

The Chancellor of Ghent University has the honour of inviting you to attend the public defense of the doctoral dissertation of

## Racha Ahmad El Hage

Title of the doctoral dissertation:

### *Ability of a Propionate-Producing Synthetic Microbial Consortium to Restore Functionality in a Dysbiosed Human Gut Microbiome*

The public defence will take place on Friday, September 13th, 2019 at 16:00 in the E2 Auditorium (E1.012), Coupure links 653, 9000 Gent.

There will be a contiguous reception to which you are heartily invited.  
Please confirm your attendance before September 7<sup>th</sup> to: [racha.elhage@ugent.be](mailto:racha.elhage@ugent.be)

#### Dissertation supervisors

**Prof. dr. ir. Tom Van De Wiele**  
Faculty of Bioscience  
Engineering,  
Ghent University

**Dr. Emma Hernandez-Sanabria**  
Faculty of Bioscience  
Engineering,  
Ghent University

#### Board of examiners

**Prof. dr. Abdul Mouazen**  
Chairman  
Department of Environment  
Faculty of Bioscience Engineering,  
Ghent University, Belgium

**Prof. dr. Andreja Rajkovic**  
Department of Food, Technology,  
Safety and Health  
Faculty of Bioscience Engineering,  
Ghent University, Belgium

**Prof. dr. ir. John VAN CAMP**  
Department of Food, Technology,  
Safety and Health  
Faculty of Bioscience Engineering,  
Ghent University, Belgium

**Prof. dr. Filip Van Immerseel**  
Department Pathology, Bacteriology  
and Poultry Diseases  
Faculty of Veterinary Medicine,  
Ghent University, Belgium

**Dr. Kristof Van Emelen**  
ProDigest, Technologiepark-  
Zwijnaarde, Ghent, Belgium

#### Abstract of the doctoral research:

Several factors can lead to the manipulation of the gut microbiota, including antibiotics, probiotics, prebiotics and other environmental factors. The misuse of antibiotics causes a disruption for the gut microbiota and thereby a disorder in short chain fatty acids production. Propionate, a major short chain fatty acid, is able to stimulate the production of anorexigenic gut hormones that can control satiety thus causing weight loss. Propionate can also contribute to metabolic health by activating the intestinal gluconeogenesis, which can maintain energy homeostasis. In this PhD, we designed a propionate-producing bacterial consortium from gut commensals by considering the three different metabolic pathways for propionate production (acrylate, succinate, and propanediol). To assess the effect of the propionate-producing consortium on the microbial functionality upon antibiotic-induced dysbiosis, we used the *in vitro* simulator for the human intestinal microbial ecosystem (M-SHIME). The impact of addition of the propionate-producing consortium was tested for different donors after which the antibiotic was added to induce dysbiosis. Our results revealed that the administration of our consortium restored functionality and caused a shift to the microbial community towards enhancing propionate production. Furthermore, we investigated the impact of the metabolites from the propionate-producing consortium and *A. muciniphila*, a propiogenic bacterium, in an *in vitro* enterohepatic model of insulin resistance. Our results showed that only the metabolites produced by our designed consortium were able to increase hepatic glycogen levels and lipoprotein lipase activity and had the tendency to decrease pro-inflammatory markers such as IL-8. These results elucidated the positive effect of the propionate-producing consortium on metabolic function and low-grade inflammation. In conclusion, this PhD research showed that the designed propionate-producing consortium is a promising strategy to restore dysbiosis and manage metabolic disorders.

#### Brief Curriculum Vitae

Racha El Hage obtained her bachelor's degree in Nutrition and Dietetics at the American University of Beirut (Lebanon) in 2011. She obtained her Licence in Dietetics in 2012. In September 2012, Racha started her MSc degree in Molecular Nutrition at the University of Aberdeen in Scotland with an experimental thesis on the "Ability of isolated human gut bacteria to utilize oligosaccharides from human milk", and obtained her degree in 2013. She then worked for one year as Research Assistant in the Department of Pediatrics and Adolescent Medicine in American University of Beirut Medical Center. In October 2014, Racha obtained her Marie Curie PhD Fellowship, and started her PhD at the Center for Microbial Ecology and Technology (CMET), University of Ghent. Her research focused on the selection of propionate producers from gut commensals and developing a propionate-producing microbial consortium that is able to restore antibiotic-associated dysbiosis, and improve markers of metabolic disorder. During her PhD, Racha participated in two major secondments that took place in the ProDigest in Ghent and in the University of Copenhagen, and she participated in other schools that were part of the European Union project. Her work has been presented in international conferences or symposiums, and she co-authored multiple publications in peer-reviewed journals. During her PhD, Racha mentored one master student, and she assisted in the lab teaching for the course of Host Microbe Interactions.