Elucidating the immunomodulatory mechanism of growth-promoting biodegradable microparticles using RNA-seq in mouse macrophages

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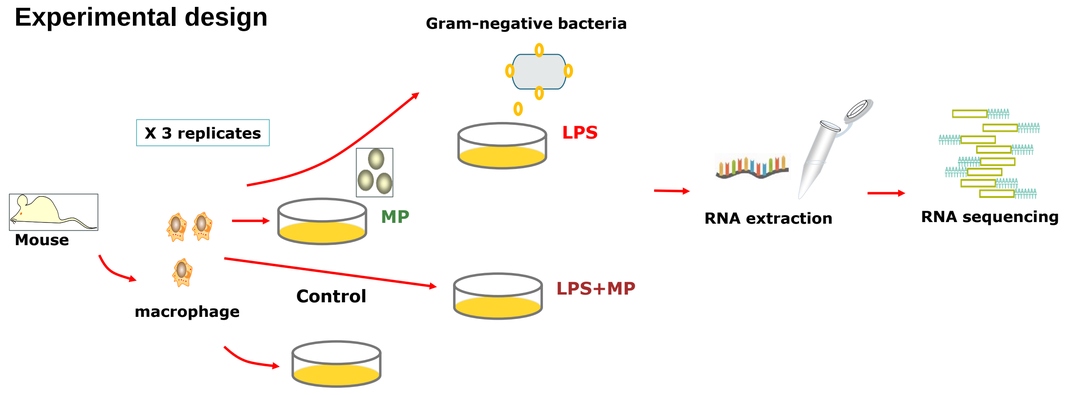
Introduction

- **Food gap by 2050:** The global population will reach 10 billion by 2050, and the demand for animal protein will increase by 56%.
- **Urgent needs:** Animal growth rates and feed efficiency must be greatly improved to achieve this.
- **Current solution:** Antibiotics in feed additives to mitigate persistent low-level infection in livestock.
- **Issues and challenges:** Overuse of antibiotics results in antimicrobial resistance in livestock. Up to 90% of antimicrobials are excreted to the environment, threatening the environment and human health.
- **Our solution:** Dr. Kaltenboeck developed and patented proprietary biodegradable microparticles as a non-antibiotic growth promotant, which were found to improve growth rates in pigs and chicken.

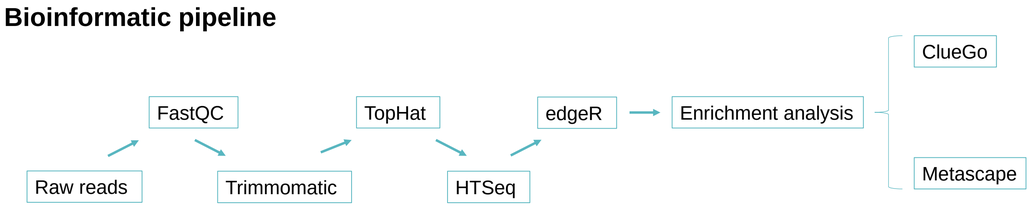
Methods

- J774A.1 macrophages from BALB/c laboratory mouse were treated by the microparticles (MP), lipopolysaccharide (LPS), or both compounds (LPSMP).
- LPS is the major component of the outer membrane of Gram-negative bacteria triggering Toll-like receptor 4 and innate immune response.

Experimental design

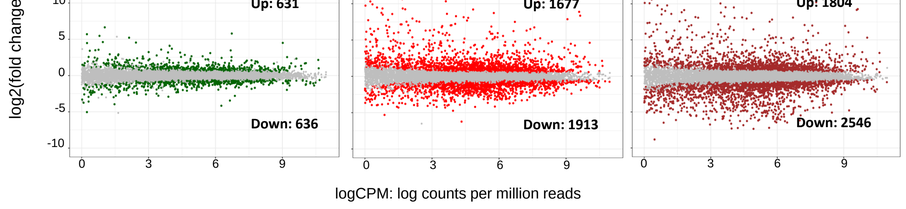


Bioinformatic pipeline

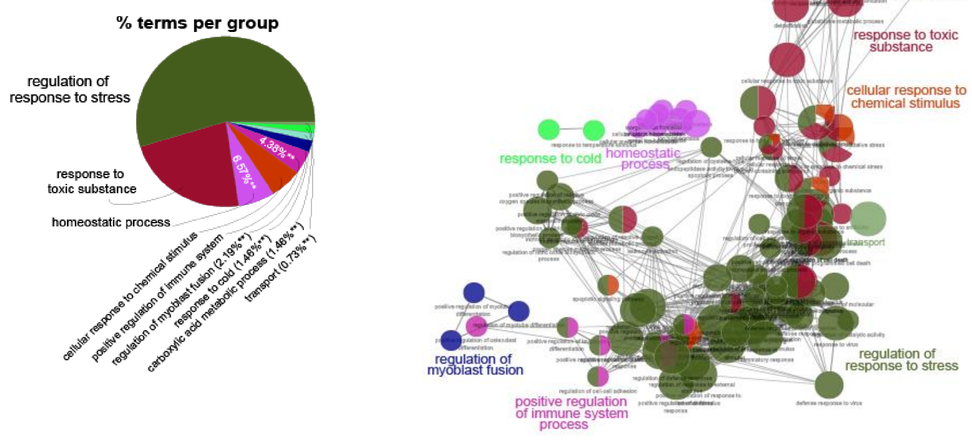


Results

- A total of 1,267 DEGs were discovered in the MP group, including 631 upregulated and 636 downregulated genes (adjusted P<0.05).

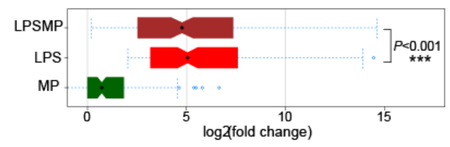


- Gene ontology analysis of the upregulated genes identified the immune system and stress response-related function categories.



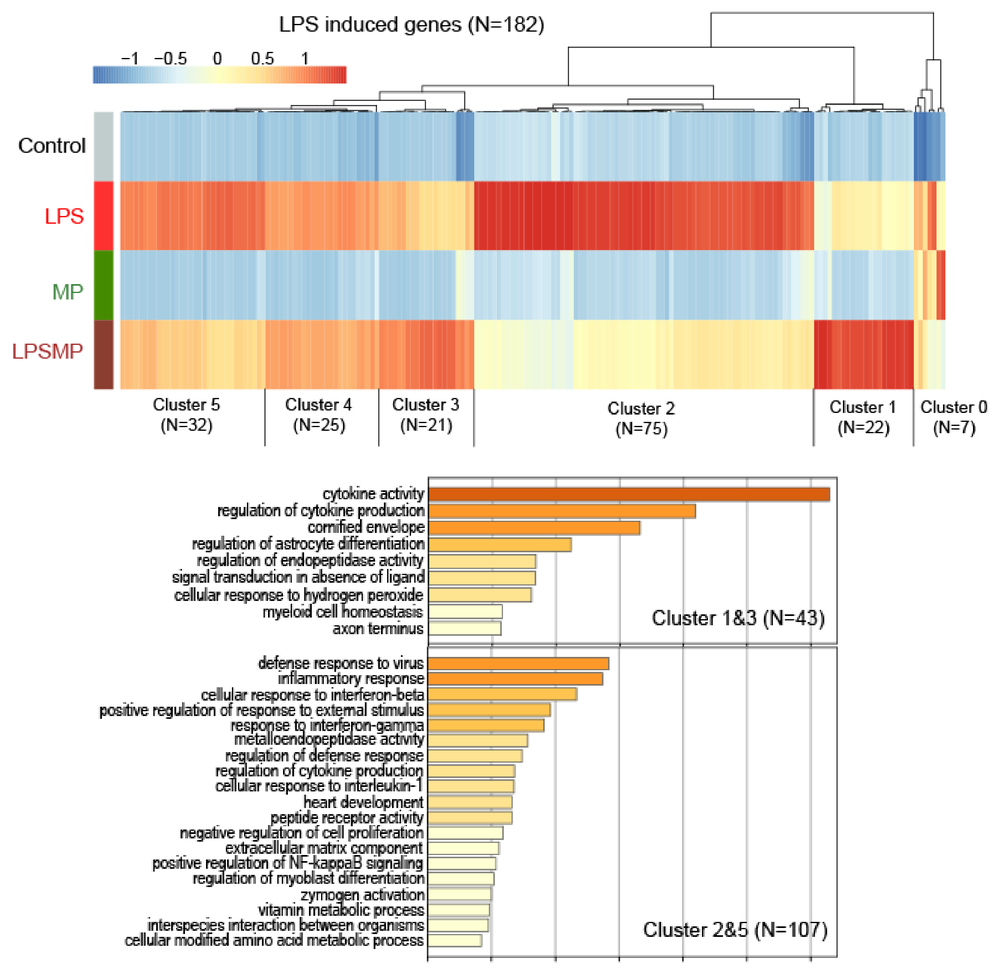
- When examined the induced genes under LPS challenge, the expression levels are slightly increased in the MP group, suggesting a slight increase in expression preparing for potential infection.
- On the other hand, the average expression fold changes in the LPSMP group is significantly lower than LPS alone, indicating the response to LPS stimulation is reduced under the presence of MP.

LPS induced genes



182 induced genes in LPS group (RPKM>2, control RPKM<1, , fold change>4

- Heatmap assigns LPS induced genes to 5 clusters. Among these clusters, there are two major expression pattern (cluster1&3 and Cluster2&5).



Conclusion

- Our preliminary results are consistent with that the MP is able to fine-tune the immune system by slightly boosting specific immune pathways under non-infected conditions and reducing the unnecessary response when bacterial pathogens are present.

Acknowledgments

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Reference

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