RESEARCH INTERNSHIP

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Description of the project

Activity-based probes targeting metalloproteases: toward the profiling of these enzymes in vivo?

MMPs (matrix metalloproteases) are a very important family of enzymes involved in many pathophysiological phenomena (cancers, wound healing, inflammation ...). Their presence, state of activation, concentration and balance between the different forms testifies to completely normal processes or, on the contrary, are markers of disease progression. It is therefore important to have tools to document their presence, spatial and temporal activation in various biological contexts. However, monitoring these proteins in low abundance in a complex environment is a real challenge. The strategy of chemical derivatization with a "tag" aims to improve the specific detection of these biomolecules of interest. By selectively reacting with functions involved in the catalytic act, **activity-based probes (ABPs)** enable an unambiguous discrimination between the active enzyme and its inactive counterparts. As previously used photoaffinity labeling technique reached its limit, facing the need for in-vivo analysis, we developed a new strategy, based on the design of a new generation of activity-based probes, to promote in-vivo identification and quantification of MMPs. [1]

As part of this study, the goal is to **synthesize a chemically derivatized biomarker for the detection/quantification of targeted proteins involved in knee arthritis**. In such context, MALDI-MS mass spectrometry is one of the methods of choice for **biomolecules multiplexing mapping**. Thus, the labeling of molecules of interest makes it possible to significantly improve their detection through the relative increase in the mass spectrometry signal of ions labeled under conventional conditions of analysis.[2,3,4]

The **objectives** of the M1/M2 level trainee will focus here on the synthesis of peptides modified by a "chemical" probe, he/she will tag proteins of interest in synovial fluids, and validate the effectiveness of MALDI labeling. The successful candidate must present proven skills in organic synthesis in order to optimize / modify the probes of interest. He/She will actively participate in the processing of biological samples, and **will be able to train in chemical, analytic and biochemical techniques mastered in the laboratory** such as solid support synthesis, chromatography, protein labeling (ABP approach), protein digestion, biological assays and mass spectrometry.

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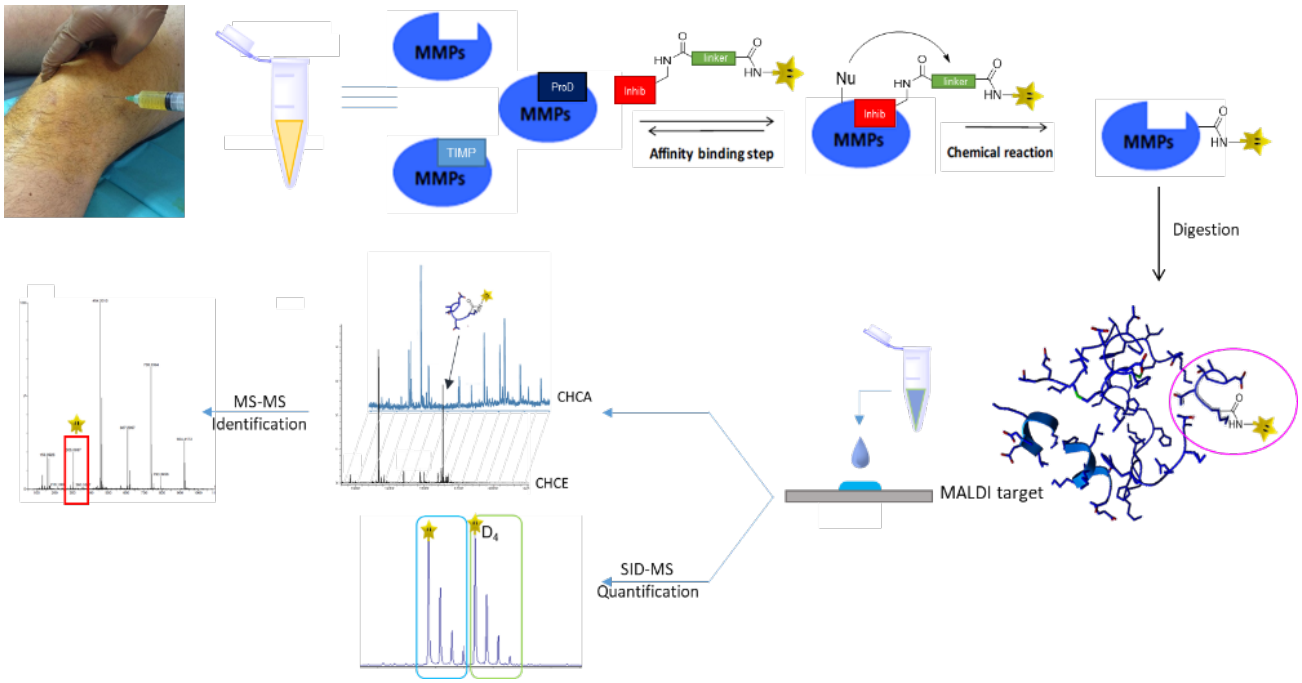
MMPs
ProD
MMPs
TIMP
MMPs
Inhib
linker
HN
HN
Affinity binding step
Nu
Inhib
MMPs
Chemical reaction
MMPs
Digestion
MALDI target
CHCA
CHCE
D4
SID-MS
Quantification
MS-MS
Identification