The use of ‘live’ beneficial lactobacilli to treat skin conditions

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YUN NV – THE COMPANY

Belgian biotech company in the centre of the world with a new vision on health
REMINDER – MICROBIOME

It is a matter of balance...

Man et al. 2017

Balance, more stable and infection resistance and resilience

Imbalance, less stable, infection and inflammation susceptibility

Nature Reviews | Microbiology
YUN is focusing on the benefits of a healthy skin microbiome.
SKIN CONDITIONS LINKED TO THE MICROBIOME

A multitude of skin conditions are currently treated with topical antibiotics

ACNE

HYDRENITIS SUPPERATIVA

IMPETIGO

FOLLICULITIS DECALVANS
CREATE A BACTERIAL REVOLUTION

The natural alternative for antibiotics

“Antibiotic resistance is one of the biggest threats to global health, food security, and developments today.”

(WHO)

“Drug resistance deadlier than cancer by 2050”

(UK Government Study)
‘Probiotic’ means ‘living’ bacteria

“live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”

TOPICAL PROBIOTIC RESEARCH

Lactobacillus spp. and the link to the skin microbiome

1. Why use ‘probiotic’ Lactobacillus spp. for skin applications?
2. Can we do a rational in vitro strain selection?
3. How to keep lactobacilli alive at sufficient dosage levels?
RATIONALE FOR USING LACTOBACILLI

Because they are the first bacteria a baby receives to build his/her immunity.

Reid et al. 2011
SCREENING PLATFORM

Key criteria we took into account during our research

RATIONALE FOR IN VITRO STRAIN SELECTION

SAFETY
- History Lactobacillus (QPS/GRAS)
- Lack of antibiotic-resistance
- No toxicity

APPLICABILITY
- Growth rate / Biomass
- Robustness (viability & stability)
- Adaptability / Niche flexibility

FUNCTIONAL ACTIVITY
- Microbiome modulation
- Immune modulation
- Epithelial modulation

UN PROBIOTHERAPY
PROBLEM

How to go from *in vitro* to a final formulation?
TOPICAL PROBIOTIC RESEARCH

*Lactobacillus spp.* and the link to the skin microbiome

1. Why use ‘probiotic’ *Lactobacillus spp.* for skin applications?
   - ✓

2. Can we do a rational in vitro strain selection?
   - ✓ ❗

3. How to keep lactobacilli alive at sufficient dosage levels?
   - ✓
Each visit:
- **Clinical evaluation** – lesion count
- **Skin swab** ⇒ DNA extraction for
  1. Library preparation (16S rRNA Sequencing⇒ Illumina MiSeq Platform ⇒ Bioinformatic analysis ⇒ **Microbiome profiling**
  2. qPCR for evaluation of **impact** of topical study cream on **pathobionts** (*Cutibacterium spp.* & *Staphylococcus spp.*)

Lebeer et al. 2018 (BioRxiv)
IN VIVO EFFICACY

Test 1: Proof-of-concept clinical trial - results

Wilcoxon matched-pairs rank test * = p<0.05 and ** = p<0.01
MOLECULAR MECHANISM OF ACTION

Probiotics are influencing pathobionts...
MOLECULAR MECHANISM OF ACTION

...inhibiting both *Staphylococcus* spp. AND *Cutibacterium* spp.
Lipase activity of cutibacteria is reduced

MOLECULAR MECHANISM OF ACTION
Molecular Mechanism of Action

... resulting in reduced inflammatory responses

Competition with pathobionts leads to:
- Reduction of metabolic activity of and inflammatory responses by pathobionts
- Competition for interaction with PRRs (e.g. TLR2)

<table>
<thead>
<tr>
<th>L. pentosus*</th>
<th>L. plantarum*</th>
<th>L. rhamnosus*</th>
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<tbody>
<tr>
<td>L- &amp; D-lactic acid</td>
<td>L- &amp; D-lactic acid</td>
<td>L-lactic acid</td>
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<tr>
<td>• StsP &amp; CPS</td>
<td>• SpaCBA pili, LTA &amp; EPS</td>
<td>Pathobionts</td>
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<tr>
<td>• Msa lectin</td>
<td>• SpaCBA pili</td>
<td>Re-epithelialization ↑</td>
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<tr>
<td>• pentocin</td>
<td>• plantaricin</td>
<td>Inflammation ↓</td>
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<td></td>
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<td>Competitive adhesion ↑</td>
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<td>Pathobionts ↓</td>
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</table>
PROBIOTIC MECHANISM OF ACTION

Multifactorial mechanism of action

- Competition for PRR’s
- Pathobiont inhibition
- Lipase activity reduction of cutibacteria
IN VIVO EFFICACY

Post-market follow-up study

Background - Study

- Feedback received
  - 52 dermatologists (6.5% of Belgian total)
  - 199 patients

- Patient population
  - Average age (n=174): 22.72 [min. 10 – max. 69]
  - Gender: 35.1 % male – 64.9% female
  - Severity: 46.6% mild – 53.4% moderate

- Global acne grading (0-4):
  - Average score by dermatologist = 2.66 [1.52-3.79]
  - Average score by patient = 2.74 [1.52-3.95]

Conclusion

- 165 patients (95%) showed improvement
- No difference between dermato & patient score

Figure - Treatment efficacy (% of patients) based on global acne grading by independant dermatologists
NEW POSTMARKET DATA

Based on the scientific mechanism of action new skin conditions show great potential

Postmarket study with cream with live lactobacilli:
- n = 70 independent dermatologists
- Total of 208 patients included
- New skin indications based on scientific rationale

GLOBAL SKIN IMPROVEMENT (0-4)
(SCORE DERMATOLOGIST / PATIENT):
- Acne rosacea = 2,53 [1,42 – 3,64] / 2,43
- Seborrheic eczema = 2,73 [1,70 – 3,76] / 2,76
- Folliculitis = 2,75 [1,64 – 3,86] / 2,72
YUN – PRODUCT RANGE

- ACNE
- SENSITIVE AND DRY SKIN
- VAGINAL IRRITATIONS
- ATHLETE’S FOOT
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THANK YOU AND...
DON’T FORGET TO LOVE YOUR BACTERIA

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