Houda ABLA, PharmD

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First stage researcher

Pharmacology, Biochemistry, Drug discovery

Motivated, autonomous, team-spirit

PhD Position – TRANSMIT Project ESR9

Professional experience

Jan-Jul 2016 **6 months**

Research Assistant - Internship- Screening for inhibitors of phospholipase D as potential anticancer drugs.

➔ Screening for Phospholipase D inhibitors: 3120 molecules, assay validation, hit selection
➔ Cloning and expression of recombinant human phospholipase D in *P. pastoris* expression system

Institute for Molecular and Supramolecular Chemistry and Biochemistry UMR 5246 CNRS Lyon, FRANCE. Supervisors: Abousalham A. and Noiriel A.

Skills

- **Biochemistry** - protein expression and purification, SDS-PAGE, western blotting
- **Molecular biology** - PCR, gene cloning, site-directed mutagenesis, transformation (yeast, bacteria)
- **Enzymology** - *in vitro* compounds screening, enzymatic assays (phospholipase D activity), Z' factor
- **Metabolism biochemistry, cell and cancer biology**
- **Microbiology**: growth medias, plating techniques
- Oral communication - **Scientific poster presentation, Journée Scientifique de l'IMBL**

Jan-Jul 2015 **6 months**

Junior researcher- Internship - Effect of novel vasodilators iontophoresis on the healing of scleroderma-related ulcers.

➔ **Preclinical model** of scleroderma: effect of novel vasodilators on healing of provoked ulcers
➔ **Safety/toxicity studies**: effect of drug iotophoresis on skin structure and arterial blood pressure

HP2 Laboratory UMR 1042 INSERM- Grenoble, FRANCE. Supervisors: Roustit M. and Kotzki S.

Skills

- **Vascular biology, experimental pharmacology** – *ex vivo*, *in vivo* drug candidates testing
- **Laboratory animals** handling, injection, anaesthesia - rats, mice ★★★★☆
- **Imaging techniques** - Laser Doppler Imaging, light microscopy ★★★☆☆
- **Immunohistochemistry** - paraffin-embedded samples, slide preparation, stainings
- **Analytical chemistry** - HPLC, CE, TLC ★★☆☆☆
- **Theoretical courses**: Computer aided drug design, **SPR**, homology modelling, medicinal chemistry ★★★☆☆

2013-2014 **18 months**

Technical Director - Global DistriMed (pharmaceutical products wholesale), Constantine-Algeria

Other skills

- Excellent **oral communication and written skills:** lab meetings, reports
- **Respect of good practises**, correspondence with **health authorities** and collaborators
- Medicine stocks management and follow up
- Computer skills - Microsoft Office (word, excel, powerpoint), *Sybyl*® software
- **First aid diploma** - April 2016 Lyon, France

Education

2015-2016 University Diploma - Grenoble Alpes University
2014-2015 **Research Master's degree M.Sc** - Drug and Health Engineering, Grenoble Alpes University
Speciality "***Medicinal Chemistry and Pharmacological Innovation***" (*MCL* Distinction)
2006-2012 **PharmD** Pharmacist Diploma - Constantine University – Algeria (*Magna Cum Laude* Distinct)

Languages

- **English** Advanced (TOEFL ibt score **102/120**)
- **French** Bilingual (DALF C1 diploma)
- **Arabic** Mother tongue
- **Spanish** Intermediate, written and spoken

Congresses and Scientific articles

*Rahier R, Abla H, Arhab Y, Noiriel A, Abousalham K. **Direct and Continuous Measurement of Phospholipase D Activities Using the Chelation-Enhanced Fluorescence Property of 8-Hydroxyquinoline.** Methods in Molecular Biology 2nd Ed. New York. Springer (Submitted)

*16th IMBL Scientific days, Lyon, FRANCE. **Screening for phospholipase D inhibitors as potential anticancer drugs**. *Scientific poster presentation (2016)*

Hobbies

Reading	Detective and adventure novels
Sports	Modern jazz, running, swimming
Pastry	
Photography	

Research projects

1. Screening for phospholipase D inhibitors as potential anticancer drugs

Phospholipase D (PLD) hydrolyses phospholipids to form phosphatidic acid (PA) and the corresponding headgroup. To date, PLD has been linked to several pathologies, including cancer, making this enzyme an important therapeutic target. However, most attempts to screen inhibitors and to characterize recombinant human PLDs (HsPLD), *in vitro*, have failed because of the lack of suitable heterologous expression systems.

Therefore, this project has been made around two axes. The first one concerns the cloning and recombinant expression of HsPLD1 in yeast *Pichia pastoris*. As indicated in Fig.1.1, after plasmid subcloning and transformation steps, successful expression was followed using western blotting experiments, supporting further purification trials and activity measurements (in process). These results, which to our knowledge have never been described before in literature, open various perspectives for directly screening chemical libraries on human PLD as well as to its biochemical characterization.

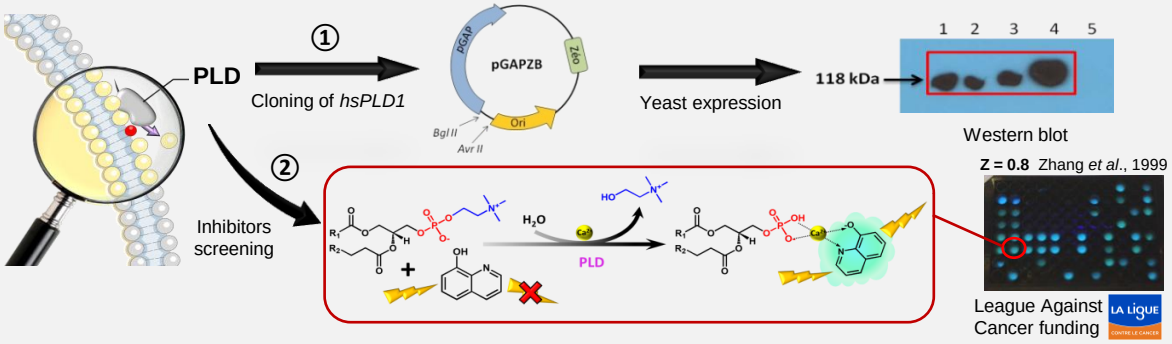

Fig 1.1 Cloning and expression of recombinant HsPLD1 in *P. Pastoris*. **2.** Principle of PLD assay and screening for inhibitors

The second part of the project aimed to screen potent inhibitors (3120 molecules) from the chemical library of the institute (Fig.1.2). This work was performed using a recombinantly expressed plant PLD (*Vigna unguiculata)*, which is homologous to HsPLDs. Screenings were realized using our newly developed PLD assay (Fig.1.2) that presents a calculated Z factor value of 0.8, qualifying it as "an excellent assay", suitable for high throughput screening. Active compounds (7% of the library) currently in characterization (IC50, inhibition mode), will further be tested *in cellulo* on human cancer cell lines and their structures optimized.

2. Cinaciguat iontophoresis, a vasodilator drug, effects on the healing of scleroderma-related ulcers

Systemic sclerosis (SSc) is a connective tissue disease that affects both the skin and internal organs. It's features include a vascular alteration, an inflammation and a fibrosis. Digital ulcers (DU) a major complication of scleroderma can lead to fingers amputation. Their treatment relies on vasodilators but is limited by severe side effects. Therapeutic cutaneous iontophoresis is a delivery technique based on the facilitated movement of charged species through the skin via the application of an electric current of low intensity. Thus, we aim to develop an innovative therapeutic scheme through local administration of drug candidates using non-invasive iontophoresis. Our objective through this work was therefore to assess iontophoresis of cinaciguat, a vasodilator drug, on wound healing speed of skin ulcers induced on a murine model of scleroderma.

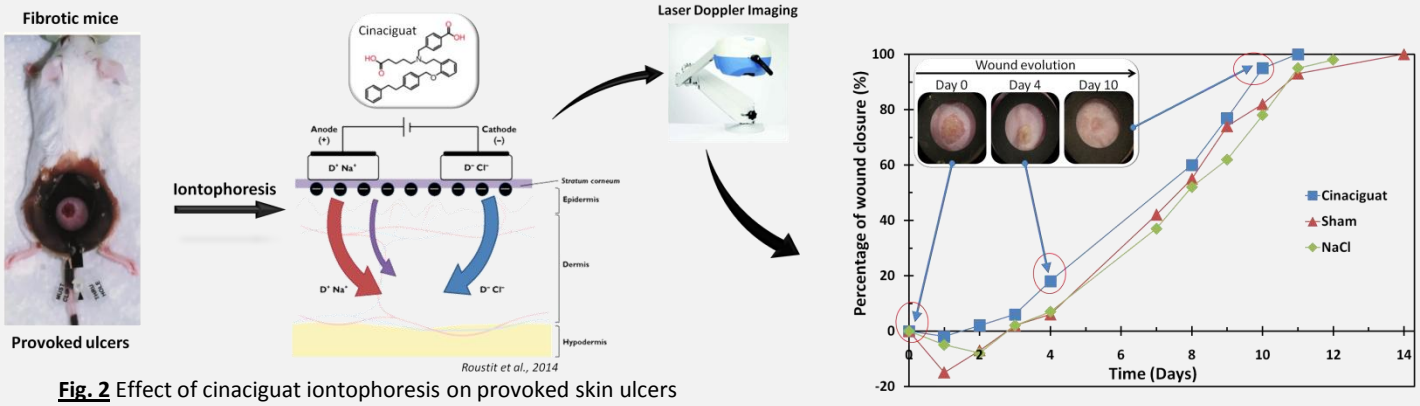

Fig. 2 Effect of cinaciguat iontophoresis on provoked skin ulcers

Firstly for proof of concept and safety studies, testing cinaciguat iontophoresis on healthy Wistar Han rats was shown to increase the animals' skin blood flow (monitored by laser doppler imaging), but severely reduced their arterial blood pressure. Excisional ulcers were then realized on fibrotic mice: A group received cinaciguat through daily iontophoresis, another received NaCl 0.9%, as a control, while the last remained untreated (sham). After calculating wound closure percentage, results showed cinaciguat iontophoresis significantly enhanced wound closure speed in comparison with both control and sham groups (Fig.2). Cinaciguat appears thus as a good candidate for the treatment of SSc and diabetic skin ulcers (in course of characterization).

References

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