

# Gold-promoted arylation of biomolecules: selenocysteine chemoselective modification by cyclometallated gold(III) compounds



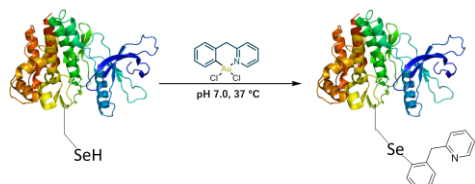
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## Introduction

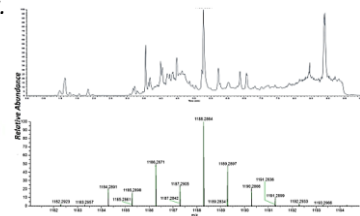
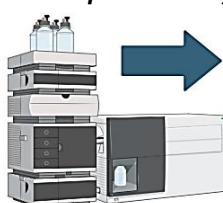
✓ A low pKa (5.2), high polarizable volume (3.8 Å), and proneness to oxidation under ambient conditions make **selenocysteine** (Sec, U) a unique, natural reactive handle present in most organisms<sup>1</sup>.

✓ Our investigation is focused on the use of cyclometallated gold(III) compounds for the **chemoselective arylation** of selenobiomolecules<sup>2</sup>

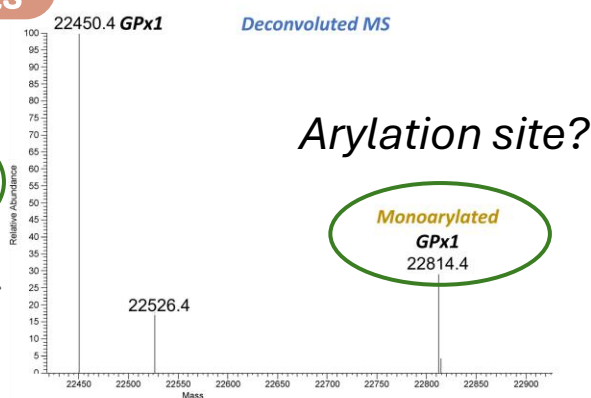
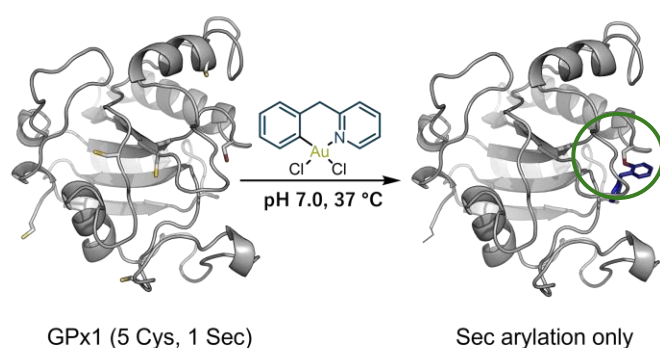


## Methods

✓ The ability of several organometallic gold(III) compounds to promote the C-Se coupling in the active sites of Glutathione Peroxidase and Thioredoxin Reductase was studied by **liquid chromatography** coupled to **electrospray tandem mass spectrometry**.



## Results



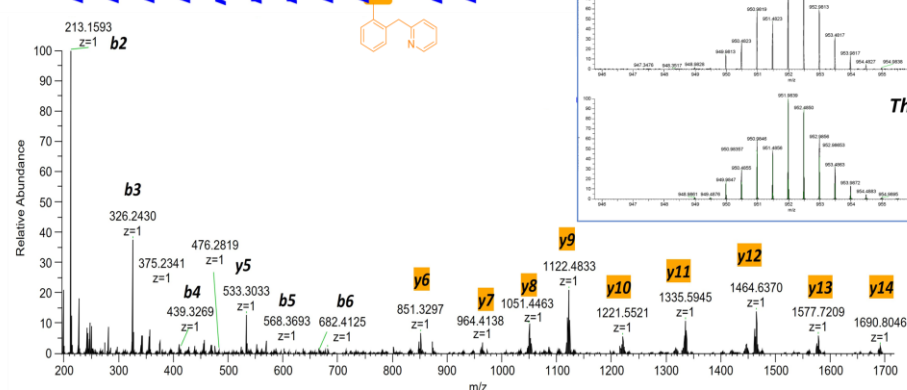
### 1. Top-down approach

N **C** A A Q R S A A **A** L L A A A A P R T V Y A F S A R P 25  
 26 L A G G E **L** P F N L S S L R G K V L L **I** E N V A **S** L 50  
 51 **U** G T T **V** R D Y T **Q** M N D L Q R R **L** G P R G L V V 75  
 76 L G F P **C** N Q F G H Q E N A K N E E I L N **C** L K Y 100  
 101 V R P G G G F E **L** P N F M L F E K **C** E V N G E K A H 125  
 126 P L **F** A F L R E V L P T **L** P S D D A T **L** A L L M **L** D P K 150  
 151 F I T W S **L** P V **C** R N D V S W **N** F E K F L V G P D **G** 175  
 176 V P V R R Y S R R F L T I D I E P D **I** E T L L S **Q** 200  
 201 G A S A **C**

✓ Elucidation of arylation site by ms/ms fragments

### 2. Bottom-up approach

V L L L I E N V I A S L L **U** G T T V R



✓ Identification of the arylated tryptic selenopeptide



The conditions enabling the **selective arylation of Se (Sec)** over S (Cys) were found in GPx1 protein, containing both Sec and Cys. Moreover, in **competitive experiments**, selenopeptides are preferentially arylated by gold(III) compounds, even in the presence of large excess of their Cys counterparts

### References

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**Acknowledgements:** This research has received funding from the European Union's Horizon H2020 Research and Innovation under the Marie Skłodowska-Curie Grant Agreement N° 945416 through the PhD fellowship of IK. This project has also received funding from "la Caixa" Foundation (ID 100010434) through the Junior Leader fellowship to RdP (LCF/BQ/PI22/11910033).