UNIVERSITÉ DE LORRAINE

DOCTORAL FELLOWSHIP

OPEN POSITION

LORRAINE Université d'Excellence

DESCRIPTION

Innovative screening methodology for metal chelating peptides with antioxidant properties using Surface Plasmon Resonance

The present cross-disciplinary project aims at discovering and testing new potential chelating antioxidant peptides (**CAPs**) produced through proteolysis and evidenced through the setting up of original screening methods on commercial hydrolysates. (i) Based on their Fe(II) chelating ability, the CAPs screening method in hydrolysate will be developed **using Surface Plasmon Resonance (SPR)** and will be validated on some laboratory-produced hydrolysates. (ii) Then, CAPs sequences will be identified by IMAC-MS, an original coupling currently under development in the frame of another out-of impact PhD thesis. (iii) In a second part of this PhD, the identified CAPs will be chemically **synthesised and modified to pseudopeptides** in order to avoid *in vivo* peptide catabolism and to **increase peptides bioavailability for potential *in vivo* application**. Finally, the antioxidant capacity of identified peptides or pseudopeptides will be investigated on **an *in vitro* model of oxidative stress based on cells representative for different majors systems** (*e.g.* immune, vascular systems). Moreover, the discovery of new Fe(II) chelating peptides with antioxidant activity from various peptide hydrolysates, especially from soy and sunflower, will enable the valorisation of local by-products.

This PhD project is divided in 2 main tasks.

Task 1. Setting up of innovative screening methodologies of iron(II) chelating peptides and identification of the metal-chelating peptides for further studying their potential antioxidant activity (B2S platform (UMS2008 IBSLor CNRS-UL-INSERM), LIBio, ENSAIA analytical platform, SRSMC, LRGP). First, SPR screening methodology of metal chelating peptides in hydrolysates previously developed on Ni(II) (Canabady-Rochelle et al, 2018) will be adapted on Fe(II). This SPR methodology has been initiated on commercial hydrolysates and on synthetic peptides (Canabady-Rochelle et al, 2016 and 2017, 2018). The developed methodologies will be first set up on commercial hydrolysates and then validated on lab-produced hydrolysates (LRGP, URAFPA). Screening will be performed at various levels for: (i) the best hydrolysates in terms of metal chelation properties and determining by SPR the best biocatalysis conditions for producing metal-chelating peptides and (ii) identifying the best chelating peptides using an original methodology coupling IMAC and MS currently under development (LRGP, LIBio).

Task 2. Producing metal-chelating peptides by chemical synthesis and studying their bioactivity (LCPM, LRGP, CITHEFOR). The best metal-chelating peptides sequences screened from Task 1 will be produced by chemical synthesis to obtain sufficient amount for bioactivity evaluation. Indeed, profusion of peptides of interest might be too low in the produced hydrolysate, constituting an experimental bolt to perform *in vitro* bioactivity tests. First, the antioxidant activity will be investigated using acellular assays (Canabady-Rochelle et al, 2015). Then, antioxidant capacity of these peptides will be evaluated on an *in vitro* model of oxidative stress based on vascular smooth muscle cells (Belcastro et al., 2017). The variation of oxidative stress markers (Parent et al, 2015; Belcastro et al., 2017) will be compared to the initial whole hydrolysate and to reference antioxidants like ascorbic acid or *N*-acetylcysteine. As peptides may suffer from *in vivo* catabolism both in the gastrointestinal tract and in the blood stream, the most bioactive peptides will be chemically modified (pseudo-peptides) (Zhou et al, 2008; Moussodia et al, 2015) and their susceptibility to peptidases will be assessed in contact with an intestinal barrier model or with whole blood to determine their bioavailability for further *in vivo* applications.

References

Megias, *et al.* (2007) Affinity purification of copper-chelating peptides from sunflower protein hydrolysates. *J. Agric. Food Chem.* **55** (16), 6509-6514.

Kalinowski D.S. and Richardson D.R. (2007). Futur of toxicology-iron chelators and differing modes of action and toxicity: the changing face of iron chelation therapy. *Chem. Res. Toxicol.* **20** (5), 715-720.

Meggias, *et al.* (2008). Production of copper-chelating peptides after hydrolysis of sunflower proteins with pepsin and pancreatin. *Food Science Technol.* **41**, 1973-1977.

Canabady-Rochelle, *et al.* 2016, 17th International Conference on Oxidative Stress Reduction, Redox Homeostasis and Antioxidants June 13-15, Institut Pasteur, Paris.

Laetitia L.S. Canabady-Rochelle, Katalin Selmeczi, Sabrina Collin, Andreea Pacs, Laurence Muhr and Sandrine Boschi-Muller. (2018) SPR Screening of Metal chelating Peptides for their Antioxidant Properties. *Food Chemistry*. 239, 478-485.

Hafeez, *et al.* (2014). Strategies of producing bioactive peptides from milk proteins to functionalize fermented milk products. *Food Res. Int*. **63**, 71-80.

Canabady-Rochelle, *et al.* (2015). Determination of reducing power and metal chelating ability of antioxidant peptides: revisited methods. *Food Chem.* **183**, 129-135.

Parent, *et al.* (2015). Nitric oxide-eluting scaffolds and their interaction with smooth muscle cells in vitro. *J. Biomed. Mater. Res. A.* **103**, 3303-3311.

Belcastro, et al. (2017). Oxidative stress enhances and modulates protein S-nitrosation in smooth muscle cells exposed to S-nitrosoglutathione. ***Nitric Oxide*** 2017, 69: 10-21.

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TERMS AND TENURE

This position will be based at the LRGP UMR 7274 CNRS-UL [ENSIC, Nancy] and the CITHEFOR EA 3452 UL [Biology-health campus, Vandoeuvre-les-Nancy]. The duration cannot exceed 36 months.

The target start date for the position is ***September or October 2018***.

HOW TO APPLY

Applications are only accepted through email. All document must be sent to laetitia.canabady-rochelle@univ-lorraine.fr and caroline.gaucher@univ-lorraine.fr
Deadline for application is ***April 30 2018***.

JOB LOCATION

Nancy, Lorraine, France

REQUIREMENTS

Applicants are requested to submit the following materials:

- CV and Motivation Letter
- Notes of your Master (first and second year) or the 3 years of French Engineering School with the certificate of success (if possible) – Higher average note of 12/20 in M2 or 3A engineer, or ranking in the first third of the promotion
- Recommendation letters
- Detailed subject of your last year trainee