah, A.; Tan, S.-B.; Teo, J.; Ng, O.-T.; Marimuthu, K.; Venkatachalam, I.; Blasiak, A.; Chow, E. K.-H.; Ho, D.; Gan, Y.-H. Discovery of Broad-Spectrum Repurposed Drug Combinations Against Carbapenem-Resistant Enterobacteriaceae (CRE) Through Artifi cial Intelligence (AI)-Driven Platform. *Adv. Ther*. **2024**, *7* (3), 2300332. https://doi.org/10.1002/adtp.202300332.
20. Boyd, N. K.; Teng, C.; Frei, C. R. Brief Overview of Approaches and Challenges in New Antibiotic Development: A Focus On Drug Repurposing. *Front. Cell. Infect. Microbiol*. **2021**, *11*. https://doi.org/10.3389/fcimb.2021.684515.
21. World Health Organization. *Global Cancer Burden growing, Amidst Mounting Need for Services*. WHO. https://www.who.int/news/item/01-02-2024-global-cancer-burden-growing--amidst-mounting-need-for-services. (accessed 2025-08-24).
22. *NCI's Role in Cancer Research - NCI*. https://www.cancer.gov/research/nci-role (accessed 2026-02-02).
23. Stokes JM, Yang K, Swanson K, *et al.* A deep learning approach to antibiotic discovery. *Cell*. 2020;180(4):688–702. https://doi.org/10.1016/j.cell.2020.01.021.

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Kayla Leung is a graduating senior at Monta Vista High School (Class of 2026) and an aspiring biomedical computation major. Her research was conducted under the mentorship of a current Cambridge PhD student, Dikshit Bhagabati. Her interest in antimicrobial resistance stems from her personal health journey, undergoing open-heart surgery to correct a ventricular septal defect. Witnessing first hand the critical role of medical intervention inspired her commitment to advancing healthcare through research. She is passionate and inspired by research, exploring the intersection of AI and its applications to expedite drug discovery and address antimicrobial resistance. Kayla hopes to draw on her patient experience to integrate computational innovation with patient-centered care, with a greater focus on the humanistic impact her research can have on people's lives.

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