Scheda di Programma

Per l'attivazione nell'ambito del Corso di Dottorato di ricerca in BIOLOGIA APPLICATA E MEDICINA SPERIMENTALE del seguente Programma di ricerca, a valere sulle risorse di cui al DM n. 351/2022, relativamente alla seguente Misura:

☐ **M4C1- Inv. 3.4** "*Didattica e competenze universitarie avanzate*" → **Dottorati dedicati alle transizioni digitali e ambientali.**

☐ **M4C1- Inv. 4.1** *"Estensione del numero di dottorati di ricerca e dottorati innovativi per la pubblica amministrazione e il patrimonio culturale"*. In particolare:

☒ **Dottorati PNRR**

☐ **Dottorati per la Pubblica Amministrazione**
(selezionare l'area/le aree CUN di riferimento del programma tra quelle di seguito indicate)

- ☐ Area 09 – Ingegneria industriale e dell'informazione
- ☐ Area 11 – Scienze storiche, filosofiche, pedagogiche e psicologiche
- ☐ Area 12 – Scienze giuridiche
- ☐ Area 13 – Scienze economiche e statistiche
- ☐ Area 14 – Scienze politiche e sociali

☐ **Dottorati per il patrimonio culturale**
(selezionare l'area/le aree disciplinare/i e la tematica del programma tra quelle di seguito indicate)

- ☐ Area 01 – Scienze matematiche e informatiche **Tematica** – Informatica, patrimonio e beni culturali
- ☐ Area 02 – Scienze Fisiche **Tematica** – Fisica applicata al patrimonio culturale e ai beni culturali
- ☐ Area 03 – Scienze chimiche **Tematica** – Chimica, ambiente, patrimonio e beni culturali
- ☐ Area 04 Scienze della Terra **Tematica** – Georisorse minerarie per l'ambiente, il patrimonio e i beni culturali
- ☒ Area 05 Scienze Biologiche **Tematica** - Ecologia, patrimonio e beni culturali
- ☐ Area 08 – Ingegneria civile e Architettura **Tematiche** 1) Architettura, ambiente antropizzato, patrimonio e beni culturali 2) Architettura e paesaggio 3) storia dell'architettura; 4) Restauro; 5) Pianificazione e progettazione dell'ambiente antropizzato; 6) Design e progettazione tecnologica dell'architettura
- ☐ Area 10 Scienze dell'antichità, filologico-letterarie e storico -artistiche **Tematiche** 1) Archeologia; 2) Storia dell'arte; 3) Media, patrimonio e beni culturali
- ☐ Area 11 – Scienze storiche, filosofiche, pedagogiche, psicologiche **Tematiche** 1) Biblioteconoma; 2) Archivistica; 3) Storia del patrimonio e dei beni culturali 4) Paleografia; 5) Estetica; 6) Didattica dell'arte; 7) pedagogia dell'Arte
- ☐ Area 12 - Scienze giuridiche **Tematica** Diritto del patrimonio culturale
- ☐ Area 13 - Scienze Economiche e statistiche **Tematiche** 1) Economia della cultura e dell'arte 2) Economia e gestione delle imprese artistiche e culturali; 3) Statistica e Data Analytics per i beni culturali
- ☐ Area 14 Scienze Politiche e sociali **Tematiche** 1) Sociologia dei beni culturali 2) sociologia dell'ambiente e del territorio

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- **Titolo del Programma di ricerca**: Environmental sustainability and circular economy: agri-food waste as a source of new nutraceuticals against inflammatory bowel diseases.

- **Descrizione** (MAX 5000 CARATTERI SPAZI ESCLUSI)**:**

The research project aims to improve the environmental, social and economic sustainability of the agri-food supply chains through the enhancement and reuse, from a health point of view, of processing waste relevant to the Italian economy, and in particular to southern Italy such as Citrus fruit production waste, focusing on the field of the inflammatory bowel diseases (IBD). The processing of Citrus fruits is extremely important for the Italian economy and generates high quantities of *pastazzo*, a waste product consisting of flavedo, albedo and pulp residues. The production of *pastazzo* is around 50-60% by weight of the original product, and only in Sicily, from the processing of oranges and lemons, 210,000/250,000 tons of *pastazzo* are produced per year [1,2]. It is rich in various bioactive compounds such as terpenes, phenolic acids and flavonoids, which make it very promising from a health point of view, although no studies have yet been conducted that specifically evaluate its anti-inflammatory activity on IBD.

IBD, including Crohn's disease and ulcerative colitis, occur fairly early (20-40 years), with no significant gender difference and are characterized by recurrent non-infectious inflammation of the gastrointestinal tract, usually accompanied by moderate to severe tissue damage [3,4]. The highest incidence rate has been found in Europe, despite the fact that several epidemiological studies have shown an increase worldwide over the last decade [3,4]. The etiopathogenesis remains partially unknown, even if it is possible to hypothesize an abnormal immune response of the intestinal mucosa, due to genetic factors and linked to an alteration of the microbiota, in turn due to a certain individual susceptibility [5]. Furthermore, it has recently been shown that the microbiota triggers epigenetic changes that could make some individuals more susceptible to intestinal inflammation [6]. Environmental, behavioral and diet factors play also a pivotal role, so much so that IBD are defined as multifactorial diseases [5].

The IBD diagnosis is difficult and conventional treatments (antibiotics, corticosteroids and immunosuppressants) are often associated with important side effects [7]. The rapid spread and chronic and progressive nature of IBD, together with their unpredictable course and health care costs, therefore, represent an important socio-economic concern for public health [4]. Over the past decade, there has been a significant increase in publications on IBD and natural compounds in order to find alternatives to conventional therapy. However, to date, research has focused mainly on natural products and extracts obtained from edible parts, and it has rarely been thought of resorting to plant-complexes obtained from agri-food waste.

This research project fits perfectly into the circular economy and new National Recovery and Resilience Plan (PNRR) having, among its main objectives, that of making agriculture more sustainable, guaranteeing greater competitiveness, significantly strengthening the basic and applied research, promote technology transfer in order to increase national growth potential, and strengthen prevention, promoting scientific research in the biomedical and health sectors.

All these goals will be pursued through an integrated approach that will go from the quality control and safety of the raw material, to the pharmacognostic evaluation through a careful phytochemical and biological characterization by using different *in vitro* cell-free and cell-based tests, in order to investigate the antioxidant, anti-inflammatory, prebiotic and epigenetic effects. This will also be achieved thanks to a collaboration with the Molecular Genetics Research Center of Complex Characters of the Bambin Gesù Pediatric Hospital (Rome). The last aim will be to select the most active plant-complex on bowel after *in vitro* simulated dynamic gastro-duodenal digestion that will be developed at the Food Innovation and Health Program Research Center, Quadram Institute Bioscience (Norwich, UK). Finally, one of the main objectives of this project will be also to develop and validate a new 3D cell co-culture model that includes two different intestinal epithelial cell lines (Caco-2 and HT29-MTX) in co-culture with two types of immune cells (MDM and MDDC). This model could be useful to reproduce, more faithfully *in vitro*, the clinical scenario of IBD, promoting new studies and reducing the use of animals according to the 3R principle.

Upon achievement of the project objectives will be expected, in addition to dissemination of the results through participation in national and international congresses and publications in international peer-review journals, the organization of webinars to update on the new experimental models developed and their potential applications, as well as the technological transfer by patenting the most promising plant-complex.

References

1. Cleano, 2019; Nat Prod Res 33, 244-251
2. Lanfranchi, 2012; J Essent Oil Res 24, 583-591
3. Ng, 2017; Lancet 390, 2769-2778
4. Mak, 2020; J Gastroenterol Hepatol 35, 380-389
5. Abraham, 2011; Gastroenterology 140, 1729-1737
6. Xu, 2022; Front Pharmacol 13:813659.
7. Musumeci, 2019 Nat Prod Res 34, 122-136

❖ PERIODO IN IMPRESA – CENTRI DI RICERCA – P.A.:

Il Programma di ricerca sarà svolto in collaborazione con il seguente soggetto:

Ragione sociale: Research Unit of Molecular Genetics of Complex Phenotypes, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy.
Sede legale: Piazza Sant'Onofrio 4, 00165 Roma (RM), Italia.
Rappresentante legale: Dr. Mariella Enoc

L'ente sopra citato ospiterà il dottorando beneficiario della borsa finanziata sulle risorse del DM 351/2022 per n. 6 mesi **(min 6 max 12)** nel corso del dottorato.

❖ **PERIODO ALL'ESTERO:**

Il Programma di ricerca prevede un periodo all'estero di n. 6 mesi (**min 6 max 18**) presso la seguente istituzione: Food Innovation and Health Programme, Quadram Institute Bioscience, Norwich, UK.

Si dichiara inoltre che il presente programma è conforme al principio "di non arrecare un danno significativo" (DHSH) ai sensi dell'art. 17 del regolamento (UE) 2020/852 in coerenza con gli orientamenti tecnici predisposti dalla Commissione Europea (Comunicazione della Commissione Europea 2021/C58/01) e garantisce il rispetto dei principi orizzontali del PNRR (contributo all'obiettivo climatico e digitale c.d. tagging, il principio della parità di genere e l'obbligo di protezione e valorizzazione dei giovani).

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