The New Generation Bacterial Lysate

Polyvalent Mechanical Bacterial Lysate

Prevention of upper and lower respiratory tract infections

LALLEMAND PHARMA
**Acute and Chronic Respiratory Infections**

- Most common diseases in developed countries
- 30 to 50% of work absenteeism
- 50-60% of school absenteeism

<table>
<thead>
<tr>
<th>Upper Respiratory Tract Infections</th>
<th>Lower Respiratory Tract Infections</th>
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<tbody>
<tr>
<td>Common cold</td>
<td>Bronchitis</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Bronchiolitis</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Epiglottitis</td>
<td>Acute Exacerbations</td>
</tr>
<tr>
<td>Laryngotracheitis</td>
<td>in Chronic Obstructive Pulmonary Disease (AECOPD)</td>
</tr>
<tr>
<td>Otitis</td>
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</tbody>
</table>

Most often viral etiology
- Epiglottitis and Laryngotracheitis: *Haemophilus influenza*
- Bacterial pharyngitis: *Streptococcus pyogenes*

Either viral or bacterial etiology
- Bronchitis and bronchiolitis: often viral
- Community acquired Pneumonia: *Streptococcus pneumoniae*
- Atypical pneumonia: *Mycoplasma pneumoniae, Chlamydia spp, Legionella, Coxiella burnetii and viruses*
- AECOPD: *Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis, Pseudomonas aeruginosa and viruses in 40% of exacerbations*

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**Risk factors of respiratory infections**

- Immunological status and age: children and elderly
- Air pollution
- Tobacco smoking
- Social promiscuity

1. Bellos et al. The burden of acute respiratory infections in crisis-affected populations: a systemic review, Conflict on Health, 4-3, 2010
3. V. Purushothama et al. Infection of the respiratory system, Medical Microbiology, Chap 93, 1996

http://www.ariatlas.org/

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PMBL, Unique process and formulation

- Multiple inactivated strains (13) derived from the most common pathogens responsible for Respiratory Tract Infections
- Mechanical lysis
- Preservation of the antigenic structure
- Removal of capsule
- 10-100 times more efficient than other lysates (single strain lysates or chemical lysates) \( \textit{in vitro} \)
- Sublingual route

Original mode of action

- Acts on each step of the whole immune cascade
- Stimulates both innate and adaptive immunity
- Sublingual route allows interacting directly with respiratory mucosa to trigger a loco regional immune answer

PMBL, Optimal immunogenic profile in clinical results

- Better reduction of upper respiratory tract infections than CLBL (Chemical lysate)
- Better reduction of work absenteeism than CLBL (Chemical lysate)
- No patient with PMBL required antibiotic during 6 months study

1. B. Morandi et al. A mixture of bacterial mechanical lysates is more efficient than single strain lysate and of bacterial-derived soluble products for the induction of an activating phenotype in human dendritic cells, Immunology letters, 2011
2. E. Villa et al. May We Strengthen the Human Natural Defenses with Bacterial Lysates?, WAO journal, 3:S17-S23, 2010

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PMBL is able to induce a potent maturation of dendritic cells which expressed CD 80, CD 83 and CD 86 markers1 2 3 4 5 6

2 Mature dendritic cells are able to present antigen

3 PMBL is able to increase the reservoir of naïve B cells and early memory B cells to allow the immune system to be ready to fight infections3 7 8

4 PMBL is able to increase secretion of proinflammatory cytokines1 3 9

5 PMBL is able to increase the total number of Natural Killer cells9

6 PMBL is able to increase CD 4 T helper cells 7 8 9

7 PMBL is able to recruit a larger number of precursor B cells to be differenciated in plasma cell7

8 PMBL is able to increase specific and opsonising immunoglobulins1 3 9 10

9 PMBL is able to induce efficient opsonization to allow the destruction of bacteria10

1 B. Morandi et al. A mixture of bacterial mechanical lysates is more efficient than single strain lysate and of bacterial-derived soluble products for the induction of an activating phenotype in human dendritic cells, Immunoology letters, 2011
4 E. Villa et al. May We Strengthen the Huma h Bacterial Lysates?, WAO journal, 3:S17-S23, 2010
6 G. Melioli et al. A polyvalent Mechanical bacterial lysate induces a powerful and specific immunoresponse in vivo by activating a cross-talk between innate and adaptative immunity, Clinical and Investigative Medicine, vol.27, no. 4, 2004
10 G. Melioli, Opsonization: to eat or be eaten, Gior.It.Mal.Tor, 56, 4, 245-248, 2002

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## PMBL, Proven clinical efficacy

<table>
<thead>
<tr>
<th>Journal</th>
<th>Publication Title</th>
<th>Results (compared to control or placebo)</th>
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<tbody>
<tr>
<td>World Allergy Organization journal&lt;sup&gt;1&lt;/sup&gt;</td>
<td>“May we strengthen the Human Natural Defenses with Bacterial Lysate”</td>
<td>- Improvement of immunogenicity thanks to preservation of antigenic structure by mechanical lysis - PMBL stimulates both innate and specific immune response</td>
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<tr>
<td>European Journal of Aerobiology, environmental medicine and Air-borne infections&lt;sup&gt;2&lt;/sup&gt;</td>
<td>“Evaluation of the clinical efficacy of a new polyvalent bacterial lysate obtained by mechanical lysis (PMBL) in a population of 180 school-aged children with recurrent respiratory infections”</td>
<td>- Reduction of mean number of infections by 53.6% - Reduction of school absenteeism by 49.7%</td>
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<tr>
<td>Acta Bio Medica Ateneo Parmense&lt;sup&gt;3&lt;/sup&gt;</td>
<td>“Strategies for optimizing compliance of paediatric patients for seasonal antibacterial vaccination with sublingually administered Polyvalent Mechanical Bacterial Lysates (PMBL)”</td>
<td>- Reduction of mean number of infections by 29.5% - Increase of B lymphocytes by 67.8%</td>
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<tr>
<td>GIMMOC&lt;sup&gt;4&lt;/sup&gt;</td>
<td>“Immunoprophylaxis of recurring bacterial infections of respiratory tracts in paediatric age: clinical experience through a new immunostimulating vaccine”</td>
<td>- Higher proportion of healthy children (no respiratory infections) with PMBL: 67.5% - Reduction of complementary medicine use (antibiotics/antipyretics/antiphlogistics) by 66.7%</td>
</tr>
<tr>
<td>ArzneimForschDrugRes&lt;sup&gt;5&lt;/sup&gt;</td>
<td>“Prevention of Recurrent Upper Respiratory tract infections in a community of cloistered Nuns using a new immunostimulating Bacterial lysate”</td>
<td>- Reduction of the number of infections by 77.4% after treatment and by 81.2% after 3 months follow-up - Increase of secretory IgA by 110%</td>
</tr>
<tr>
<td>Trends in Medicine&lt;sup&gt;6&lt;/sup&gt;</td>
<td>“A new bacterial lysate protects by reducing infectious exacerbations in moderate to very severe COPD”</td>
<td>- Reduction of episodes of acute exacerbations/patient by 20.7% - Reduction of the hospitalization rate by 44.6%</td>
</tr>
<tr>
<td>Gior It Mal Tor&lt;sup&gt;7&lt;/sup&gt;</td>
<td>“Prophylaxis of episodes of winter airway infections with a sublingual antibacterial vaccine obtained by mechanical lysis, PMBL (Ismigen-Zambon): clinical trial in patients with a case history of tuberculosis”</td>
<td>- Reduction of bronchial infections by 63.4% - Reduction of antibiotic use by 50.6%</td>
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### Easy posology scheme

<table>
<thead>
<tr>
<th>10 days/Month during 3 months</th>
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<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td>22</td>
</tr>
<tr>
<td>29</td>
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</tbody>
</table>

### PMBL Key advantages
- Higher immunogenic profile (mechanical lysis, sublingual route, acts on the whole immune cascade)
- Stimulation of both innate and specific immune response
- Dual action on prevention of viral and bacterial Respiratory Tract Infections
- Significant reduction of number of upper and lower respiratory infections
- Significant reduction of antibiotics use

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1. E. Villa et al. May We Strengthen the Human Natural Defenses with Bacterial Lysates?, WAO journal, 3:S17-S23, 2010
6. M. Cazzola, A new bacterial lysate protects by reducing infectious exacerbations in moderate to very severe COPD, Trends in Medicine, 2006
7. V. M. Boris, Prophylaxis of episodes of winter airway infections with a sublingual antibacterial vaccine obtained by mechanical lysis, PMBL (Ismigen-Zambon): clinical trial in patients with a case history of tuberculosis, Gior It Mal Tor, 57, 3, 2003

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PMBL Worldwide presence

- Brazil and Colombia
- Saudi Arabia, Kuwait, Oman, Yemen, Iran, Syria, Lebanon, Iraq, Jordan, Bahrain, Qatar, Egypt
- Russia, Kazakhstan, Bielorussia, Uzbekistan, Kyrgyzstan, Turkmenistan, Moldova, Tajikistan, Armenia, Azerbaijan

ARGENTINA
Imigen

CENTRAL AMERICA
Imigen

ECUADOR
Imigen

MEXICO
Imigen

PERU
Imigen

URUGUAY
Imigen

VENUEZUELA
Imigen

Immubron

UKRAINE
Resipbron

INDIA
Imigen

Immubron

ITALY
Imigen

SOUTH KOREA
Imigen

POLAND
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PORTUGAL
Provax

SRI-LANKA
Imigen

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