The Promise of the Human Microbiome

Next generation targeted pre, pro, and synbiotics

March 2016
Company Overview

- Founded in March 2012, LSE listing 2014

- Developing products and ingredients to modify the human microbiome to prevent and manage human disease

- Technology platforms
  - **OptiScreen®**: High throughput screening platform to allow the identification of probiotics with specific health benefits
    - Cholesterol reducing supplement: successful clinical studies completed Sep 2015
  - **OptiBiotix®**: High throughput technology platform(s) which generates novel sugars which act as strain, species, and genus specific prebiotics

- Extensive portfolio of patents and strain registrations

- Partnership model: commercial partners across all platforms
Current pre, pro, and synbiotics

- Traditional focus on general health benefit (dairy origins)
- Growing trend towards products with a specific health benefit
  - Absence of targeted approach toward specific biomarkers which evidence a health benefit
- Mechanism of action often not understood
- Lack of scientific rationale in probiotic and prebiotic selection
  - Use of multistrain preparations common
  - Market view ‘more means better’ – more strains and greater numbers
- Synbiotics: lack of information on ability of the prebiotic to support probiotic activity and enhance survival (definition)
- Few good human studies evidencing health benefits of pro, pre, or synbiotic
  - Poor study design: Lack of appropriate controls, Statistical power, Probiotic recovery
**OptiScreen®: Targeted probiotics**  
**First product: Cholesterol reduction**

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<tr>
<th>Biomarker</th>
<th>Target biomarker identification: <strong>Cholesterol</strong></th>
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<tr>
<td>Mechanism</td>
<td>Target mechanism: <strong>Bile Salt Hydrolysis (BSH)</strong></td>
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| Screening| High throughput screening for BSH activity and bile resistance (~4000 strains)  

- 353 *Lactobacillus* strains
| Selection| 45 lactobacilli selected for quantitative determination of BSH activity and bile tolerance  

- 24 strains with the highest BSH activities selected to quantify cholesterol assimilation capacity *in vitro*.  
3 strains showed *in vitro* cholesterol reductions of 72-81%
| Pilot scale| Final selection (high manufacturability): **Lactobacillus plantarum strain**  

- Bacterial growth optimisation and pilot scale production
| Human study| Determination of the cholesterol lowering efficacy of *L. plantarum*  

- **Human intervention study** (12 wk randomized, dbl-blind, placebo-controlled, parallel-group trial)

- **☑ LDL Cholesterol lowering efficacy:** -7.2% all groups, -15% in 50-59 age group  
- **☑ Clinically significant hypertension reduction:** 6mmhg (-5.1%)
OptiBiotix®: Targeted prebiotic Systematic development process

- **Species selection**
  - Microbial genera are selected based on their safety, potential health benefits, production, & enzymatic potential activity to synthesize prebiotics (e.g. galactooligosaccharides)

- **Screening**
  - Bacterial strains are screened for the expression of their enzymic capability
  - c.500 strains from 3 genera screened to date. High intra and interspecies variability

- **Selection**
  - Strain growth and enzyme expression used to predict prebiotic yield
  - Potential to hyperinduce enzyme expression if required

- **Synthesis/IP**
  - Lab scale bacterial growth and prebiotic yield optimisation
  - Structural analysis for novelty and patent filings (HPLC-RID, GC-MS, HPAEC-PAD)

- **In vitro**
  - In vitro assessment of functional properties: strain, species, genus level specificity (gut models)
  - Pilot scale up, organoleptic testing

- **Human study**
  - Prebiotics with high yields, novelty, and potential in vivo functional properties: human studies

- ✓ Prebiotics with evidence of genus and species specificity
- ✓ Prebiotics with potential strain specify: requires higher purity
Strains selected for optimisation and yield analysis:
L. delbruckii (2)
L. helveticus (9)
L. reuteri (18)
L. plantarum (30)
L. fermentum (31)

High inter-species/strain variation in ability to produce prebiotic

Cut off for predicted prebiotic synthesis
Optibiotix®: Pure culture on GOS synthesized by *L. rhamnosus* β-galactosidases

- Highest growth rate/ shorter lag phase observed for *L. rhamnosus*
- No growth for *C. difficile* and *B. longum*, *B. bifidum* moderate growth
Overview of OptiBiotix’s next generation Pre, Pro, Synbiotics:

**OptiScreen®**
A proprietary high throughput screening & optimisation technology platform designed to identify microbes with metabolic pathways with can interact with human physiological processes and bring health benefits.

Probiotic with specific health benefit (e.g. cholesterol reduction)

**OptiBiotix®**
A proprietary technology which generates novel prebiotics & screens them for their ability to modulate individual species within the human microbiome.

Prebiotic which selectively enhances the growth of a specific strains, species, or genera of bacteria

**OptiBiotics®**
Combination of a targeted probiotic and prebiotic in which the prebiotic selectively enhances the in vivo growth of the probiotic and accentuates its functional properties and health benefits.

Potential for designer prebiotics specific for a microbial genera, species, or strain associated with a health benefit and the ability to mix and match sugars to shape the human microbiome.
Conclusions

- OptiBiotix has developed two high throughput technology platforms

- **OptiScreen®**: allows the identification of probiotics with specific health benefits
  - Developed safe, efficacious cholesterol supplement with human data
  - Potential for product line extension into foods such as yoghurts, fruit & vegetable juices
  - Diabetes and bone health supplements to follow

- **OptiBiotix®**: allows the creation of targeted prebiotics
  - Evidence of genus and species specificity
  - Evidence of potential strain specify but may require higher purity prebiotic
  - Potential for designer prebiotics for specific microbial genera, species, and strains

- New concept: **OptiBiotics®**: A combination of a targeted probiotic and prebiotic which selectively enhances the *in vivo* growth of the probiotic and accentuates its functional properties and health benefits

- Systematic approach to development will create next generation pre, pro, and OptiBiotics® with functionally superior formulations of rationally selected probiotics and strain/species/genus specific prebiotics