Baylor College of Medicine

taiΦr

Tailored **A**ntibacterials and **I**nnovative **L**aboratories for phage (**Φ**) **R**esearch

A Baylor College of Medicine initiative empowering clinicians with capable antibacterials to treat the most vulnerable patients.

MISSION

TAILΦR delivers personalized and effective treatments for challenging antibiotic-resistant bacterial infections by cultivating scientific and medical expertise, technology, and innovation to generate an expedited bench-to-bedside pipeline. We TAILΦR infection and biocontrol for healthcare, animal care, agricultural and industrial settings.

VISION

TAILΦR strives to provide personalized solutions for infectious disease and industrial biocontrol. We develop new technologies that facilitate the discovery and evolution of novel phages with enhanced attributes for your unique applications. Through these efforts, we will compile the largest characterized library of therapeutic phages for all major drug-resistant bacterial species. TAILΦR aims to kick-start an adaptable medicine revolution, wielding the same weapon that empowers diseases to resist traditional treatments: directed change.

VALUES

TAILΦR is a non-profit initiative providing at-cost services designed to help the most pressing medical and industrial needs that are threatened by bacterial infection or contamination. The TAILΦR team strives to provide:

Need Icons

1 ▸ Safe, targeted antibacterial products that are thoroughly characterized and documented.

2 ▸ Quantitative and reproducible results that can be trusted and verified.

3 ▸ Transparent collaborations with a team-like culture that meet the specific needs the project requires.

OUR LOCATION

LARGEST MEDICAL CENTER IN THE WORLD

Clinical/Research Institutions	Patients Annually	Surgery Performed Every
54	10M	3 Minutes

TAILΦR is a Baylor College of Medicine initiative located in the heart of the Texas Medical Center (TMC) – the largest medical center in the world.

A top-ranked medical school, BCM is renowned for world-class research and patient care. The institution's scientists and physicians were awarded nearly $300 million in research grants for fiscal year 2019. BCM boasts hundreds of basic science faculty, thousands of clinicians, and over 25 core facilities housing state-of-the-art equipment and expertise.

In 2022 the TMC3 campus will be established to bring together industry, medical research, and biomedical start-ups. TAILΦR's proximity to TMC3 can facilitate the commercialization of your antibacterial products.

THE PROBLEM IS CHANGE

BACTERIA CHANGE

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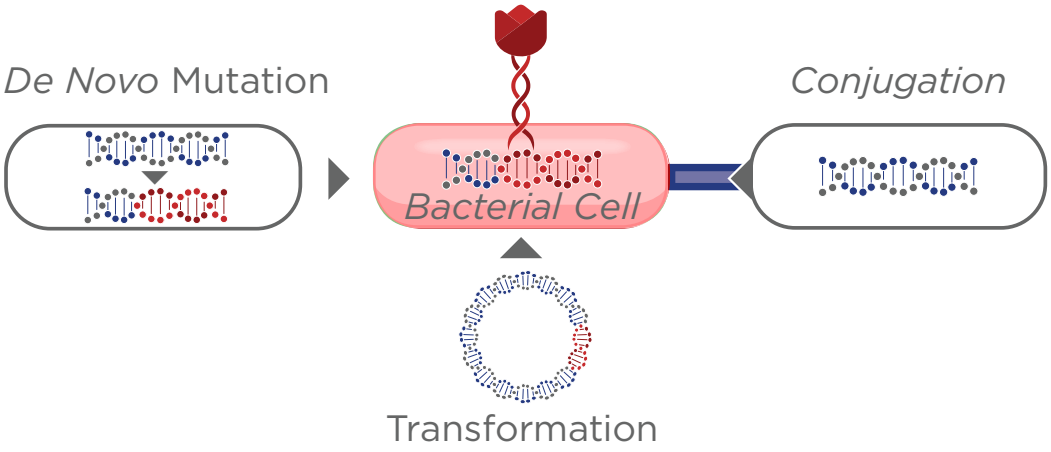
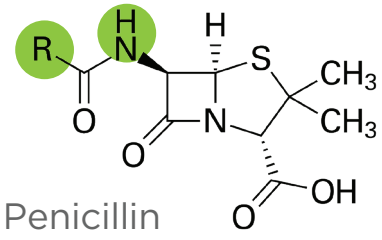


BACTERIA ARE REMARKABLY ADAPTABLE...AND THAT'S THE PROBLEM!

Four intersecting mechanisms of change, what we call the mutagenic tetrasect, come together to facilitate the ability of bacteria to change and adapt. Each of these means of acquiring new DNA contributes to the success of bacteria in undermining our attempts to control them. Bacteria can mutate their way around antibiotics, vaccines, biocides, and engineering controls.

MEDICINES DON'T CHANGE



Penicillin

EVERY ANTIBIOTIC THAT TARGETS PATHOGENIC BACTERIA HAS A FIXED CHEMICAL STRUCTURE LIKE PENICILLIN ABOVE, upon which chemists can add a few more atoms (highlighted green circles) to make the antibiotic more effective. Eventually, bacteria mutate and find ways to overcome these new structures. In return, chemists develop new modifications of the same core structure. Bacteria become resistant once more, and so on. Eventually, chemists run out of places to make modifications!

AND IT'S EXACERBATING A CRISIS!

It takes around 10 years and $1 billion for a company to bring a new antibiotic to market. Bacteria quickly evolve resistance to these drugs, sometimes within months. This undercuts the economic incentives to invest in the discovery and development of new antibiotics. Unsurprisingly, as bacterial resistance has **increased**, the number of companies developing new antibiotics has **decreased**.

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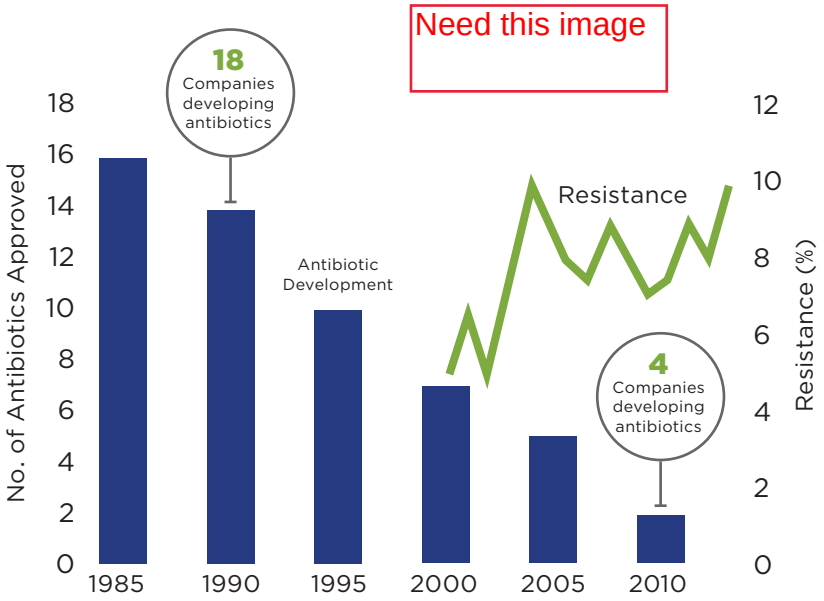

EITHER WE CHANGE THE WAY WE APPROVE AND REGULATE NEW DRUGS, OR WE DEVELOP AND APPROVE NEW DRUGS THAT CHANGE.

THE SOLUTION IS BACTERIAL KILLERS THAT CHANGE!

PHAGE ARE THE MOST NUMEROUS REPLICATING ENTITY ON EARTH.

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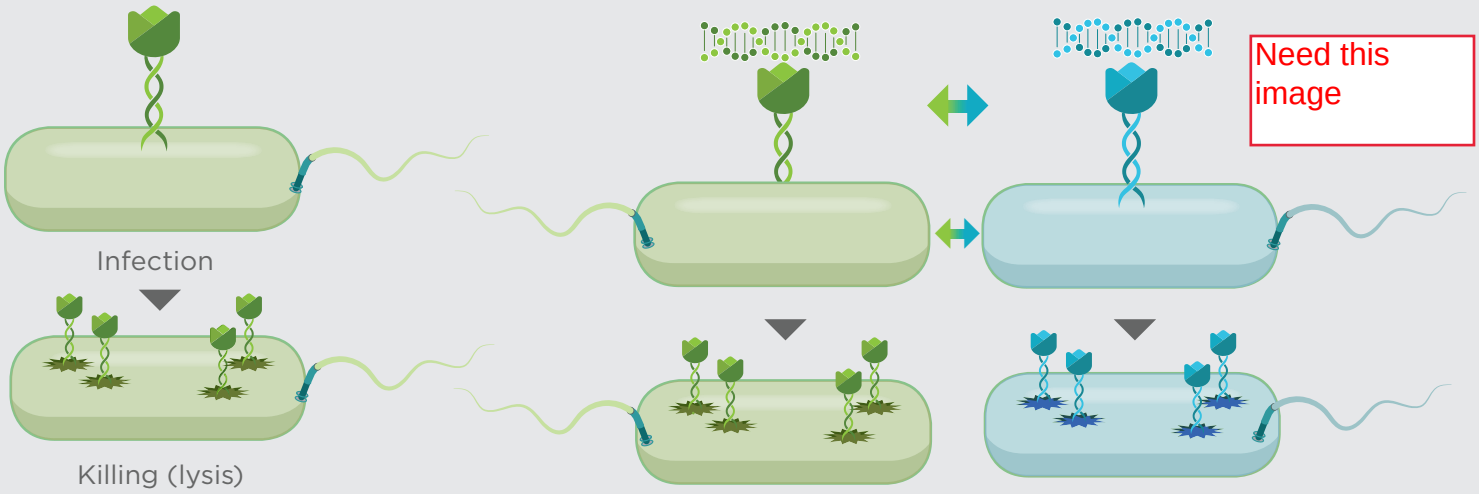

They are like a flu for bacteria, and specifically infect them. Phage replicate inside until they burst free, killing the cell.

Unlike chemical antibiotics, phage have DNA. By mutating their DNA, phage can evolve as quickly as bacteria.

TAILΦR can wield this evolution to develop the best bacterial killers quickly!

PHAGES ARE PRECISION MEDICINES TAILORED TO **YOUR** ILLNESS

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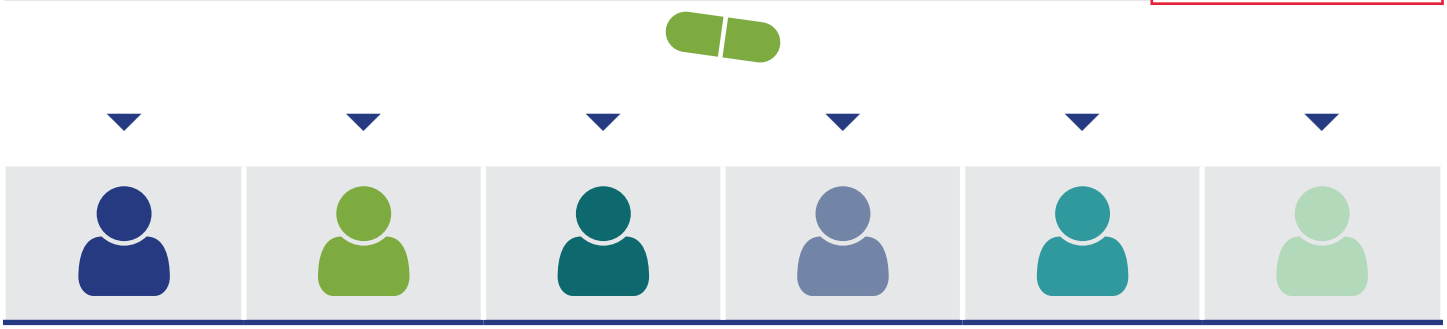
Traditional Medicine



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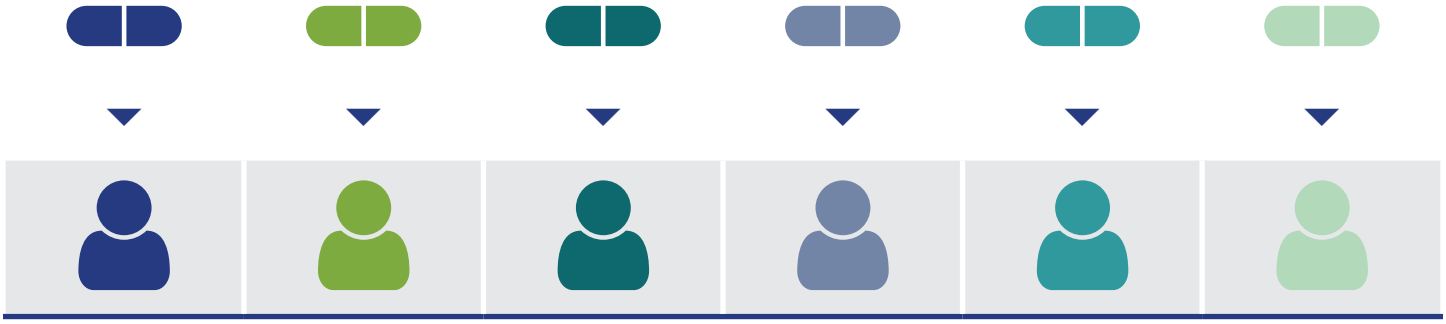
Precision Medicine

PERSONALIZATION



For some diseases that are fundamentally caused by and progress with change, we may need medicines that change as well.

For example, engineering patients' own T cells to attack their cancer is a precision medicine. CRISPR-based correction of your DNA to remove mutations that cause blindness is another example. Both of these approaches, landmark in their concept, were recently approved by the FDA.

Personalized medicines are desperately needed to combat antibiotic resistance. Doctors already tailor patients' treatments based on their bacterial strain's antibiotic susceptibility. TAILΦR can personalize treatment by discovering and developing the most effective antibiotic and phage combinations.

THE PROCESS

STEP 1 CONSULTATION

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step is to understand your needs and determine if we can reliably meet them. We will formulate a scientific plan tailored to your unique situation.

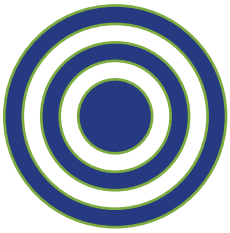
STEP 2 DISCOVERY

If we don't already have phage(s) in our library, we will find them for you. See page 9.

STEP 3 CHARACTERIZATION

Whether you need your phage to be sequenced; certified for pyrogenicity and sterility; tested for activity in blood, urine (or other host environments) or animal efficacy; our characterization services are designed to meet application needs. See page 10.

STEP 4 DELIVERY



You receive ready-to-use phage and all corresponding data. Should your project require further improvement and refinement, we will work to meet those custom needs. See page 11.

STEP 1: CONSULTATION

For PHYSICIANS:

- Make tailored phages that kill your patient's specific drug-resistant
- ing for an IND or emergency IND from the FDA
- Deliver phages that are safe, effective, and characterized

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For HEALTHCARE FACILITIES:

- Make tailored phages that kill drug-resistant bacteria circulating at your institution
- Formulate a strategy for biocontrol of bacteria in rooms, instruments, etc.

For FOOD BUSINESS:

- Make tailored phages that kill bacteria that contaminate foodstuffs, including poultry and beef products
- Formulate the product to work best in the environment you need

For INDUSTRY:

- Make phages that kill bacteria that foul, corrode, or contaminate your lines, equipment, or products
- Customize the phage for the conditions you need

For HEALTHCARE PRODUCTS:

- Make phages that kill bacteria that contaminate your medicines, probiotics, or supplements
- Help keep your products safe by removing "bad" bacteria from the preparations

For PET HEALTH:

- Make phages that kill bacteria that cause common pet ailments

STEP 2: DISCOVERY

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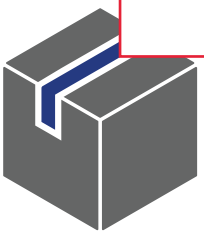
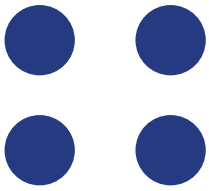


SEND US YOUR STRAIN

Give us the problematic bacterium or have us isolate it from the sample you provide.

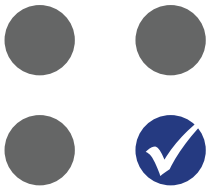


SCREEN

We will screen our well-characterized library of therapeutic phages that kill many pathogenic species of bacteria.

SEARCH

If we don't have the phage, we will ask Mother Nature for help. In this phase, we search environmental reservoirs (soil, water, sewage, bodily fluids—you name it!) for phages that are effective against your strain.



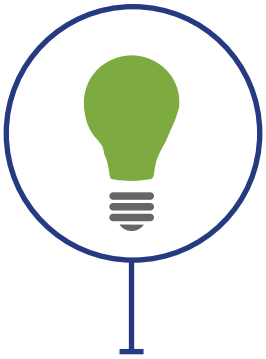
IDENTIFY

We identify lead candidates, evaluate their effectiveness, and pick the best ones to purify.

PURIFY

We scale up, use several techniques to purify, and test the purity of the phage. This gives us a clear picture of the product for the next stage of development: Characterization.

STEP 3: CHARACTERIZATION



BASIC SERVICES

- Basic characterization (titer, plaque size, plaque morphology)
- Efficiency of Plating (Host Range)
- Infection kinetics (adsorption rate, latent period, burst size)
- pH Sensitivity
- Endotoxin quantification[1]
- TEM Imaging*
- Whole genome sequencing*
- Standard genome annotation*

PREMIUM SERVICES

- Phage purification
- Full genome annotation*
- Genome curation*
- Sterility testing[1]
- Efficacy testing in blood, urine, stool, or other media*
- Efficacy testing in animal models*,[2]
- Microbiome editing*
- Biofilm disruption on catheters*
- Industrial applications (surfaces, fluids, etc.)*

** Should be performed with purified phage.*

[1] Tested in accredited and certified laboratories for FDA approval.

[2] We have established murine models of sepsis/bacteremia, immunocompromised infections, UTI, granuloma, and microbiome gut editing. If we don't already have it, we will develop it for you.

EXAMPLE REPORT FOR YOUR PHAGE

Characteristics	
Source Species	Human
Source Location	Raw Sewage
Isolation Date	9/25/2019
Isolation Strain	Your Strain
Plaque Size (mm)	1.0–1.5
Plaque Morphology	Clear
Plate stock (PFU/ml)	1.2×10^{10}
Electron Microscopy Morphology	Myovirus

Sequencing	
Genome (BP)	168,502
G + C (%)	43.68%
ORFs	275
tRNAs	2
Toxin/Virulence Genes	None
Lysogeny Genes	None
Antibiotic-Resistance Genes	None
Closest Relative	NPC
Genus	T4-like

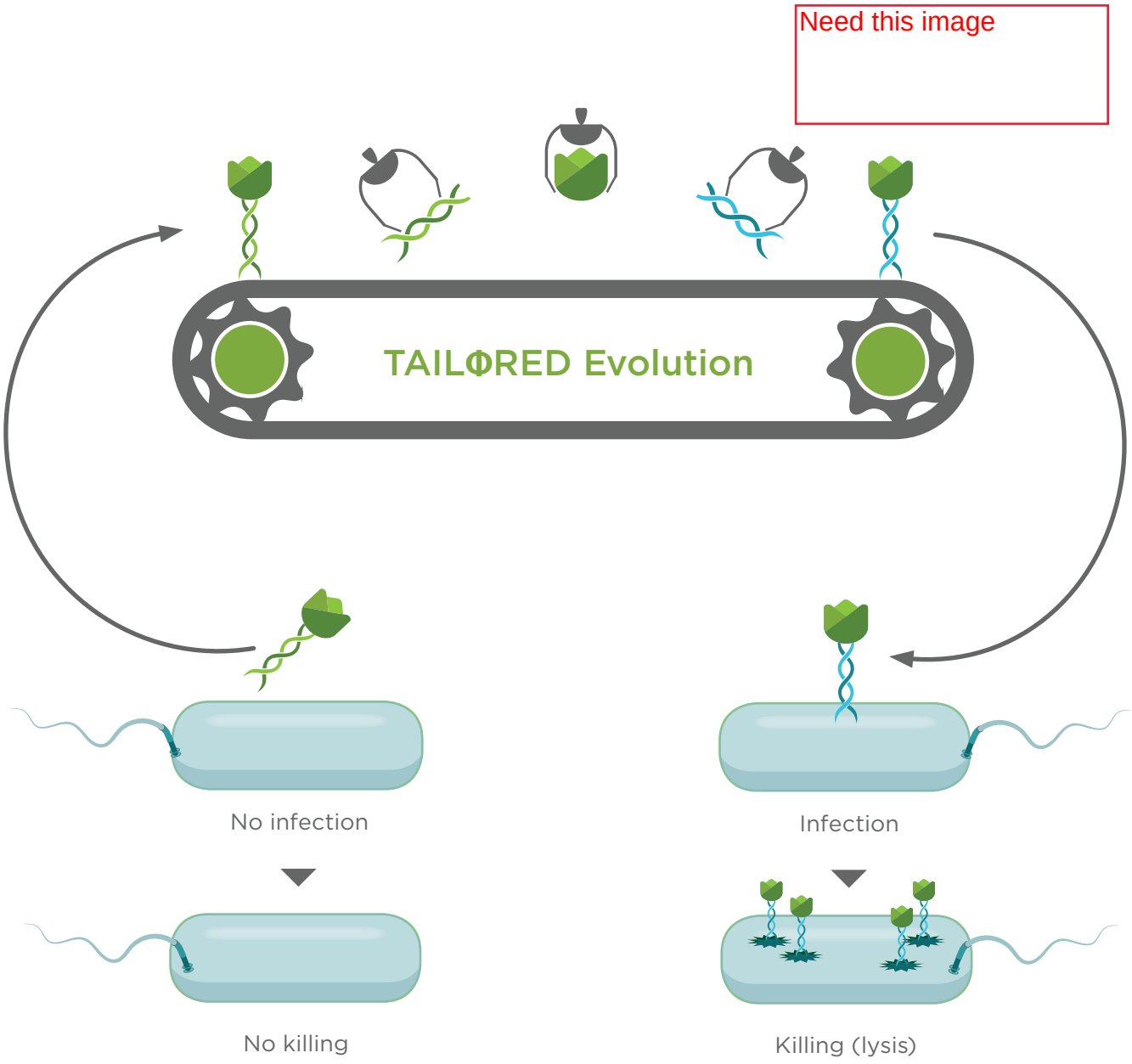
Infection Kinetics	
Adsorption Constant (mL/min)	8.92×10^{-7}
% Adsorbed (10 min)	99
Latent Period (Min)	20
Burst Size (PFU/cell)	18.2

Formulation	
Type	CsCl Purified Phage
Volume (mL)	4.3
Titer (PFU/mL)	2.2×10^{11}
Sterility (Aerobic/Anaerobic)	Pass
Endotoxin Quantification (EU/mL)	5.6×10^{3}

AT THIS LAST STEP, WE HAND OVER THE FINAL PRODUCT.
WE CAN DELIVER:

Phage(s) or phage cocktails designed to target your bacterial strain(s), formulated in whatever media you request.	Chemical, manufacturing, and control information to verify the product's safety, stability, and sterility.	Quantifiable reports tailored to your project's requests. (Example above)

QUICKLY EVOLVE PHAGE TO TARGET RESISTANT BACTERIA



Phages are small, but powerful killers of bacteria. This selective pressure may lead bacteria to evolve resistance and escape from phage, similar to antibiotic resistance. If this happens, TAILΦR can discover new phages or employ proprietary technology to evolve new phage that kill resistant bacteria.

YOUR SOLUTION STARTS HERE

SOURCE

YOU MAY SAMPLE FROM A WIDE VARIETY OF SOURCES:

Patient

Animal

Agriculture

Industry

COLLECT

WE ACCEPT SPECIMENS OF MANY KINDS!

Complex sample

Bacterial isolate

Swab

PACK

DOMESTIC: FedEx.com/packaging
INTERNATIONAL: Contact Us

Primary container

Secondary container

Label

SHIP

WE WILL INCUR SHIPPING COSTS!

Forms

Ship cool
NO dry or wet ice!

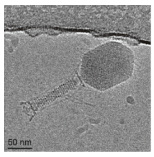
READY FOR THE NEXT TIME

Bacteria will adapt...
Resistance or new strains may appear...

The TAILΦR team will be ready!

TAILΦRED Results

All the parameters important for understanding your phage's efficacy will be retained and organized into a document we term the Phage Desk Reference, or PDR. A phage with useful PDR properties can be identified to solve future bacterial problems should they arise.



Name: HP3
Storage:
Plate stock: 4°C
Purified stock: 4°C
Frozen infective center: -80°C
Location: 217C, Box#

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Isolation:
Date isolated: 3/23/15
Biological source: feces
Source species: Avian
Source location: Herman park
Isolation strain: *E. coli* K12
Sequenced: ☑ (#KY608976)

Genetics:
Species: Myovirus
Genome size: 168,188 Bp
G + C (%): 35.4
ORFS: 274
tRNAs: 11

Infection parameters:
Tested pathogen(s) (+ Plaques):
ExPEC (+), UPEC (+), EAEC(+)

Animal tested: ☑
Tested species: Mus
Tested pathogens: ExPEC

Plaque size (mm): 0.5
Plaque morphology: Clear
Adsorption constant (mL/min): $5.63X10^{-9}$
% Adsorbed (10 min): 98
Burst size (PFU/cell): 60
Latent period (min): 22.5

Safety:
Toxin/virulence genes: None
Lysogeny casettes: None
ABX resistance genes: None
Lysogen formation: None detected

Formulation:
CsCl purified: ☑
Titer (CFU/mL): $1.9X10^{12}$
Endotoxin: $2.16X10^{3}$EU/mL

Stability
PH sensitivity: stable pH >3

TAILΦRED Libraries

If you prefer, we will store your strain(s) and your phage(s) against that strain in our library. Should your bacterial strain arise again to cause problems, or should a related but new strain appear, we can quickly screen the library for activity against these bacterial strains, thereby saving precious time and cost.

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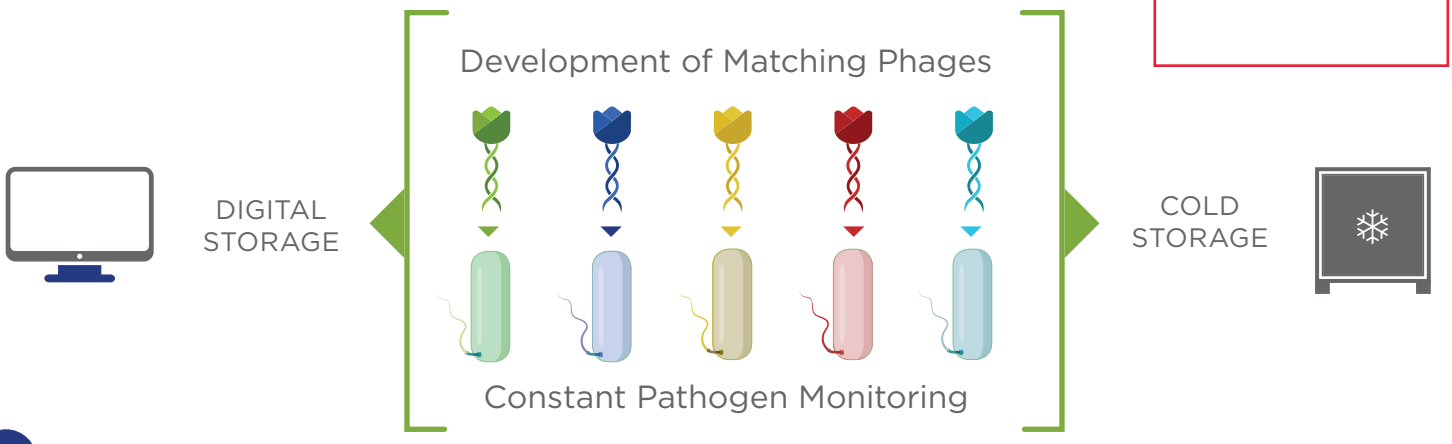
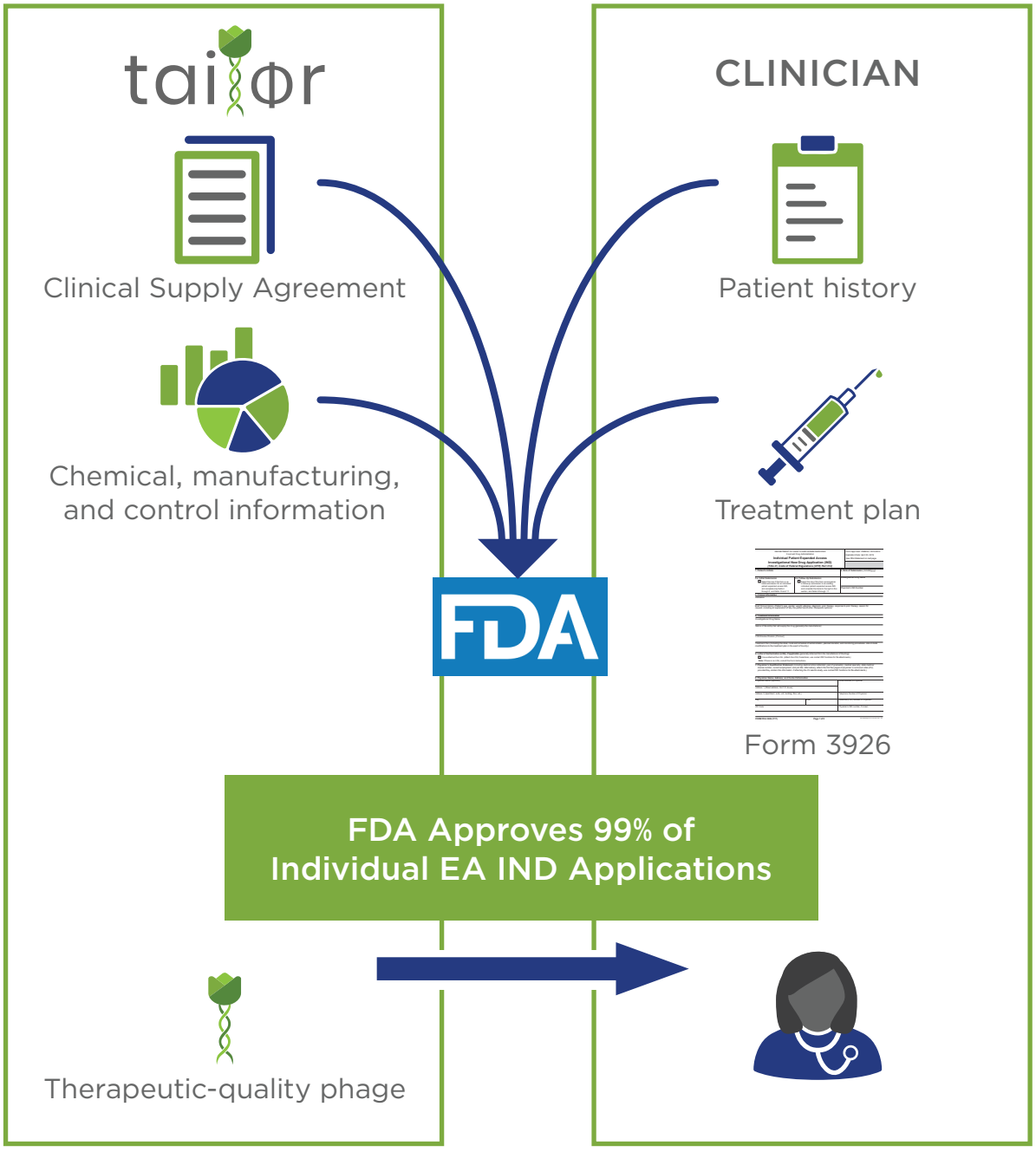


COMPASSIONATE USE/EA IND

(Expanded Access for an Investigational New Drug)

EIND: For emergency use when a patient must be treated prior to a formal written submission to the FDA.



MEET YOUR TAILORS

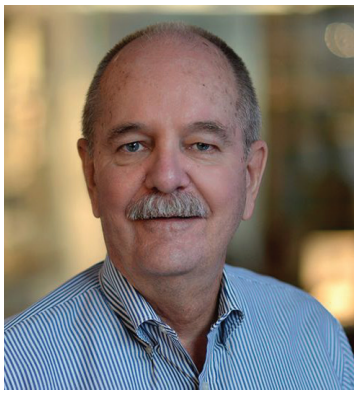
DIRECTOR OF OPERATIONS

Austen Terwilliger, Ph.D.

CLINICAL

Barbara Trautner, M.D., Ph.D.

VIROLOGY



Frank Ramig, Ph.D.

MICROBIOME

Sabrina Green, B.S.

BIOINFORMATICS

Justin Clark, Ph.D.

ANTIBIOTIC SYNERGY

Carmen Gu Liu, B.S.

EVOLUTION & RESISTANCE

Keiko Salazar, B.S.

LEAD TECHNICIAN

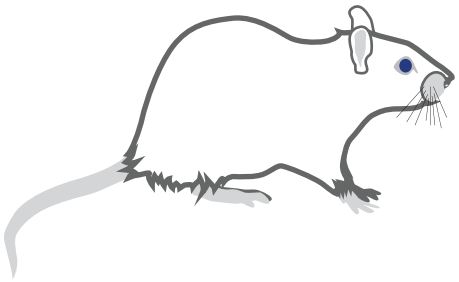
Haroldo Santos, B.S.

FACULTY FOUNDER

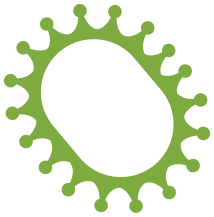
Anthony Maresso, Ph.D.

WE CAN HELP...

Have other projects in mind? Let us know.

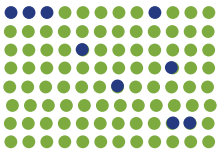


Develop animal models of infection



Bacterial identification

Vaccine development



Bacterial genetics/screening/culturing

We welcome collaborations of many kinds!

CONTACTS

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