

MCB6XXX: Probiotics (3 credits)
Spring 2018

MCB6XXX is an upper division course on probiotics. This course will cover the use of microorganisms to promote a health status in the animal and human host. This course will provide a conceptual background in microbiology and immunology for the use of microorganisms for the prevention or treatment of animal and human diseases.

Student Learning Outcomes – After successful completion of this course, students will be able to:

- Understand the history of probiotics
- Compare and contrast the use of lactic acid bacteria, *Bifidobacterium* and *Propionibacterium* as probiotics
- Understand the range of proposed probiotics and the challenges in ensuring their safety and efficacy
- Compare and contrast the mechanisms used by probiotic microorganisms to modulate the host immune responses in the animal and in the human host
- List the proposed uses of probiotic microorganisms for the prevention or treatment of animal and human diseases
- Compare and contrast the applications of prebiotics, probiotics and symbiotics
- Discuss current research efforts and proposed applications of probiotics for animal and human health
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Lectures: Online through Canvas

Instructor: Dr. Graciela L Lorca

Office: Genetics Institute, Room 307

WebPage: Canvas (<https://ufl.instructure.com/>). Please select MCB6XXX.

On line help with classroom technology: <http://helpdesk.ufl.edu/>

Pre-requisite: MCB3020 or MCB3023

Communication: for questions regarding class and textbook content use the Discussion Board, for issues on Home Work Assignments, class organization check first the syllabus, the announcements and calendar on Canvas, then post your questions on the discussion board. For all other issues contact Dr. Graciela Lorca.

VIRTUAL OFFICE HOURS: will be available every week through the BLUE BUTTON tool in Canvas. To participate go to Conferences in the left of your screen and join! You will receive a weekly reminder by email.

Students in Gainesville can also come for in person office hours:
Fridays 2-3 PM at Genetics Institute, Room 307.

All students: If you cannot make it to office hours you can request an appointment. Send an e-mail with three suggested times and I will choose one for us to meet.

Contact Information: Use TEACHER in your emails through Canvas ONLY (personal emails should only be used in a case of emergency)

Dr. Graciela L Lorca:

Email (the most efficient): ONLY use Canvas e-mail (If you do not have access to the e-learning platform and need to contact me for an **emergency**, use glorca@ufl.edu)

Phone: 273 8090 (please leave a message).

Office hours: Fridays 2-3 PM at Genetics Institute, Room 307. By appointment: (only if you cannot make it to office hours) send an e-mail with three suggested times and I will choose one for us to meet.

- **Discussion Board:** A discussion board is available in Canvas. It is very useful, please post and answer your questions on class content and organization there. Postings and answers are monitored by the instructor to make sure no mistakes get propagated. There are several discussion themes. Please post your questions in the adequate section.

Material

- **Textbook:** no textbook is required, this course is based on peer reviewed papers either available for free through the links provided or through the UF library (ejournals).

- **Suggested readings:** For each module, suggested readings will be posted as pdf documents on Canvas or as links to download them from PUBMED (see working list at the end of the document)

Assessment of learning

- **Assignments (250 points):** Activities will be assigned by Unit. The activities include online research on diverse topics such as “co-evolution of beneficial bacteria and its hosts”, “GMO’s and probiotics”, “Market claims: is there scientific evidence?”. The

activities are mandatory and count towards the final grade. They should be completed by the deadline indicated on Canvas.

- **Topic reviews (300 points):** The research topics will involve the search and writing of a critical review of at least 5 scientific articles (original research, no reviews will be allowed). The student will have to complete the review on five topics that will be listed on Canvas. Examples are listed below:
 - Conflicts between study of probiotics as foods, dietary supplements and drugs in the US
 - Use of Omics technologies to help understand the microbiome and probiotic functionality
 - Psychobiotics: the microbiome as a key regulator of Brain and behavior
 - Improving probiotic specificity – ‘designer probiotics’
- **Exams (450 points):** Exams will assess your knowledge of the concepts covered during the lectures. Students must sign up on ProctorU at least 72h in advance. The assessment will be performed in **Three Mandatory Mid-term exams**. The student will be given the option to take a final cumulative exam to improve the grade obtained through the mid-term exams.
 - *Mid-terms (450 points):* There will be three 50 minutes proctored mid-term exams (150 points each) with multiple choice questions, true/false, fill in the blanks questions and short answers questions. **All exams are mandatory and will count towards the final grade.** Exams will test learning and understanding of material presented in lectures, assigned readings and in assignments.
 - *Optional Final to replace ONE test (with the lowest grade) will be available during Finals Week.* The students **MUST** have taken all three tests to qualify for the Optional Final. This cumulative test will include all the content included in Units 1 to 5 and will be worth 150 points.

Make-Up policy: No make-up exams. If one exam is missed, it will result in a score of 0 for the test (see below for “Excused absences”).

Excused absences:

Documentation **MUST** be provided for absences caused by serious illness, accident, jury duty, or death in the immediate family. You must contact the instructor **IN ADVANCE** of the missed exam and I will arrange an alternative time for the exam.

After the exam: The grades will be available on Canvas three days after the exam, unless notified by an announcement. Test questions will be made available through Canvas. After we release the questions, the student will have **5** days to submit questions about the test or claim mistakes in grading. No claims will be considered after that time.

Grading: Straight scale

Grading Scale

A	900 or above
A-	860-899
B+	830-859
B	790-829
B-	750-789
C+	720-749
C	690-719
C-	660-689
D+	630-659
D	600-629
D-	570-599
E	560 or below

Schedule of Classes

Date	Unit	Module. Topic
	Unit 1	Probiotics: definitions, history and classification
8-Jan		1. Definitions and History
10-Jan		Review: Bacterial cell structure
12-Jan		Review: Bacterial metabolism
17-Jan		2. Classification and physiology: Lactic acid bacteria (LAB)
19-Jan		3. Classification and physiology: <i>Bifidobacterium</i> and <i>Propionibacterium</i>
22-Jan		4. Impact of genomics on the characterization of probiotics_Intro to genomics
24-Jan		4. Impact of genomics on the characterization of probiotics_LAB part 1
26-Jan		4. Impact of genomics on the characterization of probiotics_LAB part 2
29-Jan		Assignment 1 due
	Unit 2	Biotechnological applications of Lactic acid bacteria
31-Jan		5. The uses of LAB in food fermentation -part 1
2-Feb		5. The uses of LAB in food fermentation -part 2
5-Feb		6. Antimicrobials components of LAB
7-Feb		7. Bacteriophages from LAB
9-Feb		8. Nutraceuticals and high value metabolites produced by LABs
12-Feb		Assignment 2 due

14-Feb		Test 1
	Unit 3	Interactions of probiotics with the host immune system
16-Feb		Overview on the adaptive and innate immune response - Part 1
19-Feb		Overview on the adaptive and innate immune response - Part 2
21-Feb		9. Immunomodulatory properties of probiotics: bacterial surface proteins
23-Feb		10. Immunomodulatory properties of probiotics: interactions with the immune system
26-Feb		11. Engineering LAB and <i>Bifidobacterium</i> for mucosal delivery of health-associated molecules: Genetic tools
28-Feb		12. Engineering LAB and <i>Bifidobacterium</i> for mucosal delivery of health-associated molecules
2-Mar		Assignment 3 due
	Unit 4	Probiotics safety and efficacy
12-Mar		13. FAO/WHO Guidelines on Probiotics
14-Mar		14. Safety studies and proposed uses of probiotics - Animal studies
16-Mar		14. Safety studies and proposed uses of probiotics - Human studies
19-Mar		15. Efficacy of probiotics in Human Subjects: Healthy populations
21-Mar		16. Efficacy of probiotics in Human Subjects: Clinical populations - Part 1
23-Mar		16. Efficacy of probiotics in Human Subjects: Clinical populations - Part 2
26-Mar		17. Probiotics in Animal Production and Health - Part 1
28-Mar		17. Probiotics in Animal Production and Health - Part 2
30-Mar		Assignment 4 due
2-Apr		Test 2
	Unit 5	New frontiers in probiotic's development
4-Apr		18. Overview on the microbiome
6-Apr		19. Manipulation of the microbiome by probiotics
9-Apr		20. Microbiome research to identify new probiotic microorganisms
11-Apr		21. Fecal transplants as probiotics
13-Apr		22. Probiotics, prebiotics and symbiotic
16-Apr		23. Interactions of probiotics with food components
18-Apr		24. Psychobiotics and the Manipulation of Bacteria–Gut–Brain Signals
20-Apr		25. Lactic Acid Bacteria Biofilms: Formation and their Health and Biotechnological Potential
23-Apr		Test 3
2-May		Optional Final

University of Florida Policies

Students Requiring Accommodations

Students with disabilities requesting accommodations should first register with the Disability Resource Center (352-392-8565, www.dso.ufl.edu/drc/) by providing appropriate documentation. Once registered, students will receive an accommodation letter which must be presented to the instructor when requesting accommodation. Students with disabilities should follow this procedure as early as possible in the semester.

Campus Resources

Resources are available on campus for students having personal problems or lacking clear career and academic goals, which interfere with their academic performance. These resources include:

Health and Wellness

- U Matter, We Care: If you or a friend is in distress, please contact umatter@ufl.edu or 352 392-1575 so that a team member can reach out to the student.
- Counseling and Wellness Center: <http://www.counseling.ufl.edu/cwc/Default.aspx>, 392-1575;
- Sexual Assault Recovery Services (SARS) at the Student Health Care Center, 392-1161.
- For emergencies call: University Police Department, 392-1111 (or 9-1-1 for emergencies). <http://www.police.ufl.edu/>

Academic Resources

- E-learning technical support, 352-392-4357 (select option 2) or e-mail to Learning-support@ufl.edu. <https://lss.at.ufl.edu/help.shtml>.
- Career Resource Center, Reitz Union, 392-1601. Career assistance and counseling. <http://www.crc.ufl.edu/>
- Library Support, <http://cms.uflib.ufl.edu/ask>. Various ways to receive assistance with respect to using the libraries or finding resources.
- Teaching Center, Broward Hall, 392-2010 or 392-6420. General study skills and tutoring. <http://teachingcenter.ufl.edu/>
- Writing Studio, 302 Tigert Hall, 846-1138. Help brainstorming, formatting, and writing papers. <http://writing.ufl.edu/writing-studio/>

Course Evaluation

Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at <https://evaluations.ufl.edu>. Evaluations are typically

open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at <https://evaluations.ufl.edu/results/>.

Class demeanor

Students are expected to arrive to class on time and behave in a manner that is respectful to the instructor and to fellow students. Please avoid the use of cell phones and restrict eating to outside of the classroom. Opinions held by other students should be respected in discussion, and conversations that do not contribute to the discussion should be held at minimum, if at all.

Netiquette guide for online courses

It is important to recognize that the online classroom is in fact a classroom, and certain behaviors are expected when you communicate with both your peers and your instructors. These guidelines for online behavior and interaction are known as netiquette.

<http://teach.ufl.edu/wp-content/uploads/2012/08/NetiquetteGuideforOnlineCourses.pdf>

University Honesty Policy

UF students are bound by The Honor Pledge which states, “We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honor and integrity by abiding by the Honor Code. On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: “On my honor, I have neither given nor received unauthorized aid in doing this assignment.” The Honor Code (<https://sccr.dso.ufl.edu/process/honor-code/>) specifies a number of behaviors that are in violation of this code and the possible sanctions. Furthermore, you are obligated to report any condition that facilitates academic misconduct to appropriate personnel. If you have any questions or concerns, please consult with the instructor or TAs in this class.

Additional comments regarding academic integrity:

Students are encouraged to discuss material with each other from the course, help each other understand concepts, study together, and even discuss assessment questions with each other once the quiz window is closed. However, the following is considered academic dishonesty, and I expect that no student will ever do any of the following:

- Have another person complete a quiz in this course
- Copy another student’s quiz in this course
- Collaborate with anyone during a quiz in this course
- Discuss the questions and answers of a quiz with other students while the quiz window is still open
- Manipulate and/or distribute any materials provided in this course for any purpose (including course lecture slides).
- Use any materials provided by a previous student in the course

Software Use

All faculty, staff and students of the university are required and expected to obey the laws and legal agreements governing software use. Failure to do so can lead to monetary damages and/or criminal penalties for the individual violator. Because such violations are also against university policies and rules, disciplinary action will be taken as appropriate.

Microsoft Office 365 Software is free for UF students

<http://www.it.ufl.edu/gatorcloud/free-office-365-downloads/>

Other free software is available at:

<http://www.software.ufl.edu/>

To check for availability of the media and technical requirements, contact the UF Computing Help Desk at (352)392-HELP(4357).

University of Florida Complaints Policy and Student Complaint Process

Most problems, questions and concerns about the course will be resolved by professionally communicating with the instructor or the TAs.

The University of Florida believes strongly in the ability of students to express concerns regarding their experiences at the University. The University encourages its students who wish to file a written complaint to submit that complaint directly to the department that manages that policy.

If a problem really cannot be resolved by communicating with the instructor or the TAs you can contact

- Residential Course: https://www.dso.ufl.edu/documents/UF_Complaints_policy.pdf.
- Online Course: <http://www.distance.ufl.edu/student-complaint-process>.

University of Florida Complaints Policy and Student Complaint Process

The University of Florida and most instructors believe strongly in the ability of students to express concerns regarding their experiences at the University. Most problems, questions and concerns about courses can be resolved by professionally communicating with the instructor. Please try to meet your instructor in person, make an appointment to call, or try to set up a remote meeting through Skype or other media.

If this does not help the University encourages the students who wish to file a written complaint to submit that complaint directly to the department that manages that course. If a problem really persists and cannot be resolved by communicating with the instructor and the department, contact... for

Residential Course: https://www.dso.ufl.edu/documents/UF_Complaints_policy.pdf.

Online Course: <http://www.distance.ufl.edu/student-complaint-process>

This said, professionalism is a two-way-street. Unprofessional behavior of students includes, among other things: lack of communication, blaming other people or external factors, lying, affecting others negatively in a group or in the class, not accepting criticism and not being proactive in solving problems or seeking help. Furthermore, faculty often have family and other obligations to tend to. Over the weekend, replies to your inquiries or questions maybe delayed.

If a student is lacking professionalism repeatedly, the instructor has the rights to file formal complaint against the student through the Dean of Student office.

Elective Readings and Sources (this is not a complete list)

Unit 1. Probiotics: definitions, history and classification

Module 1. Definitions and History

Gogineni VK, Morrow LE, Gregory PJ, Malesker MA. 2013. Probiotics: History and Evolution. J Anc Dis Prev Rem 1:107. doi:10.4172/2329-8731.1000107

<https://www.omicsonline.org/open-access/probiotics-history-and-evolution-2329-8731.1000107.php?aid=14832>

Lauzon HLL, Dimitroglou A, Merrifield DL, Ringo E, Davies SJ. 2014. Probiotics and Prebiotics: Concepts, Definitions and History. In Aquaculture Nutrition: GutHealth, Probiotics and Prebiotics, First Edition. Edited by Daniel Merrifield and Einar Ringø. © 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

https://www.researchgate.net/profile/Einar_Ringo/publication/277698316_Prebiotics_in_Finfish_An_Update/links/55aca24808aea9946727b630.pdf

SOCOL CR, de Souza Vandenberghe, Spier MR, et al. 2010. The Potential of Probiotics, Food Technol. Biotechnol. 48:413-434.

hrcak.srce.hr/file/92463.html

Module 2. Classification and physiology: Lactic acid bacteria (LAB)

Axelsson L. 1998. Lactic acid bacteria: Classification and Physiology. Ch. 1. In Lactic acid bacteria, Microbiology and Functional Aspects. Salminen S and von Wright A, Editors. Marcel Dekker, Inc. New York. Basel.

Stiles MH, Wilhelm H Holzapfel WH. 1997. Lactic acid bacteria of foods and their current taxonomy. International Journal of Food Microbiology 36 (1997) 1~ 29

https://ac.els-cdn.com/S0168160596012330/1-s2.0-S0168160596012330-main.pdf?_tid=a6501a32-a85d-11e7-a6ca-0000aabb0f02&acdnat=1507050763_1b66a6717549ec5cf7ddcfd8fadbdb13

Module 3. Classification and physiology: *Bifidobacterium* and *Propionibacterium*

Sela DA, Price NPJ, Mills DA. 2010. Metabolism of Bifidobacteria. In *Bifidobacteria: Genomics and Molecular Aspects* (Edited by: Baltasar Mayo and Douwe van Sinderen). Caister Academic Press, U.K. (2010)

https://www.researchgate.net/profile/David_Sela/publication/285787411_Carbohydrate_metabolism_of_the_bifidobacteria/links/09e415140bc3c3e8fd000000/Carbohydrate-metabolism-of-the-bifidobacteria.pdf

Zarate G., 2012. Dairy Propionibacteria: Less Conventional Probiotics to Improve the Human and Animal Health. Ch 8. In "[Probiotic in Animals](#)", book edited by Everlon Cid Rigobelo, ISBN 978-953-51-0777-4, Published: October 3, 2012 under [CC BY 3.0 license](#). © The Author(s).

Poonam, Pophaly SD, Tomar SK, De S, Singh R. Multifaceted attributes of dairy propionibacteria: a review. *World J Microbiol Biotechnol.* 2012 Nov;28(11):3081-95.

<https://link.springer.com/content/pdf/10.1007%2Fs11274-012-1117-z.pdf>

Module 4. Impact of genomics on the characterization of probiotics

Frese SA, Benson AK, Tannock GW, Loach DM, Kim J, et al. (2011) The Evolution of Host Specialization in the Vertebrate Gut Symbiont *Lactobacillus reuteri*. *PLoS Genet* 7(2): e1001314. doi:10.1371/journal.pgen.1001314

Van Pijkeren J-P, O'Toole PW. Comparative and Functional Genomics of the Genus *Lactobacillus* (2009). *Lactobacillus molecular biology: From genomics to probiotics*. Ed. Ljungh, A., & Wadström, T. Norfolk, UK: Caister Academic.

Kelleher et al. Comparative and functional genomics of the *Lactococcus lactis* taxon; insights into evolution and niche adaptation *BMC Genomics* (2017) 18:267.

<https://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-017-3650-5>

Oksana Lukjancenka, David W. Ussery, Trudy M. Wassenaar. 2012. Comparative Genomics of Bifidobacterium, Lactobacillus and Related Probiotic Genera. *Microb Ecol.* 2012 Apr; 63(3): 651–673. Published online 2011 Oct 27. doi: 10.1007/s00248-011-9948-y

Lugli GA, Milani C, Turrone F, Duranti S, Mancabelli L, Mangifesta M, Ferrario C, Modesto M, Mattarelli P, Jiří K, van Sinderen D, Ventura M. [Comparative genomic and phylogenomic analyses of the Bifidobacteriaceae family](#). *BMC Genomics.* 2017 Aug 1;18(1):568. doi: 10.1186/s12864-017-3955-4. <https://bmcgenomics.biomedcentral.com/track/pdf/10.1186/s12864-017-3955-4?site=bmcgenomics.biomedcentral.com>

Unit 2. Biotechnological applications of Lactic acid bacteria

Module 5. The uses of LAB in food fermentation

V. K. Shiby & H. N. Mishra (2013) *Fermented Milks and Milk Products as*

Functional Foods—A Review, *Critical Reviews in Food Science and Nutrition*, 53:5, 482-496,

Zannini E, Waters DM, Coffey A, Arendt EK. Production, properties, and industrial food application of lactic acid bacteria-derived exopolysaccharides. *Appl Microbiol Biotechnol*. 2016 Feb;100(3):1121-35. doi: 10.1007/s00253-015-7172-2. Epub 2015 Dec 1. Review.

Leroy F, Verluuyten J, De Vuyst L. Functional meat starter cultures for improved sausage fermentation. *Int J Food Microbiol*. 2006 Feb 15;106(3):270-85. Epub 2005 Oct 5. Review.

De Vuyst L, Weckx S. The cocoa bean fermentation process: from ecosystem analysis to starter culture development.

J Appl Microbiol. 2016 Jul;121(1):5-17. doi: 10.1111/jam.13045. Epub 2016 Feb 13. Review.

Add later comple ref of the book online <http://www.crcnetbase.com/doi/preview-pdf/10.1201/9781315370378>

Module 6. Antimicrobials components of LAB

Alvarez-Sieiro P, Montalbán-López M, Mu D, Kuipers OP. Bacteriocins of lactic acid bacteria: extending the family. *Appl Microbiol Biotechnol*. 2016 Apr;100(7):2939-51. doi: 10.1007/s00253-016-7343-9. Epub 2016 Feb 10. Review.

Module 7. Bacteriophages from LAB

Mullan, W.M.A. (2002). Morphology of bacteriophages for lactic acid bacteria. [On-line]. Available from: <https://www.dairyscience.info/index.php/morphology-of-bacteriophages-for-lactic-acid-bacteria.html> . Accessed: 14 October, 2017. Revised December 2012.

Mahony J, McDonnell B, Casey E, van Sinderen D. Phage-Host Interactions of Cheese-Making Lactic Acid Bacteria. *Annu Rev Food Sci Technol*. 2016;7:267-85. doi: 10.1146/annurev-food-041715-033322. Epub 2016 Jan 6. Review.

Mahony J1, Ainsworth S, Stockdale S, van Sinderen D. Phages of lactic acid bacteria: the role of genetics in understanding phage-host interactions and their co-evolutionary processes.

Virology. 2012 Dec 20;434(2):143-50. doi: 10.1016/j.virol.2012.10.008. Epub 2012 Oct 22.

[HTTPS://WWW.RESEARCHGATE.NET/PUBLICATION/282442175_BACTERIAL_DEFENSE_MECHANISMS_AGAINST_BACTERIOPHAGES](https://www.researchgate.net/publication/282442175_BACTERIAL_DEFENSE_MECHANISMS_AGAINST_BACTERIOPHAGES)

Module 8. Nutraceuticals and high value metabolites produced by LABs

Sauer M, Russmayer H, Grabherr R, Peterbauer CK, Marx H. The Efficient Clade: Lactic Acid Bacteria for Industrial Chemical Production. *Trends Biotechnol.* 2017 Aug;35(8):756-769. doi: 10.1016/j.tibtech.2017.05.002. Epub 2017 May 23. Review.

Bosma EF, Forster J, Nielsen AT. Lactobacilli and pediococci as versatile cell factories - Evaluation of strain properties and genetic tools.

Biotechnol Adv. 2017 Jul;35(4):419-442. doi: 10.1016/j.biotechadv.2017.04.002. Epub 2017 Apr 7. Review.

Song AA, In LLA, Lim SHE, Rahim RA. A review on *Lactococcus lactis*: from food to factory.

Microb Cell Fact. 2017 Apr 4;16(1):55. doi: 10.1186/s12934-017-0669-x. Review. Erratum in: *Microb Cell Fact.* 2017 Aug 9;16(1):139.

Lee NK, Paik HD. Bioconversion Using Lactic Acid Bacteria: Ginsenosides, GABA, and Phenolic Compounds.

J Microbiol Biotechnol. 2017 May 28;27(5):869-877. doi: 10.4014/jmb.1612.12005. Review.

Brown L, Pingitore EV, Mozzi F, Saavedra L, Villegas JM, Hebert EM. Lactic Acid Bacteria as Cell Factories for the Generation of Bioactive Peptides. *Protein Pept Lett.* 2017;24(2):146-155. doi: 10.2174/0929866524666161123111333. Review.

Unit 3. Interactions of probiotics with the host immune system

Module 9. Immunomodulatory properties of probiotics: bacterial surface proteins

Hynönen U, Palva A. 2013. Lactobacillus surface layer proteins: structure, function and applications. *Appl Microbiol Biotechnol.* 2013 Jun;97(12):5225-43. doi: 10.1007/s00253-013-4962-2. Epub 2013 May 16. Review.

Sánchez B, Bressollier P, Urdaci MC. 2008. Exported proteins in probiotic bacteria: adhesion to intestinal surfaces, host immunomodulation and molecular cross-talking with the host. *FEMS Immunol Med Microbiol.* 2008 Oct;54(1):1-17. doi: 10.1111/j.1574-695X.2008.00454.x. Epub 2008 Jul 8. Review.

Module 10. Immunomodulatory properties of probiotics: interactions with the immune system

O'Callaghan J, O'Toole PW. Lactobacillus: host-microbe relationships. *Curr Top Microbiol Immunol.* 2013;358:119-54. doi: 10.1007/82_2011_187. Review.

<https://link.springer.com/content/pdf/10.1007%2F978-3-642-36560-7.pdf>

Lebeer S, Vanderleyden J, De Keersmaecker SC. Genes and molecules of lactobacilli supporting probiotic action. *Microbiol Mol Biol Rev.* 2008 Dec;72(4):728-64, Table of Contents. doi: 10.1128/MMBR.00017-08. Review.

Hevia A, Delgado S, Sánchez B, Margolles A. Molecular Players Involved in the Interaction Between Beneficial Bacteria and the Immune System.

Front Microbiol. 2015 Nov 18;6:1285. doi: 10.3389/fmicb.2015.01285. eCollection 2015. Review.

<https://www.frontiersin.org/articles/10.3389/fmicb.2015.01285/full>

Lebeer S, Vanderleyden J, De Keersmaecker SC. 2010. Host interactions of probiotic bacterial surface molecules: comparison with commensals and pathogens. *Nat Rev Microbiol.* 8:171-84. doi: 10.1038/nrmicro2297. Review.

Tsai YT, Cheng PC, Pan TM. 2012. The immunomodulatory effects of lactic acid bacteria for improving immune functions and benefits. *Appl Microbiol Biotechnol.* 96:853-62. doi: 10.1007/s00253-012-4407-3. Epub 2012 Sep 23.

Bermúdez-Humarán LG, Aubry C, Motta JP, Deraison C, Steidler L, Vergnolle N, Chatel JM, Langella P. 2013. Engineering lactococci and lactobacilli for human health. *Curr Opin Microbiol.* 2013 Jun;16(3):278-83. doi: 10.1016/j.mib.2013.06.002. Epub 2013 Jul 11. Review.

http://ac.els-cdn.com/S1369527413000763/1-s2.0-S1369527413000763-main.pdf?_tid=4cc981b0-989a-11e7-8f07-00000aacb362&acdnat=1505317613_e64c7ca73aa48be60170eaf13552e365

Bosma EF, Forster J, Nielsen AT. Lactobacilli and pediococci as versatile cell factories - Evaluation of strain properties and genetic tools. *Biotechnol Adv.* 2017 Jul;35(4):419-442. doi: 10.1016/j.biotechadv.2017.04.002. Epub 2017 Apr 7. Review.

Module 12. Engineering LAB and *Bifidobacterium* for mucosal delivery of health-associated molecules

Song AA, In LLA, Lim SHE, Rahim RA. A review on *Lactococcus lactis*: from food to factory. *Microb Cell Fact.* 2017 Apr 4;16(1):55. doi: 10.1186/s12934-017-0669-x. Review. Erratum in: *Microb Cell Fact.* 2017 Aug 9;16(1):139.

Bermúdez-Humarán LG, Aubry C, Motta JP, Deraison C, Steidler L, Vergnolle N, Chatel JM, Langella P. 2013. Engineering lactococci and lactobacilli for human health. *Curr Opin Microbiol.* 2013 Jun;16(3):278-83. doi: 10.1016/j.mib.2013.06.002. Epub 2013 Jul 11. Review.

http://ac.els-cdn.com/S1369527413000763/1-s2.0-S1369527413000763-main.pdf?_tid=4cc981b0-989a-11e7-8f07-00000aacb362&acdnat=1505317613_e64c7ca73aa48be60170eaf13552e365

Unit 4. Probiotics safety and efficacy

Module 13. FAO/WHO Guidelines on Probiotics

FAO/WHO. 2002. Guidelines for the evaluation of Probiotics in Food.

http://www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf?ua=1

Module 14. Safety studies and proposed uses of probiotics

http://ac.els-cdn.com/S0168160598001287/1-s2.0-S0168160598001287-main.pdf?_tid=5fc1a4ca-988e-11e7-8f07-00000aacb362&acdnat=1505312472_b39e10978aea3e76ae26ff126aebbde6

<http://www.sciencedirect.com/science/article/pii/S0168160598001287?via%3Dihub>