INTER·DISCIPLINARY & IN·LAB GRADUATE PROGRAM

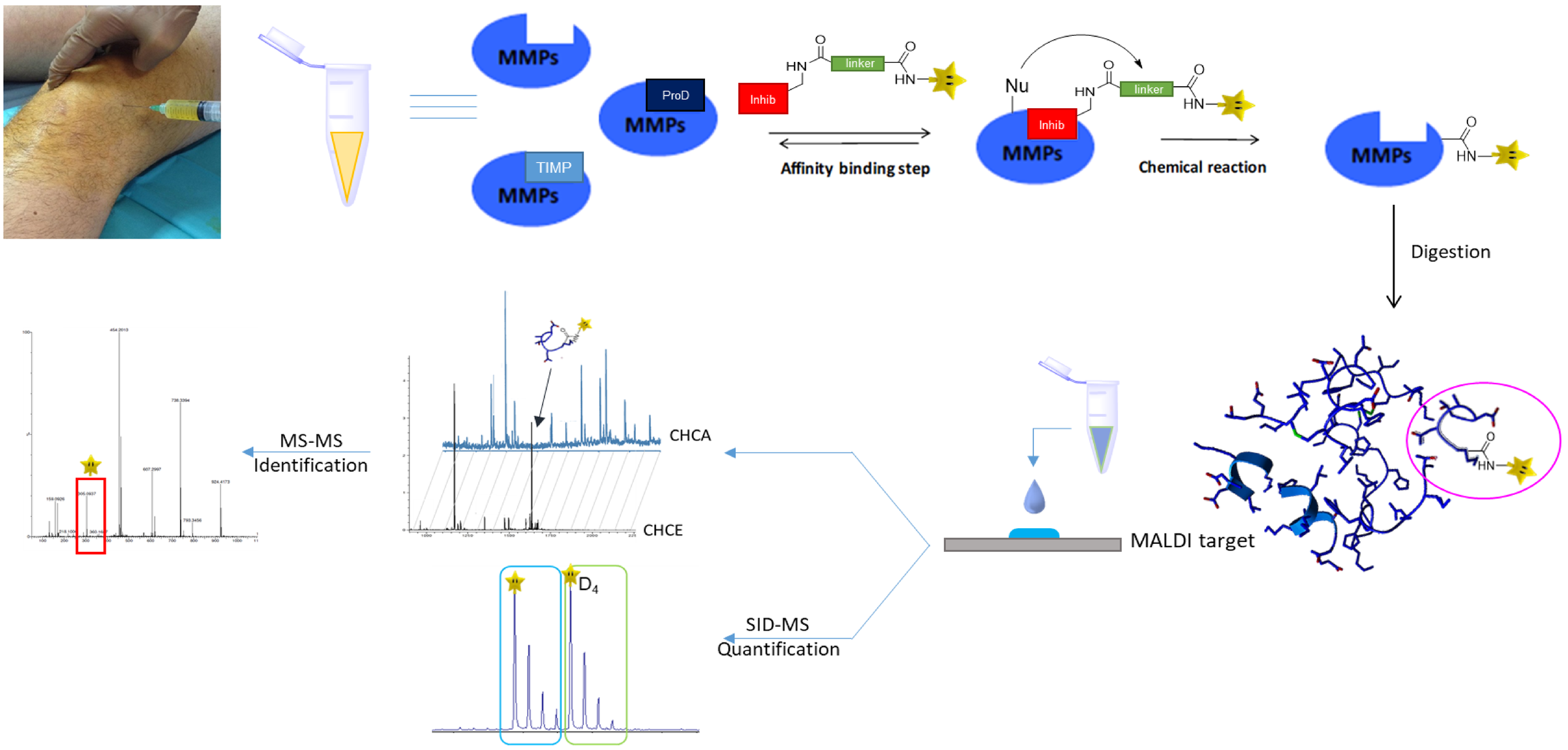
Development of novel molecular targeted probes for profiling metalloproteases activities by MALDI-mass spectrometry in synovial fluid

Goal:

Osteoarthritis (OA) is the most common form of arthritis, affecting millions of people worldwide. Detection of MMP activity in biological samples provides important information for diagnosis, prognosis, and therapeutic monitoring of these diseases.

Thanks to dedicated engineered biomolecular constructions based on (i) very affine ligands of MMPs, (ii) a reactive spacer and (iii) MS probes, we are able to transfer these activity based probes (ABP) on active MMPs, in the idea of identifying them by mass spectrometry (MS).

The objective is here to show the presence of specific active MMPs and quantify them in healthy synovial fluid or issued from osteoarthritis/ arthritis suffering patients. By varying designed probes and assisted by MALDI Mass spectrometry detection, we could hope to operate a multiplexing detection on several MMPs and define signature for each active MMP present in the synovial fluid via the generation of a specific fragment, thus allowing easier identification/activity/involvement of MMPs in such pathologies.



Collaboration / Contact

IBMM AAPPS Team - UMR 5247, leading the synthesis and mass spectrometry characterization of the designed chemical tools
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IRMB Inserm UMR 1183 (Biology of Mesenchymal stem cell and cartilage therapies) leading the synovial fluids processing.
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The successful candidate must present skills in chemistry / biochemistry in order to optimize / modify biomolecules of interest. He will evaluate fragments candidates by MALDI mass spectrometry, optimizing sample preparation (solvant, deposit mode,...) and study their limit of detection and quantification in complexed biological fluids.

He will also work at the **chemistry-biology interface** involving the need of performing chemical protein reactions, and deal with low quantities/ biological media. He will have to optimize bioconjugation experiments, protein enrichment and digestion experiments, suitable with MALDI mass spectrometry analyses.

In return, the trainee will be able to train in mastered techniques as support solid organic/peptide synthesis, LC/MS-ESI chromatography and MALDI Mass spectrometry.

[1] Simin L, Qiping S, Junyuan C, Huajun W, Wenrui W, Zhengang Z, Expression and Significance of MMPs in Synovial Fluid, Serum and PBMC Culture Supernatant Stimulated by LPS in Osteoarthritis Patients With or Without Diabetes, Exp Clin Endocrinol Diabetes **2019** ; 127: 195–202
[2] a) D. Paramelle, G. Subra, L. L. Vezenkov, M. Maynadier, C. Andre, C. Enjalbal, M. Calmes, M. Garcia, J. Martinez, M. Amblard, *Angew. Chem. Int. Ed.,* **2010**, 49, 8240–8243. b) M. Rossato, G. Miralles, C. M'Kadmi, D. Gagne, M. Maingot, M. Amblard, B. Mouillac, J. Martinez, G. Subra*, C. Enjalbal and S. Cantel*, "Quantitative MALDI-MS Binding Assays: an Alternative to Radiolabeling", *ChemMedChem*, **2016**, 11 (23), 2582-2587.
[3] L.Devel, M. Kaminska, P. Bruyat et al., "Ligand-directed modification of active Matrix Metalloproteases: New activity-based probes with no photolabile group" *Angew. Chem. Int. Ed.,* **2021,** doi.org/10.1002/anie.202106117.