Phage therapy: a new paradigm for food industry

Catalin Iancu, PhD
Scientist, Micreos Food Safety
April 2016, Timisoara, Romania
Why me and phages for food safety?

Common point: Food-born pathogens
History of bacteriophage therapy

1917 – “an invisible, antagonistic microbe of the dysentery bacillus”

1921 – First administration of phages at Hopital des Enfants-Malade, Paris

1945 – “Golden Era of Antibiotics” in the Western world – phage therapy left behind

2006 – First phage-based antilisterial product approved by FDA

“You can't really move forward until you look back”. Cornel West
Facts about phages

Natural enemy of bacteria, forced to kill.
Ubiquitous in the environment and in the human body;
Most abundant microorganism on earth (>10^{32});
Outnumber bacteria 10 to 1;
Up to a billion phages in 1 ml seawater;
2 distinct "lifestyles": lytic and lysogenic.

Moineau, S. et al., 2010. Nature Reviews
MICREOS

Est. in 2005

Technology leader

Privately owned

Targeted anti-bacterial solutions

50 employees

Food Safety

Human Health

Food Safety

Human Health
Phages and food safety

Phages are best on surface or liquid applications;

- RTE Meats
- Smeared Cheese
- Fish
- Food Contact Surfaces
- Vegetables
- Raw Poultry

Two main phage providers the food safety arena:
Rules of the game

- Strictly lytic phages;
- Do not carry undesirable genes (e.g. pathogenicity; antibiotic resistance)
- Do not transduce host DNA (transduction experiments)
- Food regulations compliance;
Phages vs common antimicrobials

Compared to other antimicrobials the numbers are in reality tiny:

→ Nisin 12.5 mg/kg ⇒ 2.24 x 10^{15} molecules/g

→ Octanoic acid 400ppm ⇒ 1.6 x 10^{18} molecules/g

→ 1 g of sodium lactate treats a small hotdog to prevent outgrowth of *Listeria*

→ 2 uL of phage particles (5 x 10^6 PFU/cm^2) can kill 10^5 of *Listeria* cells;

→ 1 g of phages will treat between 2-200 million hotdogs
Resistance and sustainable use

- Inherent phage resistance mechanisms (R/M systems, CRISPRs) are easily circumvented by testing candidate phages against a large strain collection or are of no concern (ABIs, super-infection exclusion systems)

- Mutations are generally detrimental (only phage pressure gives an advantage)

- 1 in $10^6$ or $10^7$ contaminations will not be removed but if food is treated there is no feed-back loop to the environmental niche
LISTEX™

- Extremely broad host range;
- Receptors: N-acetylglucosamine and rhamnose substituents of cell wall teichoic acids;
- High affinity towards *Listeria* cells;
- FDA approved - GRAS status;
- Used mainly in RTE and cheese;

**P100 phage (TEM)**
LISTEX™ on Hot dogs

Hot dogs, *L. monocytogenes* WSLC1001 SV1/2c

- **Control**
  - $3 \times 10^8$ PFU/g
- **3x10^7 PFU/g**

- **Hot dogs weight : surface ratio 1:2**;
- **1.5 \times 10^7 and 1.5 \times 10^8** PFU/cm²

Efficacy of LISTEX™ on read-smear soft cheese during ripening

**Data generated by ETH (Swiss Federal Institute of Technology Zurich)**
LISTEX™ as an additional hurdle

LISTEX™ in combination with Potassium Lactate-Sodium Diacetate

Extend the shelf life of RTE products

**SALMONELEX™**

- **Cocktail of two phages**
  - S16 - T4-like phage which attaches to OmpC protein – an osmoregulatory membrane protein present in all strains regardless of serovar;
  - Felix O1 - Attaches to a sugar residue of the outer core of the LPS molecule;

- FDA – GRAS status;
- Used mainly in raw meats (poultry, pork, beef);
SALMONELEX™ on chicken skin

4°C

Phage concentrations $1 \times 10^7$ pfu/cm² or $2 \times 10^7$ pfu/cm²;
Contamination with $\sim 1 \times 10^4$ cfu/cm²
SALMONELEX™ on chicken breast fillet

4°C

Phage concentrations 1x10^7 pfu/cm² or 2x10^7 pfu/cm²;
Contamination with ~1x10^4 cfu/cm²
SALMONELEX™ on raw pork

Phage concentrations $1 \times 10^7$ pfu/cm² or $2 \times 10^7$ pfu/cm²;
Contamination with $\sim 1 \times 10^4$ cfu/cm²
Concluding Remarks

WHY?
Phage therapy
(food safety)

- Effective
- Natural solution
- Available
- Sustainable
- Friendly
- Clean label
THANK YOU!