



Peptides for microbiota modulation

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Ph.D. Course in Chemical Sciences 38 cycle, University of Napoli "Federico II" Department of Chemical Sciences,
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Supervisor: Professor Angela Lombardi

Co-supervisor: Professor Angela Arciello



UNIVERSITÀ DEGLI STUDI
NAPOLI FEDERICO II







University degrees



**Bachelor of Science, Biology specialization
Microbiology (2019)**
Supervisor/tutor name: PhD Katarzyna Guz-Regner

"Biodiversity of microflora in the peatlands"



Uniwersytet Wrocławski, The Faculty of Biological Sciences,
Institute of Genetics and Microbiology



WROCLAW UNIVERSITY
OF ENVIRONMENTAL
AND LIFE SCIENCES

**Master of Science, Biology specialization Laboratory techniques
in Biology (2021)**

Supervisor/tutor name: PhD Paulina Cholewinska

"The effect of changes in the level of Firmicutes and
Bacteroidetes in Charolaise cattle"



Wrocław University of Environmental and Life Science, Faculty: The Faculty of
Biology and Animal Science, Institute of Animal Husbandry and Breeding

Previous expertise



Research project manager:

06.2020-06.2021

Wrocław University of Environmental and Life Science (Poland) as the individual student research project „Młode umysły – Young Minds Project” (project number N00000000.218.2020)



Author and co-author of 8 scientific publications



Internship in Ludwig Maximilian University, The Chair for Fish Diseases and Fisheries Biology, Munich, Germany

1.09-30.11.22

Supervisor: Univ. Prof. Dušan Palić, D.V.M., MVSc, Ph.D., CertAqV, Dipl. ECAAH

Objectives



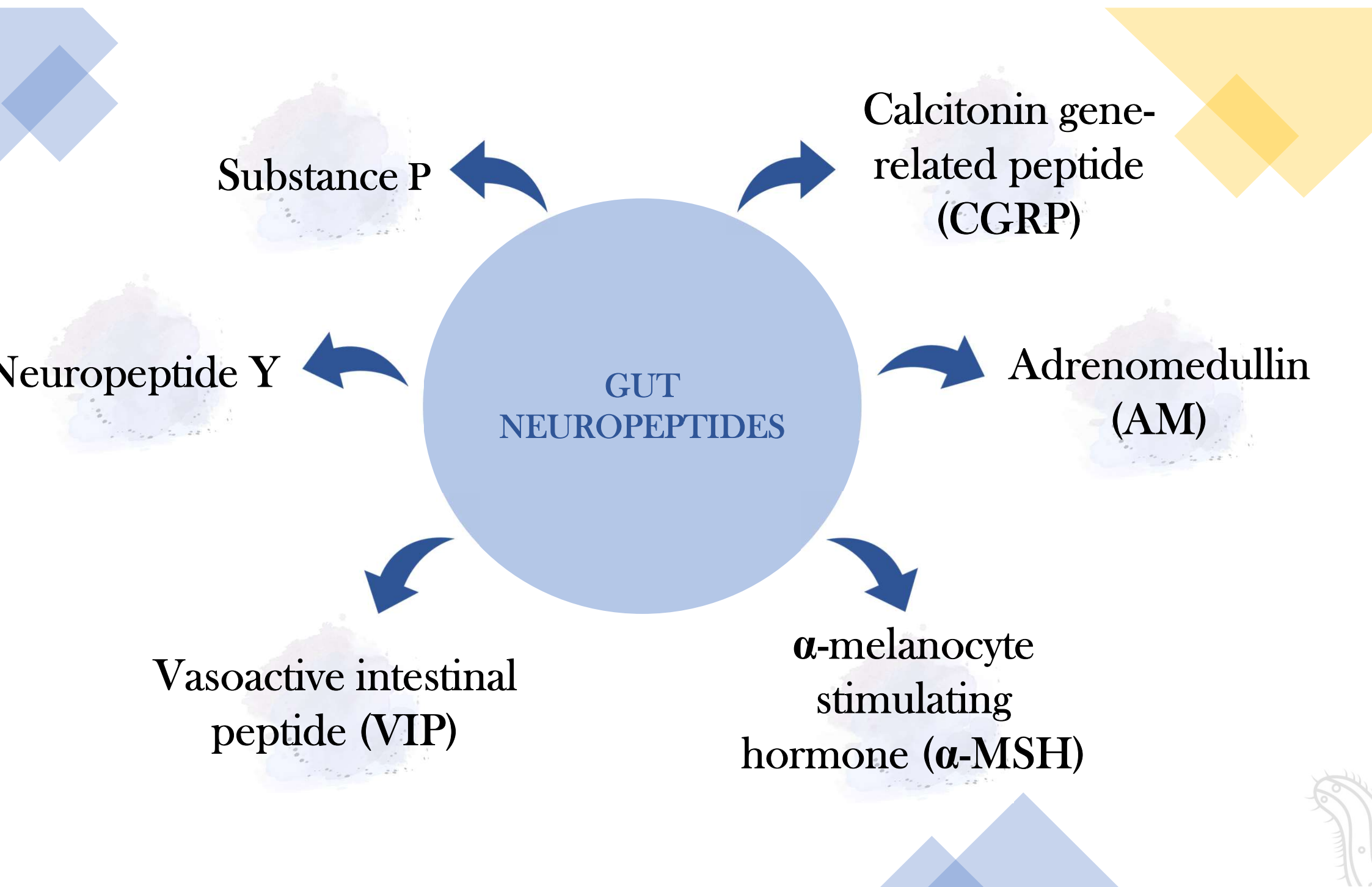
Development of NP/peptide active in gut or skin microbiome modulation



Design of modified peptide with improved activity, higher stability in serum and reduced toxicity



Evaluation of therapeutic applicability of identified peptide



GUT neuropeptides



Produced in the ENS (enteric nervous system) and in intestinal epithelium



Structurally similar to AMPs - small (<5 kDa), cationic, and amphipathic molecules

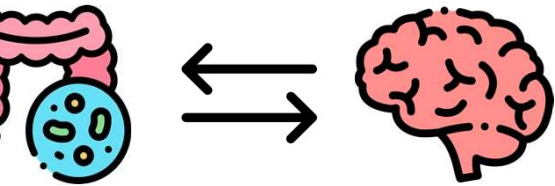


They are part of an extremely complex network between the nervous, immune systems where they are playing a key modulatory role and they play important role in gut-brain axis

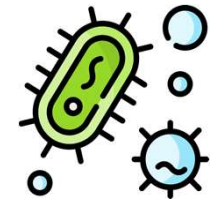
Function of NP in human body



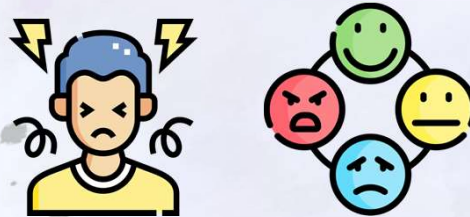
Immune function



Communication between
the gut and the brain

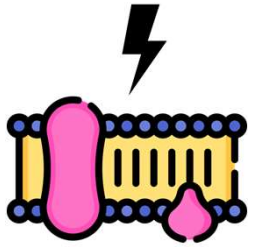


Antimicrobial properties

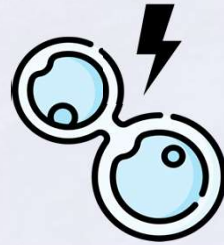


Role in inflammatory responses, pain, emotion, mood,
cognition, stress, ingestion, homeostasis, intestine motility

Mechanism of NP antimicrobial activity



Membrane disruption




Interference with cell division

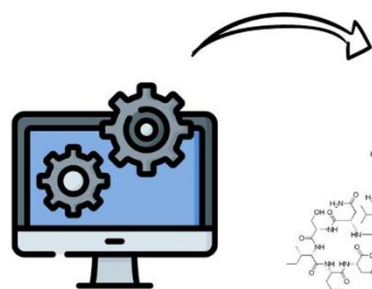


Disruption of ATP synthesis

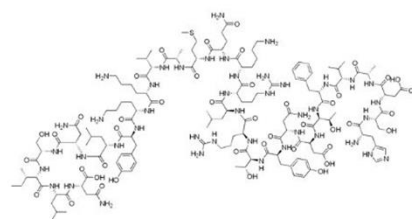


Novel insight of NP in PhD project

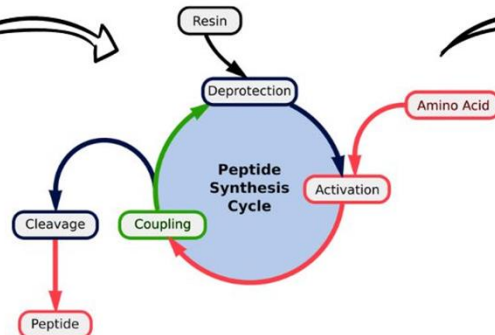
- Commensal skin microbiota activity
 - Effects of synthesized peptides on the gut and skin microbiota
 - Understanding their mechanism of action and their activity against different bacteria strains
 - Mimicking bacteria membrane interaction with peptides in model membranes
 - Design of peptide homologs with microbiota modulation activity and antimicrobial properties against pathogenic strains without causing any negative effect to commensal bacteria strains
- 



Machine learning tools



Creation of NP/AMP



Peptide synthesis



Spectroscopic and calorimetric methods



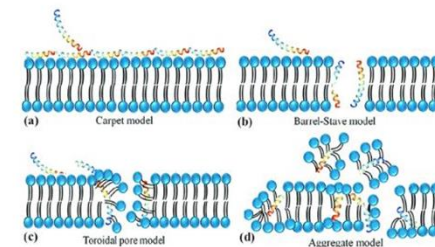
Obtaining NP/AMP with modulating/antimicrobial activity in GIT and skin microbiota



In vivo analysis of bacteria modulating/antimicrobial activity



In vitro analysis of bacteria modulating/antimicrobial activity



Peptide-membrane interaction



Nociceptin

H - FGGFTGARKSARKLANQ - OH

Peptide related to the endogenous opioid class ex. Enkephalins, Dynorphine

Widely distributed in the CNS; it is found in the hypothalamus, brainstem, and forebrain

In the gut, nociceptin has been found to have varying effects on stomach and intestinal contractility while also stimulating the increased consumption of food

Machine learning tools suggest that nociceptin could have antimicrobial activity

Nociceptin – machine learning preliminary study

nociceptin WT and homolog

Results for RF classifier

Seq. ID.	Class	AMP Probability
BASIC	AMP	0.78
1A,2A	AMP	0.93

Results for SVM classifier

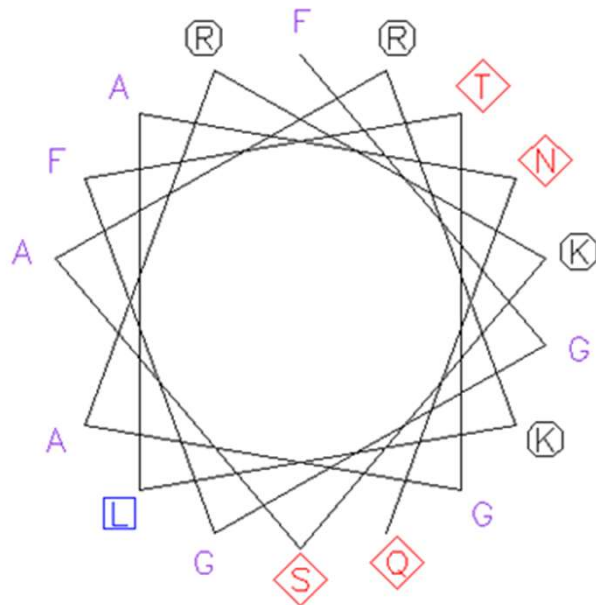
Seq. ID.	Class	AMP Probability
BASIC	AMP	0.97
1A,2A	AMP	0.98

Results for ANN classifier

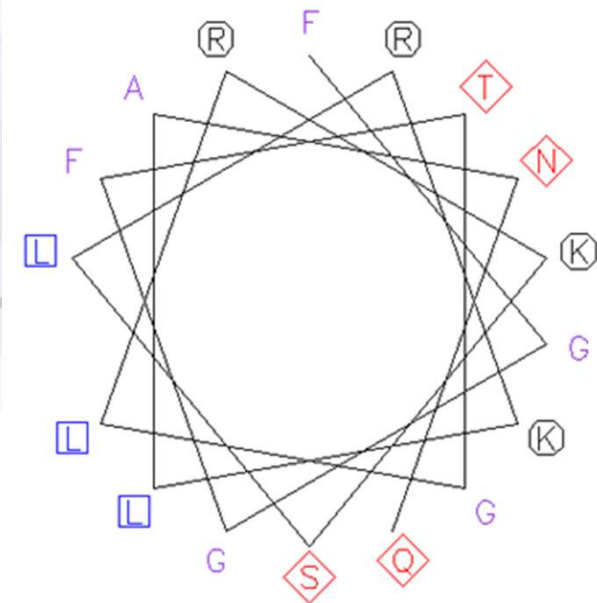
Seq. ID.	Class	AMP Probability
BASIC	AMP	0.97
1A,2A	AMP	0.98

α -helical structure

1



2



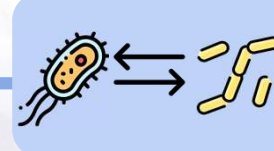
Scientific impact



Alternative methods to the use of antibiotic/probiotic therapy



Synthesis of appropriately designed NP will allow in the future using them as target drugs or supplements for humans

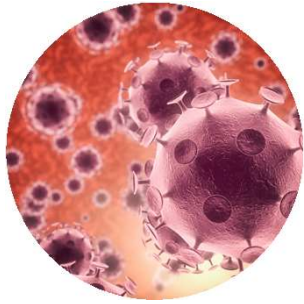


Microbiota modulating properties of NP can decrease development of many disorders



Target against specific pathogenic strains without causing any negative effects to commensal

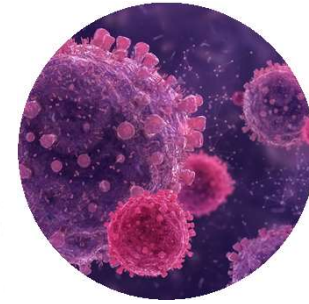
Conclusion and final goals of PhD project



Investigating the effects of NP/peptides on commensal microbiota and pathogenic strains in skin and gut



Design and creation of NP/peptides homologs demonstrating microbiota modulation capabilities



Linking the role of the obtained neuropeptide between the skin and gut microbiome



Thank you for your attention!



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