A SUSTAINABLE APPROACH TO FIGHT BACTERIA: PHAGE THERAPY

Relief healthcare systems from nosocomial resistant infections
1.1. Corporate snap shot

- **Financial resources since creation**
  - ACE Management (63 % des parts)
  - Bio-Modeling Systems (37 % des parts)
  - OSEO: Innovation agency
  - DGA: 1/3 captured
  - CIR: tax refund for R&D

  
  \[ \text{2,8 M€} \]

- **Current patents**
  - RIPh: PCT/FR2010/050796 - 2009

- **Ressources**
  - P1/P2 equiped labs in Biocitech Park (pharma site)
  - 10 scientists

- **Status**
  - SA with Directory and advisory board

- **Scientific committee**
  - International experts in bacteriophages and biodefense

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Flavie Pouillot: R&D Director

Jérôme Gabard: CEO
1.2. A highly qualified management

**CEO (Président du Directoire)**

- **Business Unit Director (2005-2009):** TMTG - 20 staff
  - Sales and service offering performances
  - Operational and strategic market studies (+30 startup and big pharma projects)
- **CEO (2001-2004):** Eurocliffe SA - 6 staff
  - Drug candidate screening: research collaboration contracts with big pharma
  - Buy out (2004) by Faust Pharmaceuticals (today Domain Therapeutics)
- **Business Developer (2000):** Qualicon - 100 staff
  - Food and beverage diagnostic: GMO detection PCR kit
- **R&D Head (1993-99):** DuPont de Nemours - 10 staff
  - From research to development then to market (Business Team)
  - Wide international exposure
- **Post Doc (1989-1993):** DuPont de Nemours Inc. (USA)
  - Plant biotechnologies R&D: mutagenesis, herbicide resistance
  - Based in Wilmington then Newark (Delaware)

**R&D Director**

- **Ph.D. in Microbiology and molecular biology (2006):**
  - Pasteur Institute and University Pierre & Marie-Curie - Paris
  - Thesis topic: the plague, in collaboration with DGA (French Defense Directorate)
  - Mutagenesis, comparative genomic & pathogenicity of Yersinia bacterial strains
- **Elaborate and drive R&D programs in Pherecydes Pharma (since 2007):**
  - Hiring and management of scientists
  - Project management
  - Scientific publication and communication
1.3. Many partnerships

- Robert Debré Hospital: *E. coli* French national reference center
- Hôpital Begin: work on hemorrhagic *E. coli* strains
- Several burn wound hospital wards: Percy (F), St. Joseph-St. Luc (F), CHU Vaudois (CH), Queen Astrid (B), Loreval (B), CHU Liège (B), CHU Nantes (F)
- Ghent University: *Pseudomonas aeruginosa* international collection
- Microbiology Institute of Orsay University: for phage characterization
- Institute for Military Biomedical Research: for preclinical testing
- Phagespoirs association: gathering 17 French intensive care units for phage therapy
- GeePhage: phage therapy patient association
- Le Lien: patient association to fight nosocomial infections
- Aix-Marseille University: for phage based diagnostic
- Clean cells: GMP bioproduction and batch control quality...
- Statitec: Clinical Research Organisation
- Laboratoires Brothier: band aid
2.1. Rediscovering phage therapy …

- **What are bacteriophages?**
  - **Natural** organisms: we breathe in and out trillions every day
  - Behave like **viruses specific to bacteria**: can be used efficiently to **cure pathogenic infections**

- Discovered in Europe in the early 20\textsuperscript{th} century, but unreliable technology at that time
  - Today Pherecydes modern technology allows reliable R&D and bioproduction
2.2. ... and the limits of antibiotics

- Multi-Resistant Bacteria (MRB):
  - Raised in the 90s with *Staphylococcus* species
  - Now expanding to gram-negative species: *E.coli* & *Pseudomonas aeruginosa* ➔ Biggest therapeutic gap

- Challenging the antibiotic model: long R&D, huge costs, high failure risks

- Antibiotics now fail to counter bacteria edgy evolution
2.3. Pherecydes core activity: Therapy

- **Positioning:**
  - Targeting **high-value orphan infections**, for which **treatments** are no longer available.
  - For hospital use (nosocomial infections)

- Focusing on the **highest medical need** and the **biggest therapeutic gap**.
  - Gram-positive species: *Staphylococcus* species
  - Gram-negative species: *E.coli* and *P. aeruginosa*, for which resistance has been expanding at a faster pace since the early 2000s (therapeutic gap)

**Altogether > 50% of nosocomial infections**
2.3. Pherecydes core activity: Therapy

Product cycle: 1<sup>st</sup> generation natural phages
L’opportunité de tester des bactériophages par voie interne dans un modèle animal et de mesurer efficacité, innocuité et pharmacodynamique.

3.2. Infection à *PYO* respiratoire

Un traitement efficace et parfaitement toléré par l’animal.

- Vérification du comportement des phages en système générateur d’aérosol: pas de réduction d’efficacité pour les générateurs de particules sans effet thermique

### Traitement des poumons de souris infectées
- Par un *Pseudomonas aeruginosa* à l’aide d’un cocktail de bactériophage
- Référence de traitement : antibiotique ciprofloxacine
- Formulation du produit cocktail de phages : eau physiologique
- Mode d’administration : aérosol
- Aucun effet secondaire du au traitement par les bactériophages

Un traitement efficace et parfaitement toléré par l’animal.
Tests précliniques chez la souris

3.3. Brulures infectées

Résultats attendus

- Guérison des animaux lorsque les antibiotiques sont inefficaces.
- Effet thérapeutique des phages équivalent à celui des AB encore actifs.

Cocktail anti COLI
Cocktail anti PYO
3.4. Evaluation of phage therapy for treating *E. coli* and *P. aeruginosa* burn wound infections

**Phase I-II clinical trial : PHAGOBURN project in selection process**

**HEALTH.2013.2.3.1-1: Drugs and vaccines for infections that have developed or are at risk of developing significant anti-microbial resistance.** Coordinator PHERECYDES PHARMA

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4.1. A compliant regulatory environment

- Favorable elements:
  - Natural origin of bacteriophages
  - Long clinical experience in Eastern Countries
  - High demand from physicians and patients

- Market authorization likely to last shorter (3-4 years)
  - Temporary authorizations of use is highly probable

- Phage cocktails classification trend: “adjustable biologics”
  - Allows yearly product update according to resistance occurrence
  - No need to pass through the regulatory pipeline again (e.g. Vaccine)
4.2. A fast bioproduction cycle (<24h)

- Bioproduction in low pressure no shear system
  - Biosafety level II
  - Product storage 4°C
  - Product shelf-life: at least 12 months

- USP: a 6 hours production timing
  - Inexpensive systems of 5-10 liters capacity

- DSP: a two steps purification within a day
  1- Clarification to remove bacterial debris
  2- Endotoxin removal and phage concentration

- Yield for a 10 liter bulk:
  1000 to 100 000 doses according to therapeutic application
4.3. Product development timeline

Coli/Pseudo. Burn-Wound
- Phase I/II
- EMA Market Approval
- FDA Market Approval
- Marketing andEU pre sales
- Marketing andUSA pre sales
- ATU EU Sales
- Standard EU Sales

Pseudo. Respiratory Cocktail
- Pre clinical
- Phase I/II

E.Coli Urinary Cocktail
- Studies
- Pre clinical
- Phase I/II
- EMA MA
- FDA MA
- ATU Sales
- Sales

Staph post-surgery Cocktail
- Phage Screening & studies
- Pre clinical
- Phase I/II
- Phase III
- EMA MA
- ATU Sales

2 products
Thank You

*Pherecydes Pharma, Paris*

Jérôme Gabard & Flavie Pouillot