

**MCB6424 Probiotics (3 credits)**  
**Spring 2023**

MCB6424 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

**Lectures:** Online through Canvas

**Instructor:** Dr. Graciela L Lorca

**Office:** Genetics Institute, Room 307

**WebPage:** Canvas (<https://ufl.instructure.com/>). Please select MCB6424

**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.

**Office hours:** Fridays 2-3 PM through ZOOM Conferences, IN PERSON (Genetics Institute Rm 307) or 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.

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

**Contact Information: Use TEACHER and TA 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](mailto:glorca@ufl.edu))

**Phone:** 273 8090 (please leave a message).

Dr. Florencia Torrez Lamberti (TA)

**Email (the most efficient):** ONLY use Canvas e-mail (If you do not have access to the e-learning platform

- **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:** textbook is not 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). Remember to connect to UF through VPN (if outside campus) before accessing the journals (<https://connect.ufl.edu/it/wiki/pages/glvpn.aspx>).

## Assessment of learning

**Activities (250 points):** Activities will be assigned by Unit.

- **Assignments 1 to 4 (40 points each)**. These assignments include online research on diverse topics such as “Introducing my favorite putative probiotic microorganism”, “Cell wall homeostasis in LAB”, “Microbiome based therapeutics”, and “Market claims: is there scientific evidence?”. These activities are mandatory and count towards the

final grade. **They should be completed by the deadline indicated on Canvas.**  
**LATE SUBMISSION POLICY:** a 5% deduction will be applied per day that the assignment is late.

- **Weekly activities “Main concepts that I should know” (9 points each).** The goal of these assignments is that the student keeps up with reading of the material on weekly basis. To achieve this goal, you are required to design questions that will assess the main concepts of this unit. The activities are mandatory and count towards the final grade. **They should be completed by the deadline indicated on Canvas.**  
**LATE SUBMISSION POLICY:** a 5% deduction will be applied per day that the assignment is late.
- **Topic review (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). Other articles can be used to introduce the topic in the introduction section. The student will have to complete the review on one of the six topics that will be listed on Canvas (ONLY) as follows:
  - Probiotics and viral infections
  - 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
  - Improving probiotic specificity – ‘designer probiotics’
  - Probiotics for animals – are they regulated?
  - Postbiotics
  - Efficacy of probiotics on disease prevention or treatment (ONLY human studies)

Notes: Two submissions are MANDATORY. Two steps are needed: Article selection pre-submission and Critical review submission. See the Canvas website for details and deadlines.

**LATE SUBMISSION POLICY:** a 5% deduction will be applied per day that the assignment is late.

- **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. You will have to start the exam before 9 PM ET for test 1-3 and before 7 PM ET for test 4 (to allow time for system check up and completion of the test before it closes at 11 PM ET).  
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, match and or true/false type of 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 (Tests 1, 2 or 3) with the lowest grade (if a higher score in the final is achieved, if not, the score from the test will be used).* It 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:* Make-up exams will **ONLY** be allowed with a **VALID** justification. 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 **as soon as possible** 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 personal meetings. After the scores release the student will have **two weeks** to submit questions about the test or claim mistakes in grading. No claims will be considered after that time.

Requirements for class attendance and make-up exams, assignments and other work are consistent with university policies that can be found at:

<https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>.

## **Grades and Grade Points**

For information on current UF policies for assigning grade points, see <https://catalog.ufl.edu/ugrad/current/regulations/info/grades.aspx>

**Grading:** Straight scale

### **Grading Scale**

<b>A</b>	900 or above
<b>A-</b>	860-899
<b>B+</b>	830-859
<b>B</b>	790-829
<b>B-</b>	750-789
<b>C+</b>	720-749
<b>C</b>	690-719
<b>C-</b>	660-689
<b>D+</b>	630-659
<b>D</b>	600-629

D- 570-599  
E 560 or below

## Schedule of Classes

Date	Unit	Module. Topic
09-Jan*	Unit 1	<b>Probiotics: definitions, history and classification</b> 1. Definitions and History 2. Classification and physiology: Lactic acid bacteria (LAB) 3. Classification and physiology: <i>Bifidobacterium</i> and <i>Propionibacterium</i> 4. Impact of genomics on the characterization of probiotics_Intro to genomics 4. Impact of genomics on the characterization of probiotics_LAB part 1 4. Impact of genomics on the characterization of probiotics_LAB part 2
27-Jan		Assignment 1 due
06-Feb	Unit 2	<b>Biotechnological applications of Lactic acid bacteria</b> 5. The uses of LAB in food fermentation -part 1 5. The uses of LAB in food fermentation -part 2 6. Antimicrobials components of LAB 7. Bacteriophages from LAB 8. Nutraceuticals and high value metabolites produced by LABs
10-11 Feb		Assignment 2 due
		Test 1
03-Mar	Unit 3	<b>Interactions of probiotics with the host immune system</b> 9. Overview on the adaptive and innate immune response - Part 1 9. Overview on the adaptive and innate immune response - Part 2 10. Immunomodulatory properties of probiotics: bacterial surface proteins 11. Immunomodulatory properties of probiotics: interactions with the immune system 12. Engineering LAB and <i>Bifidobacterium</i> for mucosal delivery of health-associated molecules: Genetic tools 12. Engineering LAB and <i>Bifidobacterium</i> for mucosal delivery of health-associated molecules
		Assignment 3 due
	Unit 4	<b>Probiotics safety and efficacy</b> 13. FAO/WHO Guidelines on Probiotics 14. Safety considerations on probiotics 15. Environmental factors influencing the efficacy of probiotics 16. Efficacy of probiotics in Human Subjects: Part 1 16. Efficacy of probiotics in Human Subjects: Part 2 16. Efficacy of probiotics in Human Subjects: Part 3 16. Efficacy of probiotics in Human Subjects: Probiotics by design 17. Probiotics in Animal Production and Health

10-11 Mar	Test 2
Unit 5	<b>New frontiers in the probiotic's field</b> 18. Overview on the microbiome – Part 1 18. Overview on the microbiome – Part 2 19. Manipulation of the microbiome with probiotics 20. Microbiome based new probiotic microorganisms 21. Fecal transplants as probiotics 22. Probiotics, prebiotics, symbiotic and postbiotics 23. Psychobiotics and the Manipulation of Bacteria–Gut–Brain Signals
24-Mar	Critical Review article selection pre-submission
31-Mar	Assignment 4 due
14-Apr	Topic review due
21-22-Apr	Test 3
01-02 May	Test 4 - Optional Final

**\*Release date for the Unit on Canvas**

**University of Florida Policies**

**Grades and Grade Points**

For information on current UF policies for assigning grade points, see <https://catalog.ufl.edu/UGRD/academic-regulations/grades-grading-policies/>

**Attendance and Make-Up Work**

Requirements for class attendance and make-up exams, assignments and other work are consistent with university policies that can be found at: <https://catalog.ufl.edu/UGRD/academic-regulations/attendance-policies/>

**Services for Students with Disabilities**

Students with disabilities who experience learning barriers and would like to request academic accommodations should connect with the disability Resource Center (<https://disability.ufl.edu/get-started/>). It is important for students to share their accommodation letter with their instructor and discuss their access needs, as early as possible in the semester.

**Campus Helping Resources**

Health and Wellness

- U Matter, We Care: If you or someone you know is in distress, please contact [umatter@ufl.edu](mailto:umatter@ufl.edu), 352-392-1575, or visit U Matter, We Care website (<https://umatter.ufl.edu/>) to refer or report a concern and a team member will reach out to the student in distress.
- Counseling and Wellness Center: Visit the Counseling and Wellness Center website (<https://counseling.ufl.edu/>) or call 352-392-1575 for information on crisis services as well as non-crisis services.
- Student Health Care Center: Call 352-392-1161 for 24/7 information to help you find the care you need, or visit the Student Health Care Center website (<https://shcc.ufl.edu/>).
- University Police Department: Visit UF Police Department website (<https://police.ufl.edu/>) or call 352-392-1111 (or 9-1-1 for emergencies).  
 UF Health Shands Emergency Room / Trauma Center: For immediate medical care call 352-733-0111 or go to the emergency room at 1515 SW Archer Road, Gainesville, FL 32608; Visit the UF Health Emergency Room and Trauma Center website (<https://ufhealth.org/emergency-room-trauma-center>).
- GatorWell Health Promotion Services: For prevention services focused on optimal wellbeing, including Wellness Coaching for Academic Success, visit the GatorWell website (<https://gatorwell.ufsa.ufl.edu/>) or call 352-273-4450.

## **Academic Resources**

- E-learning technical support: Contact the UF Computing Help Desk at 352-392-4357 or via e-mail at [helpdesk@ufl.edu](mailto:helpdesk@ufl.edu).
  - Career Connections Center: Reitz Union Suite 1300, 352-392-1601. Career assistance and counseling services (<https://career.ufl.edu/>).
  - Library Support: Various ways to receive assistance with respect to using the libraries or finding resources (<https://uflib.ufl.edu/>).
  - Teaching Center: Broward Hall, 352-392-2010 or to make an appointment 352-392-6420. General study skills and tutoring (<https://teachingcenter.ufl.edu/>).
  - Writing Studio: 2215 Turlington Hall, 352-846-1138. Help brainstorming, formatting, and writing papers (<https://writing.ufl.edu/writing-studio/>).
  - Student Complaints On-Campus: Visit the Student Honor Code and Student Conduct Code webpage for more information (<https://sccr.dso.ufl.edu/policies/student-honor-%20code-student-conduct-code/>).
- On-Line Students Complaints: View the Distance Learning Student Complaint Process (<https://distance.ufl.edu/state-authorization-status/#student-complaint>).

## **Course Evaluation**

Students are expected to provide professional and respectful feedback on the quality of instruction in this course by completing course evaluations online via GatorEvals. Guidance on how to give

feedback in a professional and respectful manner is available at <https://gatorevals.aa.ufl.edu/students/>. Students will be notified when the evaluation period opens, and can complete evaluations through the email they receive from GatorEvals, in their Canvas course menu under GatorEvals, or via <https://ufl.bluera.com/ufl/>. Summaries of course evaluation results are available to students at <https://gatorevals.aa.ufl.edu/public-results/>.

### **Class demeanor**

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>

### **Academic Honesty**

As a student at the University of Florida, you have committed yourself to uphold the Honor Code, which includes the following pledge: *"We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity."* You are expected to exhibit behavior consistent with this commitment to the UF academic community, and on all work submitted for credit 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."*

It is assumed that you will complete all work independently in each course unless the instructor provides explicit permission for you to collaborate on course tasks (e.g. assignments, papers, quizzes, exams). Furthermore, as part of your obligation to uphold the Honor Code, you should report any condition that facilitates academic misconduct to appropriate personnel. It is your individual responsibility to know and comply with all university policies and procedures regarding academic integrity and the Student Honor Code. Violations of the Honor Code at the University of Florida will not be tolerated. Violations will be reported to the Dean of Students Office for consideration of disciplinary action. For more information regarding the Student Honor Code, please see: <http://www.dso.ufl.edu/sccr/process/student-conduct-honor-code>.

### **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 instructors.**

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://sccr.dso.ufl.edu/policies/student-honor-code-student-conduct-code/>.
- 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.

## **Suggested Readings and Sources**

## 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.
- Lauzon HLL, Dimitroglou A, Merrifield DL, Ringo E, Davies SJ. 2014. Probiotics and Prebiotics: Concepts, Definitions and History. In *Aquaculture Nutrition: Gut Health, Probiotics and Prebiotics*, First Edition. Edited by Daniel Merrifield and Einar Ringø. © 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.
- Soccol CR, de Souza Vandenberghe, Spier MR, et al. 2010. The Potential of Probiotics, *Food Technol. Biotechnol.* 48:413-434.

### **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, Holzappel WH. 1997. Lactic acid bacteria of foods and their current taxonomy. *International Journal of Food Microbiology* 36:1-29.

### **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.
- 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. Published: October 3, 2012 under [CC BY 3.0 license](#). © The Author(s).
- Poonam, Pophaly SD, Tomar SK, De S, Singh R. 2012. Multifaceted attributes of dairy propionibacteria: a review. *World J Microbiol Biotechnol* . 28:3081-95.

### **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.
- Van Pijkeren J-P, O'Toole PW. 2009. Comparative and Functional Genomics of the Genus *Lactobacillus*. In *Lactobacillus molecular biology: From genomics to probiotics*. Ed. Ljungh, A., & Wadström, T. Norfolk, UK: Caister Academic.
- Kelleher et al. 2017. Comparative and functional genomics of the *Lactococcus lactis* taxon; insights into evolution and niche adaptation. *BMC Genomics* 18:267.

- Lukjancenko O, Ussery DW, Wassenaar TM. 2012. Comparative Genomics of *Bifidobacterium*, *Lactobacillus* and Related Probiotic Genera. *Microb Ecol.* 63: 651–673.
- 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. 2017. Comparative genomic and phylogenomic analyses of the Bifidobacteriaceae family. *BMC Genomics* 18:568.

## Unit 2. Biotechnological applications of Lactic acid bacteria

### **Module 5. The uses of LAB in food fermentation**

- Shiby VK, Mishra HN. 2013. Fermented Milks and Milk Products as Functional Foods —A Review, *Critical Reviews in Food Science and Nutrition* 53:482-496.
- Zannini E, Waters DM, Coffey A, Arendt EK. 2016. Production, properties, and industrial food application of lactic acid bacteria-derived exopolysaccharides. *Appl Microbiol Biotechnol.* 100:1121-35.
- Leroy F, Verluyten J, De Vuyst L. 2006. Functional meat starter cultures for improved sausage fermentation. *Int J Food Microbiol.* 106:270-85.

### **Module 6. Antimicrobials components of LAB**

- Alvarez-Sieiro P, Montalbán-López M, Mu D, Kuipers OP. 2016. Bacteriocins of lactic acid bacteria: extending the family. *Appl Microbiol Biotechnol.* 100:2939-51.

### **Module 7. Bacteriophages from LAB**

- Mullan WMA. 2002. Morphology of bacteriophages for lactic acid bacteria. [On-line].
- Mahony J, McDonnell B, Casey E, van Sinderen D. 2016. Phage-Host Interactions of Cheese-Making Lactic Acid Bacteria. *Annu Rev Food Sci Technol* 7:267-85.
- Mahony J, Ainsworth S, Stockdale S, van Sinderen D. 2012. Phages of lactic acid bacteria: the role of genetics in understanding phage-host interactions and their co-evolutionary processes. *Virology* 434:143-50.

### **Module 8. Nutraceuticals and high value metabolites produced by LABs**

- Sauer M, Russmayer H, Grabherr R, Peterbauer CK, Marx H. 2017. The Efficient Clade: Lactic Acid Bacteria for Industrial Chemical Production. *Trends Biotechnol.* 35:756-769.

- Bosma EF, Forster J, Nielsen AT. 2017. Lactobacilli and pediococci as versatile cell factories - Evaluation of strain properties and genetic tools. *Biotechnol Adv* 35:419-442.
- Song AA, In LLA, Lim SHE, Rahim RA. 2017. A review on *Lactococcus lactis*: from food to factory. *Microb Cell Fact* 16:55. Erratum in: *Microb Cell Fact*. 2017 16:139.
- Lee NK, Paik HD. 2017. Bioconversion Using Lactic Acid Bacteria: Ginsenosides, GABA, and Phenolic Compounds. *J Microbiol Biotechnol* 27:869-877.
- Brown L, Pingitore EV, Mozzi F, Saavedra L, Villegas JM, Hebert EM. 2017. Lactic Acid Bacteria as Cell Factories for the Generation of Bioactive Peptides. *Protein Pept Lett*. 24:146-155.

### Unit 3. Interactions of probiotics with the host immune system

#### **Module 10. Immunomodulatory properties of probiotics: bacterial surface proteins**

- Hynönen U, Palva A. 2013. *Lactobacillus* surface layer proteins: structure, function and applications. *Appl Microbiol Biotechnol* 97:5225-43.
- 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* 54:1-17

#### **Module 11. Immunomodulatory properties of probiotics: interactions with the immune system**

- O'Callaghan J, O'Toole PW. 2013. *Lactobacillus*: host-microbe relationships. *Curr Top Microbiol Immunol*. 358:119-54.
- Lebeer S, Vanderleyden J, De Keersmaecker SC. 2008. Genes and molecules of lactobacilli supporting probiotic action. *Microbiol Mol Biol Rev*. 72:728-64.
- Hevia A, Delgado S, Sánchez B, Margolles A. 2015. Molecular Players Involved in the Interaction Between Beneficial Bacteria and the Immune System. *Front Microbiol* 6:1285.
- 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.
- 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.

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

- Bosma EF, Forster J, Nielsen AT. 2017. Lactobacilli and pediococci as versatile cell factories - Evaluation of strain properties and genetic tools. *Biotechnol Adv.* 35:419-442.
- Song AA, In LLA, Lim SHE, Rahim RA. 2017. A review on *Lactococcus lactis*: from food to factory. *Microb Cell Fact.* 16:55. Erratum in: *Microb Cell Fact* 16:139.
- 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* 16:278-83.

## **Unit 4. Probiotics safety and efficacy**

### **Module 13. FAO/WHO Guidelines on Probiotics**

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

### **Module 14. Safety considerations on probiotics**

- Salminen S, von Wright A, Morelli L, Marteau P, Brassart D, de Vos WM, Fondén R, Saxelin M, Collins K, Mogensen G, Birkeland SE, Mattila-Sandholm T. 1998. Demonstration of safety of probiotics -- a review. *Int J Food Microbiol* 44:93-106.
- Sanders ME, Akkermans LM, Haller D, Hammerman C, Heimbach J, Hörmannspurger G, Huys G, Levy DD, Lutgendorff F, Mack D, Phothirath P, Solano-Aguilar G, Vaughan E. 2010. Safety assessment of probiotics for human use. *Gut Microbes* 1:164-85.
- Vanderhoof JA, Young R. 2008. Probiotics in the United States. *Clin Infect Dis.* 46 Suppl 2:S67-72; discussion S144-51.

### **Module 15. Environmental factors influencing the efficacy of probiotic bacteria**

- Marco ML, Tachon S. 2013. Environmental factors influencing the efficacy of probiotic bacteria. *Curr Opin Biotechnol.* 24:207-13.

### **Module 16. Efficacy of probiotics in Human Subjects**

- Salminen S, Deighton MA, Benno Y, Gorbach SL. 1998. Lactic acid bacteria in health and disease. Ch 7. In Lactic acid bacteria, Microbiology and Functional Aspects. Salminen S and von Wright A, Editors. Marcel Dekker, Inc. New York. Basel.
- Vlasova AN, Kandasamy S, Chattha KS, Rajashekara G, Saif LJ. 2016. Comparison of probiotic lactobacilli and bifidobacteria effects, immune responses and rotavirus vaccines and infection in different host species. *Vet Immunol Immunopathol.* 172:72-84.
- McCollum DL, Martin Rodriguez J. 2012. Detection, Treatment, and Prevention of *Clostridium difficile* Infection. *Clinical Gastroenterology and Hepatology* 10: 581-592.
- Varankovich NV, Nickerson MT, Korber DR. 2015. Probiotic-based strategies for therapeutic and prophylactic use against multiple gastrointestinal diseases. *Front Microbiol* 6:685.
- NASPGHAN NUTRITION REPORT COMMITTEE. 2006. Clinical Practice Guideline Clinical Efficacy of Probiotics: Review of the Evidence With Focus on Children. *J Pediatr Gastroenterol Nutr* 43:550- 557.
- Bron PA, Kleerebezem M, Brummer RJ, Cani PD, Mercenier A, MacDonald TT, Garcia-Ródenas CL, Wells JM. 2017. Can probiotics modulate human disease by impacting intestinal barrier function? *Br J Nutr.* 117:93-107.
- Dimidi E, Christodoulides S, Fragkos KC, Scott SM, Whelan K. 2014. The effect of probiotics on functional constipation in adults: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr.* 100:1075-84.
- Kim S, Lee H, Lee S, Lee J, Ha J, Choi Y, Yoon Y, Choi KH. 2017. Invited review: Microbe-mediated aflatoxin decontamination of dairy products and feeds. *J Dairy Sci.* 100:871-880.
- Azcárate-Peril MA, Sikes M, Bruno-Bárcena JM. 2011. The intestinal microbiota, gastrointestinal environment and colorectal cancer: a putative role for probiotics in prevention of colorectal cancer? *Am J Physiol Gastrointest Liver Physiol.* 301:G401-24.
- Czaja AJ. 2016. Factoring the intestinal microbiome into the pathogenesis of autoimmune hepatitis. *World J Gastroenterol.* 22:9257-9278.
- Mu Q, Kirby J, Reilly CM and Luo XM. 2017. Leaky Gut as a Danger Signal for Autoimmune Diseases. *Front. Immunol.* 8:598.
- Esmaeili SA, Mahmoudi M, Momtazi AA, Sahebkar A, Doulabi H, Rastin M. 2017. Tolerogenic probiotics: potential immunoregulators in Systemic Lupus Erythematosus. *J Cell Physiol.* 232:1994-2007.

- Gomes AC, Bueno AA, de Souza RG, Mota JF. 2014. Gut microbiota, probiotics and diabetes. *Nutr J.* 2014 13:60.
- Marinelli L, Tenore GC, Novellino E. 2017. Probiotic species in the modulation of the anticancer immune response. *Semin Cancer Biol.* 46:182-190.

### **Module 17. Probiotics in Animal Production and Health**

- Hossain MI, Sadekuzzaman M, Ha SD. 2017. Probiotics as potential alternative biocontrol agents in the agriculture and food industries: A review. *Food Res Int.* 100:63-73.
- Angelakis E. 2017. Weight gain by gut microbiota manipulation in productive animals. *Microb Pathog.* 106:162-170.
- Chaucheyras-Durand F, Durand H. Probiotics in animal nutrition and health. 2010. *Benef Microbes* 1:3-9.
- C De B, Meena DK, Behera BK, Das P, Das Mohapatra PK, Sharma AP. 2014. Probiotics in fish and shellfish culture: immunomodulatory and ecophysiological responses. *Fish Physiol Biochem.* 40:921-71.

## **Unit 5. New frontiers in probiotic's development**

### **Module 18. Overview on the microbiome**

- Workshop Slides - JCVI Blog - J. Craig Venter Institute
- Blottière HM, de Vos WM, Ehrlich, D, Doré J. 2013. Human intestinal metagenomics: state of the art and future. *Curr Opin Microbiol* 16: 232-239.
- Morgan XC, Huttenhower C. 2012. Chapter 12: Human microbiome analysis. *PLoS Comput Biol* 8:e1002808.
- Morgan XC, Huttenhower C. 2014. Meta'omic analytic techniques for studying the intestinal microbiome. *Gastroenterology* 146:1437-1448.
- Human Microbiome Project  
<https://commonfund.nih.gov/hmp/initiatives>

## **Module 19. Manipulation of the microbiome by probiotics**

- Tojo R, Suárez A, Clemente MG, de los Reyes-Gavilán CG, Margolles A, Gueimonde M, Ruas-Madiedo P. 2014. Intestinal microbiota in health and disease: role of bifidobacteria in gut homeostasis. *World J Gastroenterol* 20:15163-76.
- McFarland LV. 2014. Use of probiotics to correct dysbiosis of normal microbiota following disease or disruptive events: a systematic review. *BMJ Open* 4:e005047.
- Collado MC, Bäuerl C, Pérez-Martínez G. 2012. Defining microbiota for developing new probiotics. *Microb Ecol Health Dis.* 23.
- Walter J. 2008. Ecological role of lactobacilli in the gastrointestinal tract: implications for fundamental and biomedical research. *Appl Environ Microbiol* 74:4985-96.

## **Module 20. Microbiome research to identify new probiotic microorganisms**

- Neef A, Sanz Y. 2013. Future for probiotic science in functional food and dietary supplement development. *Curr Opin Clin Nutr Metab Care.* 16:679-87.
- El Hage R, Hernandez-Sanabria E, Van de Wiele T. 2017. Emerging Trends in "Smart Probiotics": Functional Consideration for the Development of Novel Health and Industrial Applications. *Front Microbiol* 8:1889.
- Miquel S, Martín R, Rossi O, Bermúdez-Humarán LG, Chatel JM, Sokol H, Thomas M, Wells JM, Langella P. 2013. *Faecalibacterium prausnitzii* and human intestinal health. *Curr Opin Microbiol.* 16:255-61.
- Cani PD and de Vos WM. 2017. Next-Generation Beneficial Microbes: The Case of *Akkermansia muciniphila*. *Front. Microbiol.* 8:1765.

## **Module 21. Fecal transplants as probiotics**

- Borody TJ, Paramsothy S., Agrawal G. 2013. Fecal Microbiota Transplantation: Indications, Methods, Evidence, and Future Directions. *Curr Gastroenterol Rep.* 15:337.

## **Module 22. Probiotics, prebiotics, symbiotics and postbiotics**

- Rastall RA, Gibson GR. 2015. Recent developments in prebiotics to selectively impact beneficial microbes and promote intestinal health. *Curr Opin Biotech* 32:42-46.
- Pandey KR, Naik SR, Vakil BV. 2015. Probiotics, prebiotics and synbiotics- a review. *J Food Sci Technol* 52: 7577–7587.



- Patel R, DuPont HL. 2015. New Approaches for Bacteriotherapy: Prebiotics, New-Generation Probiotics, and Synbiotics. *Clin Infect Dis* 60:S108–S121.
- Pineiro M, Asp N-G, Reid G, Macfarlane S, Morelli L, Brunser O, Tuohy K. 2008. FAO Technical Meeting on Prebiotics. *J Clin Gastroent* 42:S156-S159.
- Markowiak P, Slizewska K. 2017. Effects of Probiotics, Prebiotics, and Synbiotics on Human Health. *Nutrients* 9:1021
- Salminen S, et al. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat Rev Gastroenterol Hepatol*. 2021 Sep;18(9):649-667. doi: 10.1038/s41575-021-00440-6. Epub 2021 May 4. Erratum in: *Nat Rev Gastroenterol Hepatol*. 2021 Jun 15;: PMID: 33948025; PMCID: PMC8387231. <https://pubmed.ncbi.nlm.nih.gov/33948025/>
- Moradi M, et al. A review on preparation and chemical analysis of postbiotics from lactic acid bacteria. *Enzyme Microb Technol*. 2021 Feb;143:109722. doi: 10.1016/j.enzmictec.2020.109722. Epub 2020 Dec 3. PMID: 33375981. <https://pubmed.ncbi.nlm.nih.gov/33375981/>

### **Module 23. Psychobiotics: manipulation of bacteria–gut–brain signals**

- Wasilewski A, Zielińska M, Storr M, Fichna J. 2015. Beneficial Effects of Probiotics, Prebiotics, Synbiotics, and Psychobiotics in Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 21:1674-82.
- Liu X, Cao S, Zhang X. 2015. Modulation of Gut Microbiota-Brain Axis by Probiotics, Prebiotics, and Diet. *J Agric Food Chem*. 63:7885-95.
- Kim N, Yun M, Oh YJ, Choi HJ. 2018. Mind-altering with the gut: Modulation of the gut-brain axis with probiotics. *J Microbiol*. 56:172-182.
- Fung TC, Olson CA, Hsiao EY. 2017. Interactions between the microbiota, immune and nervous systems in health and disease. *Nature Neuroscience* 20:145–155.
- Powell N, Walker MM, Talley NJ. 2017. The mucosal immune system: master regulator of bidirectional gut–brain communications. *Nat Rev Gastroent Hepat* 14:143–159.
- Smith PA. 2015. The tantalizing links between gut microbes and the brain. *Nature News*. 14 October 2015.