Project 2

Name/title of the PhD course	**Clinical and Experimental Medicine**
Name of the PhD coordinator	Prof.Dr.Francesco Beguinot, MD
Name/Title of the PhD project	***Gut Microbiome as Target for Food Allergy: The MATFA project***
Department of reference	Department of Translational Medical Science at the University of Naples Federico II (http://www.medicinatraslazionale.unina.it/)
Working conditions, research team, infrastructures, equipment	The research activities at the Department of Translational Medical Science (DISMET) are characterized by a multidisciplinary "from bench to the bedside" approach. Data from preclinical research activities pave the way to multidisciplinary, patient-centered, and personalized intervention in clinical practice. More than 60 researchers are involved in these activities. The DISMET hosts the Research Center for Basic and Clinical Immunological Science (CISI), the European Laboratory for the Investigation of Food Induced Diseases (ELFID), and the Food Allergy Comprehensive Education, Treatment and Support Program. The Program is one of the largest providers of pediatric food allergy (FA) in Europe (www.centroallergologiapediatrica.it) with >3000 FA children currently in follow-up. The research activities of the Program are strictly connected to the activities of the ImmunoNutritionLab (http://www.immunonutritionlab.com/) dedicated to all aspects of FA, with the aim to move disease biology from the laboratory to clinical practice. The ImmunoNutritionLab is located at CEINGE Research Center(https://www.ceinge.unina.it/en/institute) and is certified by the Joint Commission International (since 2009) and ISO 9001: 2015 (Quality Management Systems). The Center is equipped with the state-of-the art of technologies for the investigation of many aspects of disease biology (including biobanking of biological samples; advanced technologies for metagenomics: last generation sequencers; metabolomics advanced technologies: HPLC, GC-MS, MALDI-TOF for proteomics; cytofluorometry and cell-sorter, microarray and Real Time PCR for epigenetics analysis; cell biology research laboratory; animal models of obesity, NAFLD/NASH, food allergy, pain, depression, anxiety, inflammatory bowel diseases, diarrhea, asthma, rhinitis; human cell lines for the study of host-microbiome interaction; human cell lines for the study nutrients-host interaction; organ cultures; Ussing's chambers for the study of transepithelial fluid transport; biostatistics team for data analysis; artificial human gut system) and for data management with machine learning approach. The Research group is a multidisciplinary team composed by allergists, immunologists, microbiologists, pediatricians, dietitians, nutritionists, biologists, allergy laboratory technicians, research nurses, biostatisticians with a great experience in preclinical and clinical research. More than 18 basic science studies and more than 16 clinical trials are conducted annually at the Food Allergy Comprehensive Education, Treatment and Support Program.
Scientific context	Food allergy (FA) prevalence, persistence and severity have been on a rise in recent decades in industrialized world under the pressure of gene-environment interactions leading to immune-system dysfunction. Evidence emphasized the role of gut microbiome (GM) in maintaining the balance of microbial signals (such as the short chain fatty acids, SCFA) required to prevent FA, and there is mounting evidence that modifications in the pattern of microbial exposure (dysbiosis) early in life represents a critical factor underlying FA development. Gut microbiome contributes to the development of a proper immune system from the early stage of life. Immune tolerance is maintained thanks to the complex interaction between gut microbiome and immune and non-immune cells. We have adopted an integrated multidisciplinary approach to investigate gut microbiome as potential target for FA prevention and treatment, and we are starting to elucidate the potential mechanisms and the potential clinical relevance of this new strategy.
Project Research plan	Project activities will be divided in work packages (WPs): WP1 - Comparative evaluation of gut microbiome structure and function (i.e., SCFAs production) in children affected by FA and in healthy controls (months 0-12) WP2 – Cellular and murine models-based investigation of the effects elicited by gut microbiome in facilitating or protecting against FA (months 13-24) WP3 – Investigations on the impact of new dietary strategies (probiotics, post-biotics and dietary peptides) on FA prevention and treatment (months 25-36)
Research and Training Innovative aspects	The results of the study will provide data of highly translational relevance with a rapid impact on innovative strategies for FA prevention and treatment. Accelerating immune tolerance acquisition will determine a significant impact for the socioeconomic costs related to FA. This would be a ground-breaking and unprecedented basic knowledge potentially opening new frontiers in translational medicine. Successful implementation of this study would lead to a much more cost-effective result to enhance disease prevention and to translate the mechanisms and utilization of innovative strategy for the management of these conditions.
Inter-Multidisciplinary aspects	During the PhD period, the student will be in contact with highly experienced multidisciplinary team (composed by neonatologists, pediatricians, immune-allergists, dietitians, pediatric nurses, microbiologists, biologists, biostatisticians) with a huge experience in all basic science and clinical aspects of pediatric nutrition and allergy, and in clinical trials.The PhD Student will have the opportunity to learn all Lab technologies that are necessary for the project that are available "in house" at the Institution.

Secondment opportunities	**Kraft-Heinz Italia** (https://www.heinz.it/). The Kraft Heinz Company is the third-largest food and beverage company in North America and the fifth-largest food and beverage company in the world, with eight $1 billion+ brands. A globally trusted producer of delicious foods, The Kraft Heinz Company provides high quality, great taste and nutrition for all eating occasions whether at home, in restaurants or on the go. The PhD will spend 3 months in Kraft-Heinz Italia. During this period, he will be involved in the characterization of the bioactive components and their stability during different fermentation processes, the design of a new "postbiotics" and of infant formulas for the prevention and treatment of FA. **Supervisor: Andrea Budelli**
Main Supervisor: Prof.Dr.Roberto Berni Canani, MD, PhD (https://www.docenti.unina.it/roberto.berni https://scholar.google.com/citations?user=mmtJSi4AAAAJ&hl=it&oi=ao).	
Brief CV	Internationally recognized as one of the leading researchers in the area of paediatric allergy, gastroenterology, food-induced diseases and nutrition. He received his MD and PhD degrees from University of Naples "Federico II", Naples, Italy. He is board certified in Paediatrics. Chief of the Pediatric Allergy Comprehensive Education, Treatment and Support Program at the University Federico II of Naples one of the largest providers of paediatric allergy services in Italy (www.allergologiapediatrica.eu). Founder and Chief of the ImmunoNutritionLab at Ceinge Advanced Biotechnologies Research Center. Founder and Member of the Advisory Board of the Task Force on Microbiome Studies and of many other national scientific societies (Italian Society of Pediatrics, Italian Society of Pediatric Gastroenterology Hepatology and Nutrition, Italian Society of Pediatric Allergy and Immunology, Italian Society of Infectious Diseases, Italian Society of Pediatric Research). Vice-president of the Italian Society of Pediatric Gastroenterology Hepatology and Nutrition (SIGENP) (2008-2012) and actual chief of the food-induced diseases working group (from 2014). He is member of the European Academy of Allergy and Clinical Immunology (EAACI) and of the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN). He has obtained several scientific prizes for the research activity. Member of the Expert Panel (from 2011) and of the Dietetic products, Nutrition and Allergies Panel of the European Food Safety Authority (EFSA) (2012-2015). From 2013 he is enclosed in the list of Top 100 Italian Scientists of VIA-Academy (http://www.topitalianscientists.org/Top_italian_scientists_VIA-Academy.aspx). **In 2019 he has been enclosed in the Plos Biology list of the most influent international scientists in the world** (https://doi.org/10.1371/journal.pbio.3000384).
Publications	He is author of more than 300 publications among scientific papers on international journals, chapters of books and reviews. His publications are widely quoted (collectively more than >18500 citations as at Sept 2021). H-index score 64. Total impact factor score: >2200. **5 most significant publications** in the microbiome field: -De Filippis F, Paparo L, Nocerino R, Della Gatta G, Carucci L, Russo R, Pasolli E, Ercolini **D, Berni Canani** R. Specific gut microbiome signatures and the associated pro-inflamatory functions are linked to pediatric allergy and acquisition of immune tolerance. Nat Commun. 2021;12(1):5958. -Roggero P, Liotto N, Pozzi C, Braga D, Troisi J, Menis C, Giannì ML, **Berni Canani R**, Paparo L, Nocerino R, Budelli A, Mosca F, Rescigno M. Analysis of immune, microbiota and metabolome maturation in infants in a clinical trial of Lactobacillus paracasei CBA L74-fermented formula. Nat Commun. 2020;11(1):2703 doi: 10.1038/s41467-020-16582-1. -Feehley T, Plunkett CH, Bao R, Choi Hong SM, Culleen E, Belda-Ferre P, Campbell E, Aitoro R, Nocerino R, Paparo L, Andrade J, Antonopoulos DA**, Berni Canani R**, Nagler CR.Healthy infants harbor intestinal bacteria that protect against food allergy.Nat Med. 2019;25(3):448-453. **-Berni Canani R**, De Filippis F, Nocerino R, Paparo L, Di Scala C, Cosenza L, Della Gatta G, Calignano A, De Caro C, Laiola M, Gilbert JA, Ercolini D. Gut microbiota composition and butyrate production in children affected by non-IgE-mediated cow's milk allergy. Sci Rep. 2018;8(1):12500. -Berni Canani R, Sangwan N, Stefka AT, Nocerino R, Paparo L, Aitoro R, Calignano A, Khan AA, Gilbert JA, Nagler CR. Lactobacillus rhamnosus GG-supplemented formula expands butyrate-producing bacterial strains in food allergic infants. ISME J. 2016;10(3):742-50
Projects participation	Dr.Berni Canani has demonstrated his research leadership potential by establishing a new independent, productive research group in 2000 (currently supporting 30 staff). To this end, he was involved in raising infrastructure funding to fully equip the new laboratories for this growing group. He has also independently raised >10 million Euros (as chief investigator) in the last 5 years. His main funded research projects focused on microbiome research are 2010-2011 Programmi di ricerca di rilevante interesse nazionale (PRIN) (prot. 2010JCWWKM); and 2011-2012 Ministero della Salute - progetto: PE-2011-02348447). Member of the reviewers panel of: "Research Projects of National Relevance (PRIN)"of the Italian Ministry of University and Scientific Research (from 2009); "The Research Projects and Fellowships Fund on Food and Nutrition with Implications on Public Health" Ministry of Health of the State of Israel (2013); "Health Research Board (HRB) Strategic Business Plan 2010- 2014 – The Future of Irish Health" (HRA-POR-2014-553)(2014); "Hertha Firnberg-Program of the Austrian Science Fund (FWF)" (2015-2017); "NWO Council for Earth and Life Sciences" (ALW), Ministry of Health Kingdom of the Netherlands (2015); "RFI Food for Tomorrow-Cap Aliment: Transition and adaptation of food systems for the future". European Community Research Grant (2015-2020); "Czech Science Foundation" (2017). "National Institute for Health Research" (NHS), UK (from 2018)