

Bacteriophage Antibiotics: Commercial Development and Application

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Antibiotics Market

- \$42 billion globally in 2009
 - 5% of global pharmaceutical market
 - ~\$50 billion global cancer therapeutics market in 2009

Organisms with emerging antibiotic resistance

- Urgent threats
 - *Clostridium difficile*
 - Carbapenem-resistant *Enterobacteriaceae* (CRE)
 - Drug-resistant *Neisseria gonorrhoeae*
- Serious threats
 - Multi-drug resistant *Acinetobacter*
 - Drug-resistant *Campylobacter*
 - Vancomycin-resistant *Enterococcus* (VRE)
 - Multi-drug resistant *Pseudomonas aeruginosa*
 - Drug-resistant *Salmonella*
 - Drug-resistant *Shigella*
 - Methicillin-resistant *Staphylococcus aureus*
 - Drug-resistant *Streptococcus pneumoniae*

Impacts of Drug Resistance

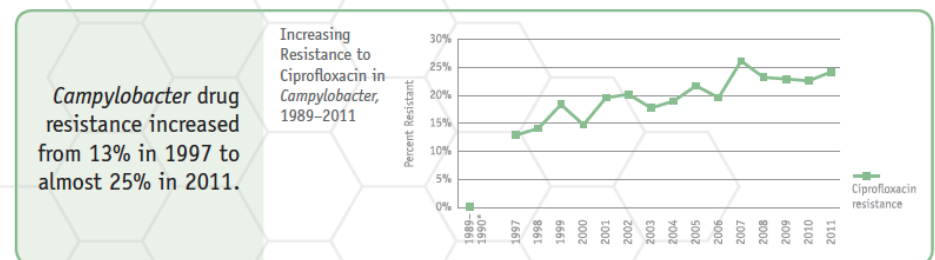
- ~2 million illnesses due to drug-resistant bacteria
 - 23,000 deaths
- 250,000 illnesses due to *C. difficile*
 - 14,000 deaths

	Percentage of Enterobacteriaceae healthcare-associated infections resistant to carbapenems	Estimated number of infections	Estimated number of deaths attributed
Carbapenem-Resistant <i>Klebsiella</i> spp.	11%	7,900	520
Carbapenem-resistant <i>E. coli</i>	2%	1,400	90

	Percentage of all <i>Acinetobacter</i> healthcare-associated infections that are multidrug-resistant	Estimated number of infections	Estimated number of deaths attributed
Multidrug-resistant <i>Acinetobacter</i>	63%	7,300	500

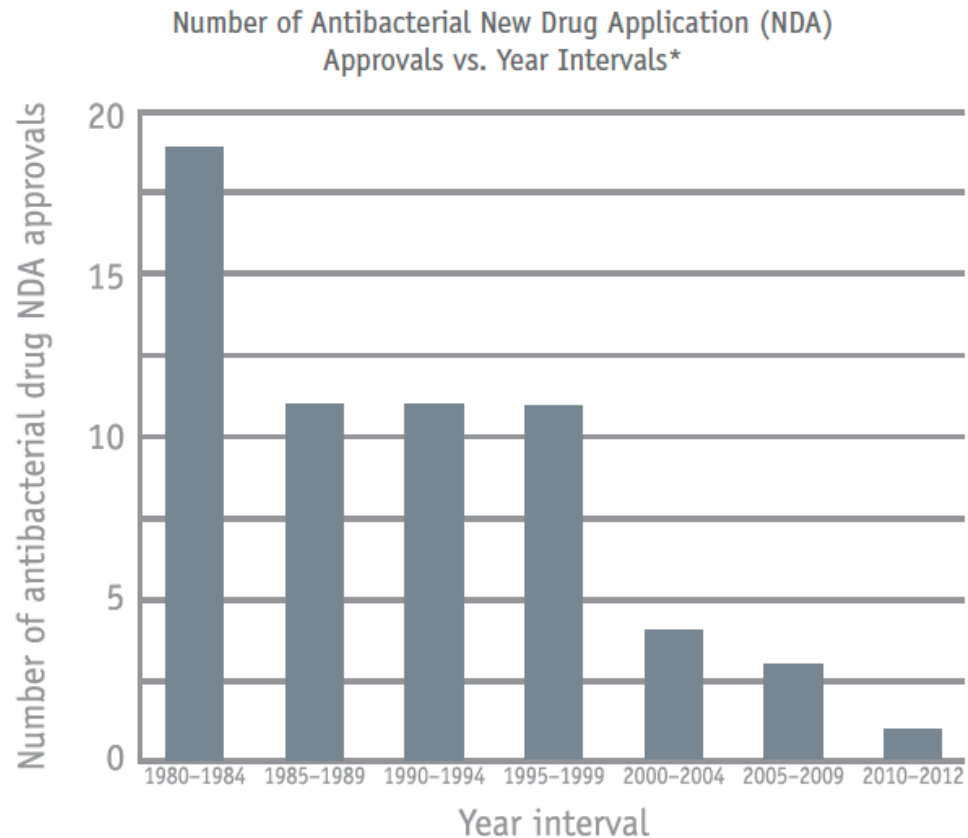
	Percentage	Estimated number of cases
Gonorrhea		820,000
Resistance to any antibiotic	30%	246,000
Reduced susceptibility to cefixime	<1%	11,480
Reduced susceptibility to ceftriaxone	<1%	3,280
Reduced susceptibility to azithromycin	<1%	2,460
Resistance to tetracycline	23%	188,600

	Percentage of all <i>Campylobacter</i> *	Estimated number of illnesses per year	Estimated illnesses per 100,000 U.S. population	Estimated number of deaths per year
Resistance to ciprofloxacin	23%	310,000	102.3	28
Resistance to azithromycin	2%	22,000	7.4	<5
Resistance to azithromycin or ciprofloxacin	24%	310,000	103.9	28



Traditional Antibiotics: Development

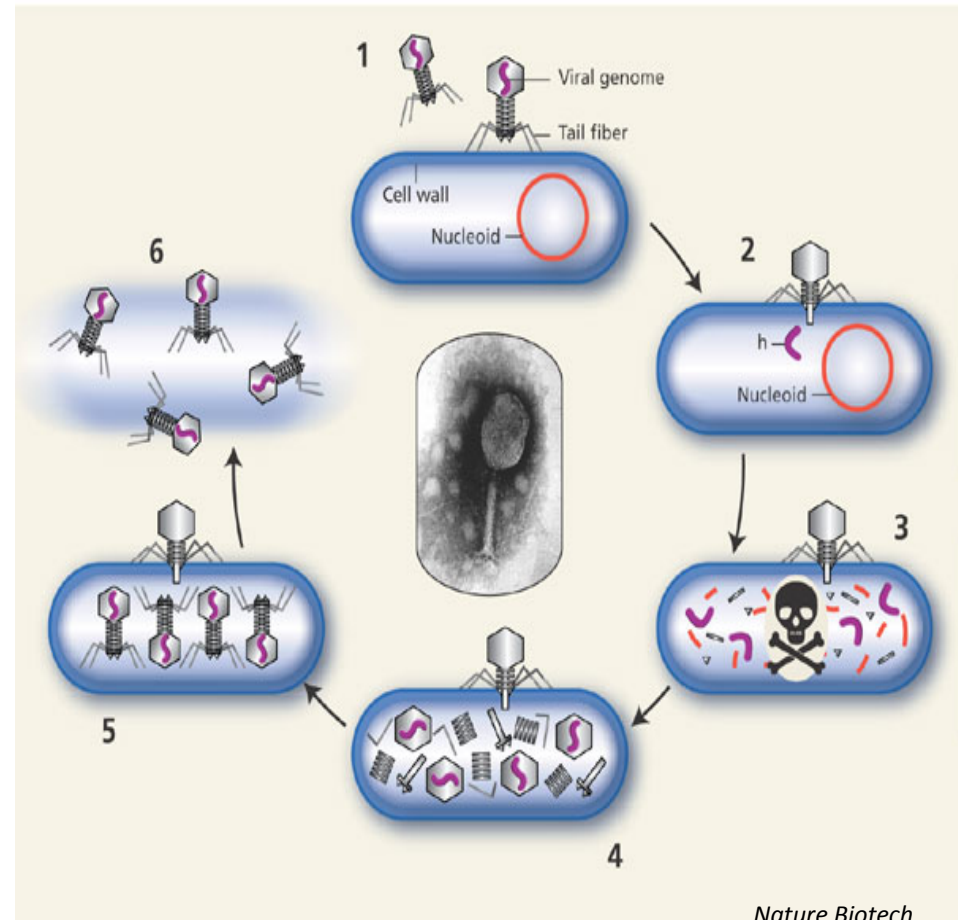
The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.



*Intervals from 1980-2009 are 5-year intervals; 2010-2012 is a 3-year interval. Drugs are limited to systemic agents.
Data courtesy of FDA's Center for Drug Evaluation and Research (CDER).

Bacteriophages as Antibiotics

- Lytic
- Lysogenic



Nature Biotech.
2004 22: 31-36

Major Players

- AmpliPhi (US-UK-Australia)
 - Public, founded 1993, in phage business since early 2000s
- Intralytix (US)
 - Private, founded 1998
- Phage International (US)
 - Private, founded 2004

Phage International

- Aim at developing clinical therapies
- Own the Phage Therapy Center in Tbilisi Georgia

Intralytix

- Develops bacteriophages for use in the food, environmental and recently clinical industries
- Products:
 - 3 food safety: approved and on the market
 - 1 probiotic for human consumption: in development
 - 1 veterinary: licensed out

Intralytix

- Partnerships:
 - USDA: Grant for phage-based application to protect hatchery-raised oysters from *Vibrio tubashii*
 - P&G: Multiple Project Agreement
 - NIFA/USDA/SBIR: Grant to develop phage preparations for reducing or eliminating *Salmonella* contamination of food
 - US Army: Probiotic against *Shigella*
 - US Army: Phage preparations for treatment of wounds infected with *Acinetobacter baumannii*

AmpliPhi

- Development and commercialization of bacteriophage-based therapeutics.
- Targeting infections resistant to existing antibiotics.
- Aims to complete clinical development in-house and then license use/commercialization to partners.
- Market capitalization: \$32 million
- Enterprise value: \$25 million

AmpliPhi

- Products:
 - Phages for acute and chronic lung infections: completing pre-clinical
 - MRSA: in pre-clinical
 - Equine endometritis: in pre-clinical

AmpliPhi

- Partnerships:
 - Cystic Fibrosis Foundation: funding development of aerosolized phage preparation for treatment of *Pseudomonae aeruginosa* in CF
 - US Army: development and commercialization of phage therapeutics to treat *Staphylococcus aureus*, *E. coli*, *Pseudomonas aeruginosa*. Initial indication are wound and skin infections of *S. aureus*.
 - University of Leicester: exclusive licenses to develop phage therapies targeting *C. difficile* (AmpliPhi will fund studies and get exclusive licenses on patents, materials, know-how)
 - Interexon Corp

AmpliPhi

- Past Business: production and development of adeno-associated viruses (AAV) vectors for gene therapy. Sold to:
 - Amsterdam Molecular Therapeutics: non-exclusive license for treatment of lipoprotein lipase deficiencies
 - Celladon Corp.: non-exclusive license for treatment of advanced heart failure through enzyme replacement
 - Genzyme: sale of IP and equipment related to AAV vector technology.

AmpliPhi

- Financials:
 - Dec. 2013: \$18 million private placement of 72,003,000 common stock shares @ \$0.25/share
 - Jun. 2013: \$7 million private placement of series B convertible preferred stock (10:1 ratio)
 - 2011 merger of BioControl Ltd and Targeted Genetics
 - 2012 acquired Special Phage Services

Industry Risks

- **Unclear Approval Process:** no FDA-approved clinical phage therapies on the market
- **Pricing**
- **Unclear IP Landscape:**
 - current patents claim methods of isolation, manufacture and use
 - unclear how robust these claims
 - unclear how strong in protecting products/applications