

# Metallothionein complexes with superoxide dismutase

Marta Zalewska

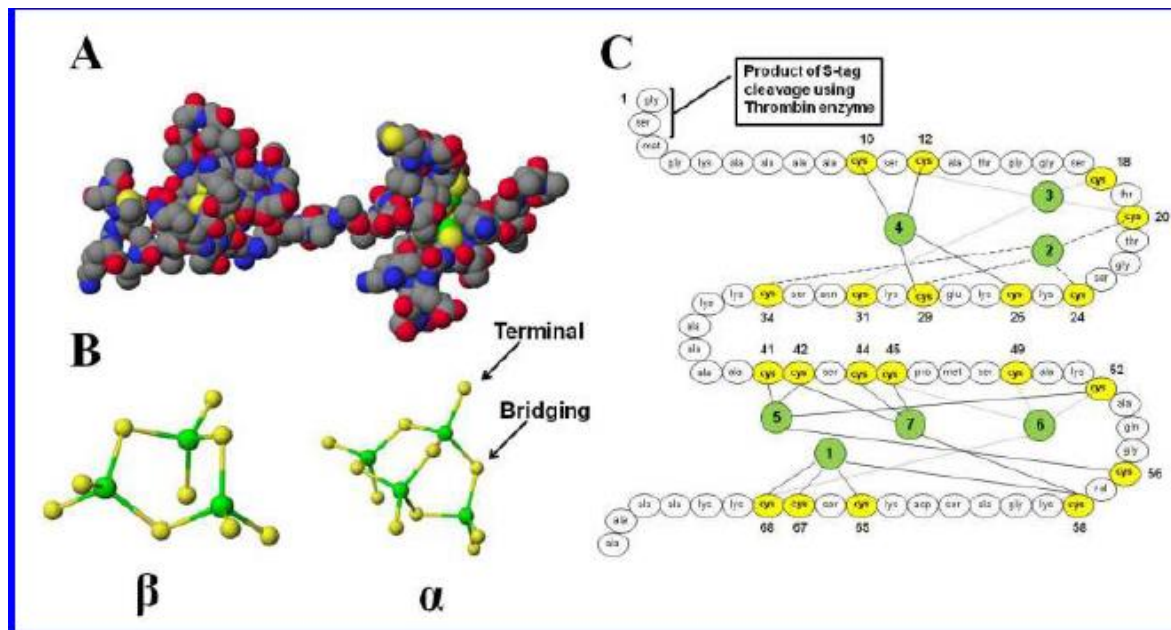
Datum : 18.7.2014

Reg.č.projektu: CZ.1.07/2.3.00/20.0148

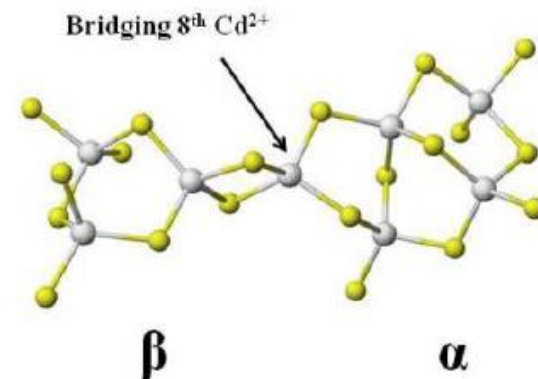
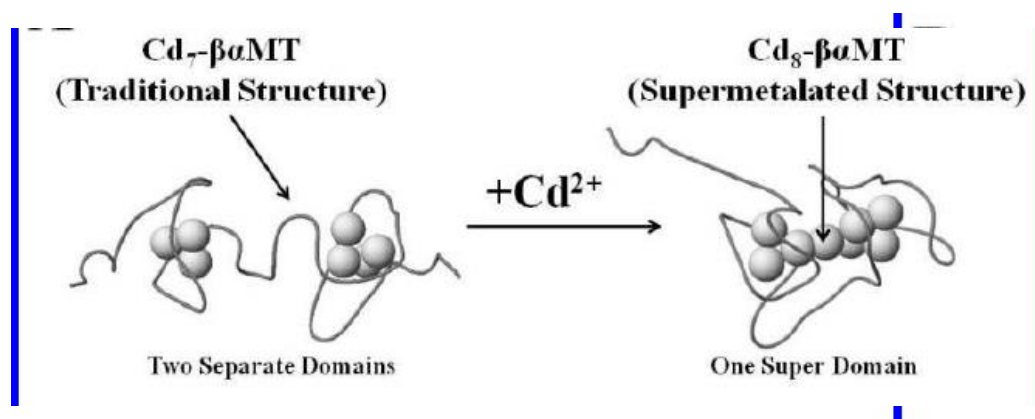
Název projektu: Mezinárodní spolupráce v oblasti "in vivo" zobrazovacích technik



# MTs



human MT 1a, well-known to coordinate 7 Zn(2+) or Cd(2+) ions with 20 cysteinyl thiols, will bind 8 structurally significant Cd(2+) ions, leading to the formation of the **supermetalated** Cd(8)-β $\alpha$ -rhMT 1a species, for which the structure is a novel single domain.



# Comparison of MT sequences in human and rabbit

**A**

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***** . **:*:.**.*:*:*****.*****:.*:***:***:***: ::* **
P04731|MT1A_HUMAN MDPNCSCAT-GG SCTCTG SCKCKECKCTSCKKSCCSCCPM SCAKCAQGCICKGASEKCSCCA 61
Q93083|MT1L_HUMAN MDPNCSCAT-GG SCSASSCKCKECKCTSCKKSCCSCCPM GCAKCAQGCVCCKGASEKCSCCA 61
P04732|MT1E_HUMAN MDPNCSCAT-GG SCTCAGSCKCKECKCTSCKKSCCSCCPV GCAKCAQGCVCCKGASEKCSCCA 61
P04733|MT1F_HUMAN MDPNCSCAA-GV SCTCAGSCKCKECKCTSCKKSCCSCCPV GCSKCAQGCVCCKGASEKCSCCD 61
P13640|MT1G_HUMAN MDPNCSCAAAGV SCTCASSCKCKECKCTSCKKSCCSCCPV GCAKCAQGCICKGASEKCSCCA 62
P80294|MT1H_HUMAN MDPNCSCEA-G S CACAGSCKCKKCKCTSCKKSCCSCCPL GCAKCAQGCICKGASEKCSCCA 61
P80297|MT1X_HUMAN MDPNCSCSP-V G S CACAGSCKCKECKCTSCKKSCCSCCPV GCAKCAQGCICKGTS DKCSCCA 61
P07438|MT1B_HUMAN MDPNCSCTT-G G S CACAGSCKCKECKCTSCKKCCCSCCPV GCAKCAQGCVCCKGSSEKCRCCA 61
Q8N339|MT1M_HUMAN MDPNCSCTT-G V S CACTG SCTCKECKCTSCKKSCCSCCPV GCAKCAHGCVCCKGTLENCSCCA 61
P02795|MT2_HUMAN MDPNCSCAA-G D S C T C A G S C K C K E C K C T S C K K S C C S C C P V G C A K C A Q G C I C K G A S D K C S C C A 61
1.....10.....20.....30.....40.....50.....60..

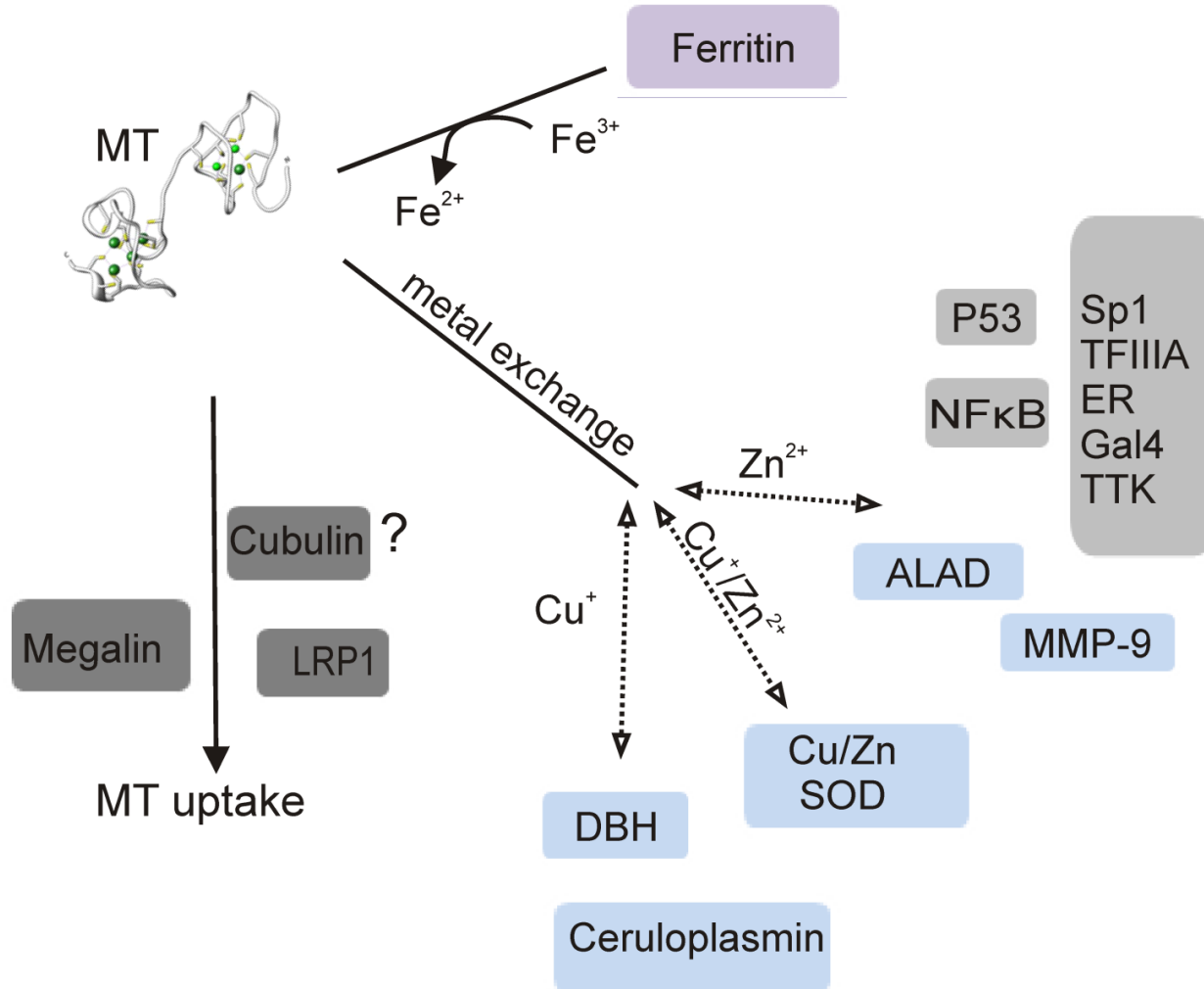
*****: : **:*:.**.* ** *****.***** **
P80291|MT2D_RABIT MDPNCSCAT-FD S CACASSCKCKECKCTSCKKSCCSCCPAG CTKCAQGCICKGASDKCSCCA 61
P80292|MT2E_RABIT MDPNCSCAT-FD S CACASSCKCKECKCTSCKKSCCSCCPAG CTKCAQGCICKGALDKCSCCA 61
P11957|MT1A_RABIT MDPNCSCAT-GN S C T C A S S C K C K E C K C T S C K K S C C S C C P A G C T K C A Q G C I C K G A S D K C S C C A 61
P80289|MT2B_RABIT MDPNCSCAT-GD S C T C A S S C K C K E C K C T S C K K S C C S C C P A G C T K C A Q G C I C K G A S D K C S C C A 61
P80290|MT2C_RABIT MDPNCSCATAGD S C T C A N S C T C K A C K C T S C K K S C C S C C P P G C A K C A Q G C I C K G A S D K C S C C A 62
P18055|MT2A_RABIT MDPNCSCAAAGD S C T C A N S C T C K A C K C T S C K K S C C S C C P P G C A K C A Q G C I C K G A S D K C S C C A 62
1.....10.....20.....30.....40.....50.....60...

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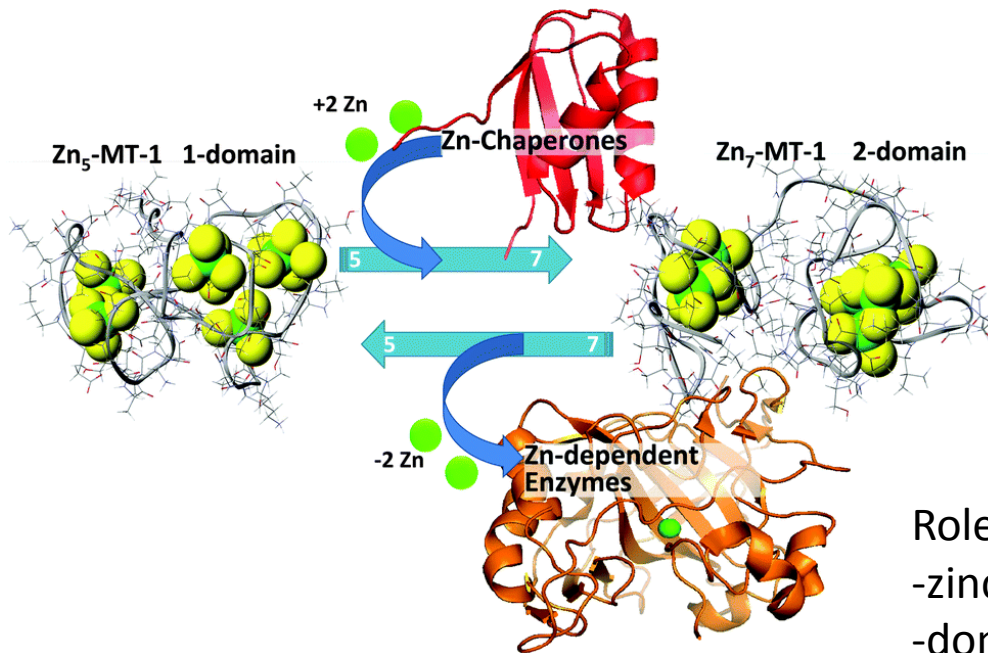
**B**

Thompson J., Higgin D., Gibson T.: CLUSTALW: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position specific gap penalties and weight matrix choice. Nuc. Acids Res., 1994, 22, 4673-4680.

# MT interactions



# The role of Zn-MT in providing homeostatic control in cells



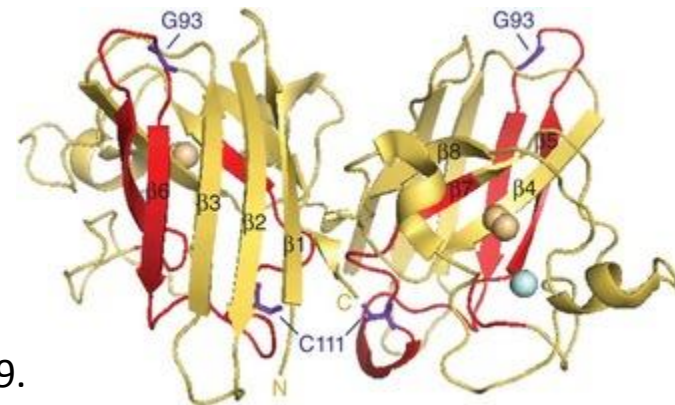
Roles of MT in Zn<sup>2+</sup> trafficking

- zinc sequestering and zinc storage proteins
- donate zinc ions to apoproteins
- upon oxidation releasing bound metal ions
- intracellular zinc reservoirs and as ROS 'sensors'
- exchanging metal ions, such as Cd<sup>2+</sup> for Zn<sup>2+</sup>
- cellular antioxidant reducing agent

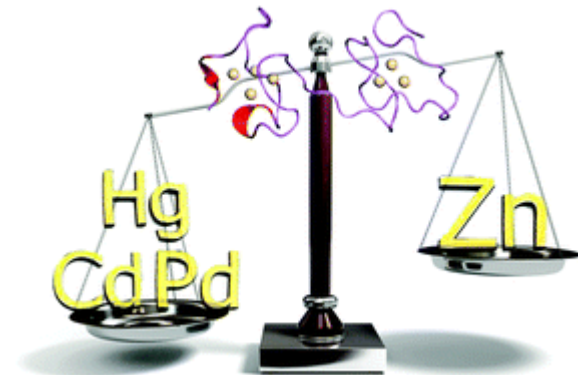
# Superoxide Dismutase



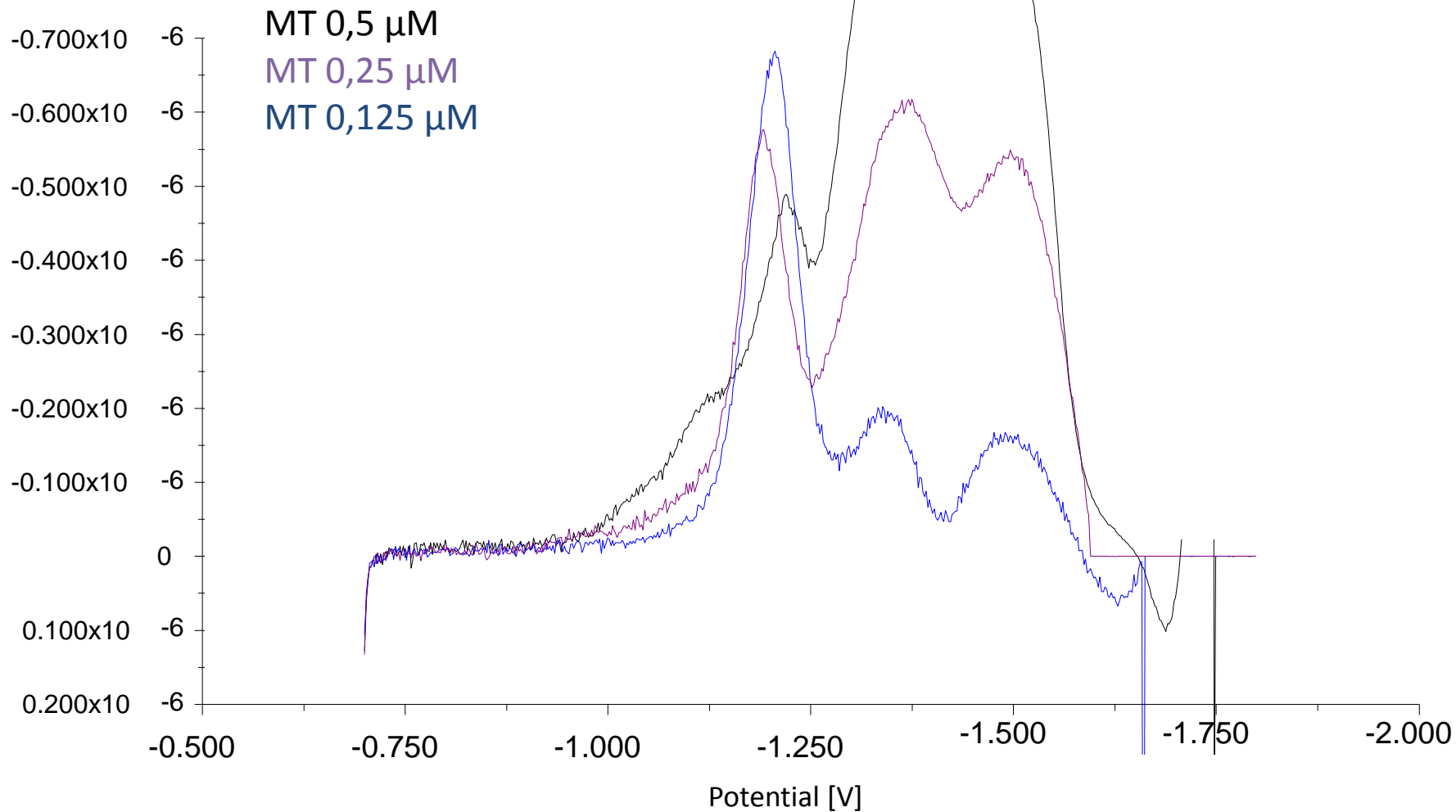
- SOD is a representative of the primary defense against oxidative damage.
- It is a metalloenzyme that exists in all oxygen consuming organisms.
- There are three forms of SOD differentiated by the metal ions:
  - **Cu<sup>2+</sup>/Zn<sup>2+</sup> SOD** => cytoplasm, mitochondrial intermembrane space
  - **Mn<sup>2+</sup>SOD** => mitochondrial matrix space
  - **Fe<sup>2+</sup>SOD** => Procaryota, and some plants



- MT and SOD have been proposed as biomarkers indicative of metal exposure and oxidation stress.
- They also could act as parameters for estimating the efficiency of the detoxification and antioxidation mechanisms in organisms.
- Interaction of Zn-MT with Cu/Zn-SOD will be analyzed.
- Apo and holo forms of MT and SOD and influence of Zn association with proteins on their interaction will be verified.

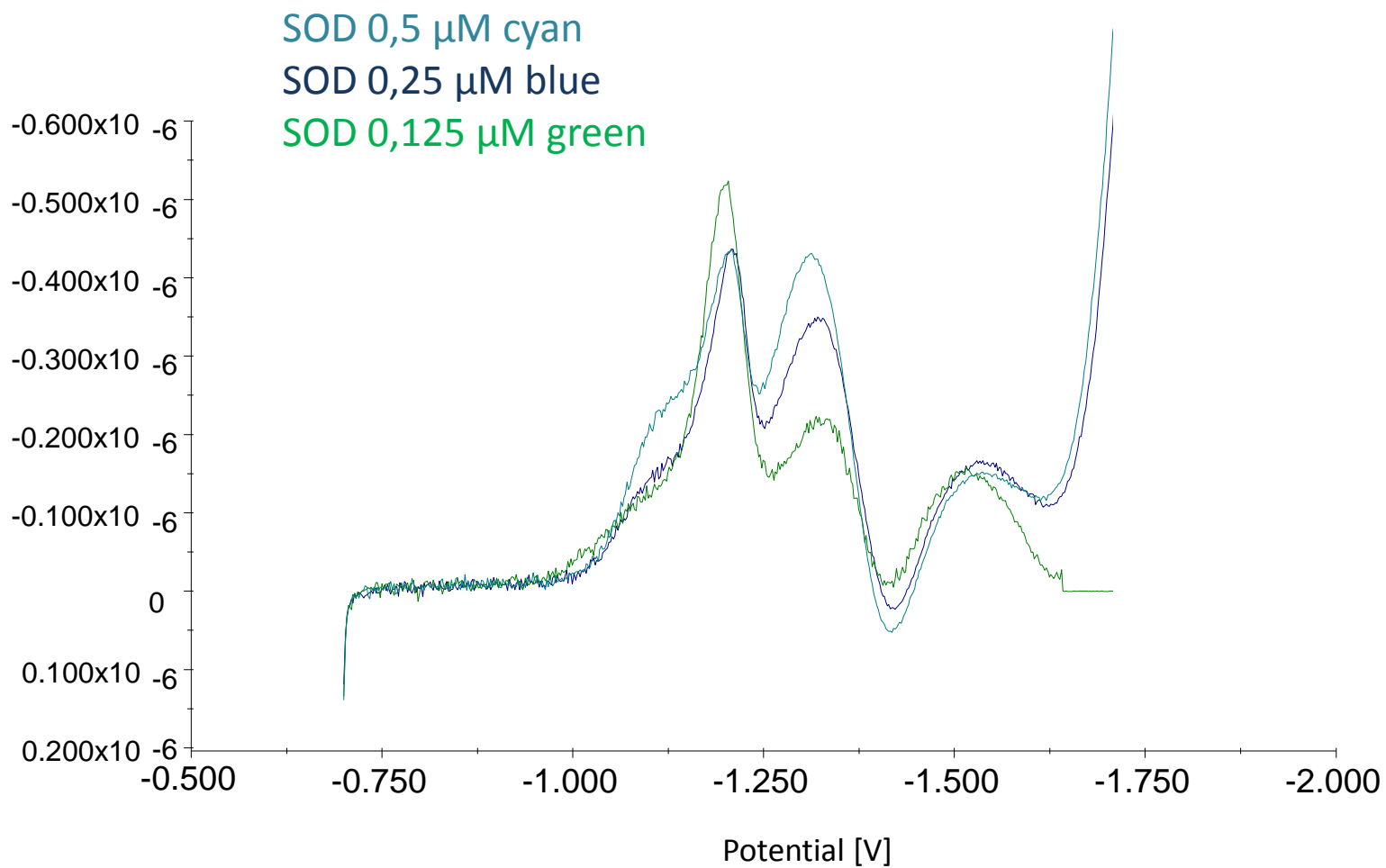


# Metalothionein on Brdicka reaction

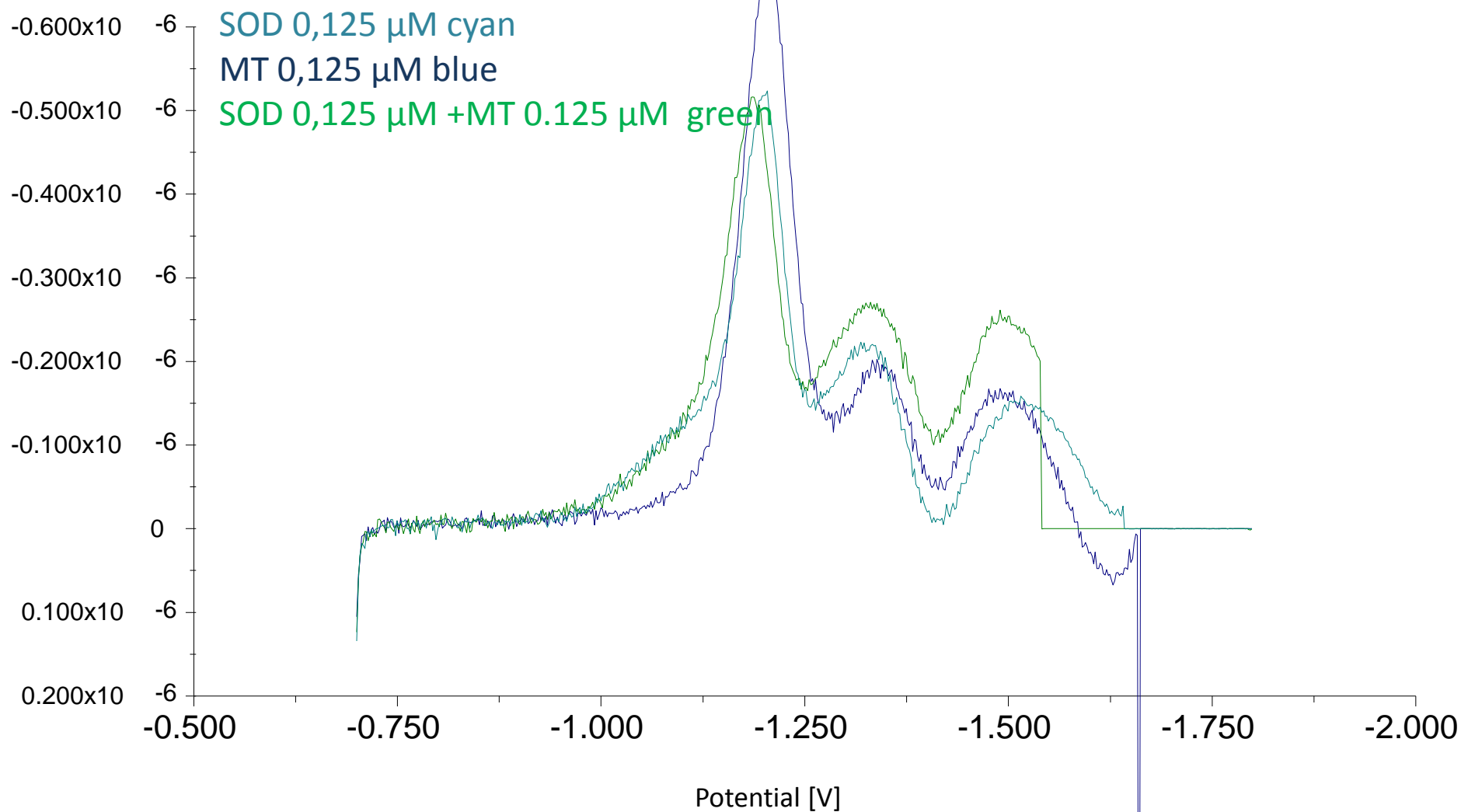




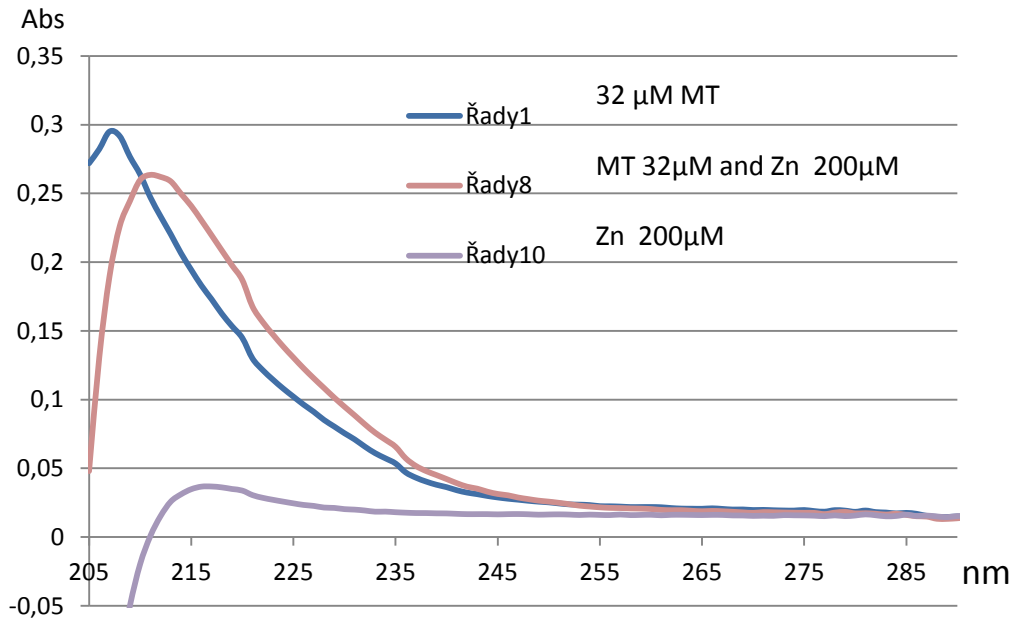
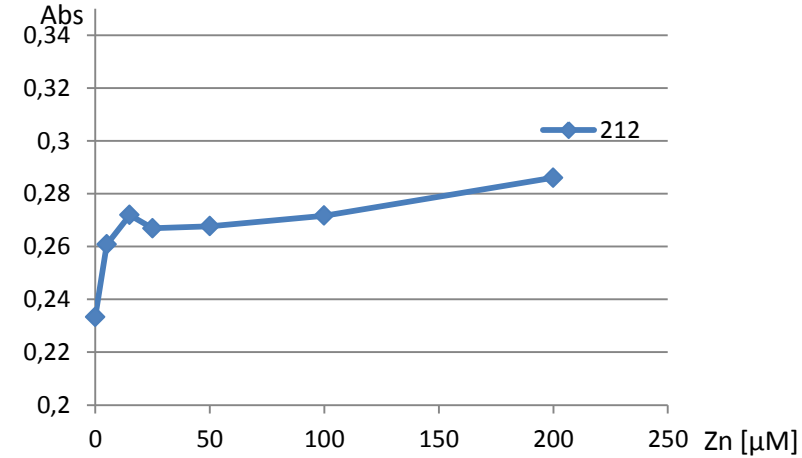
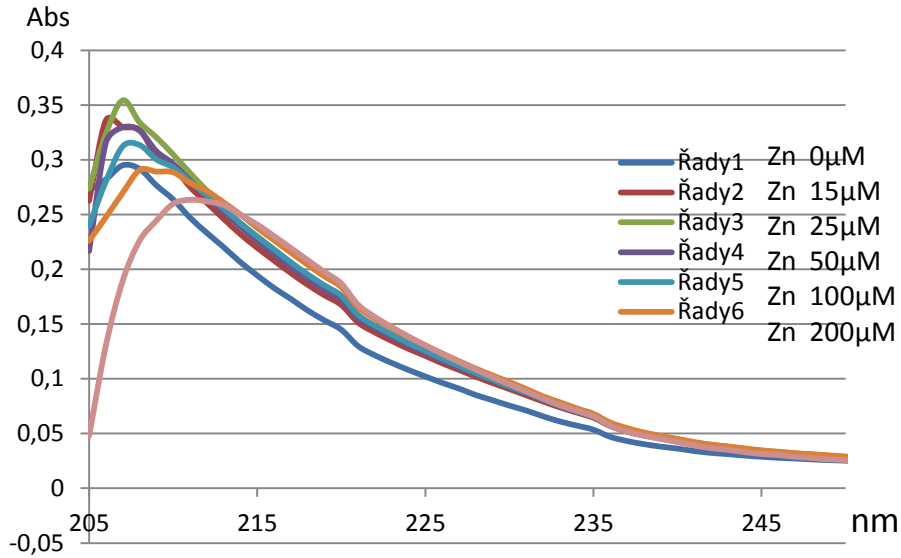
# Superoxide dismutase on Brdicka reaction



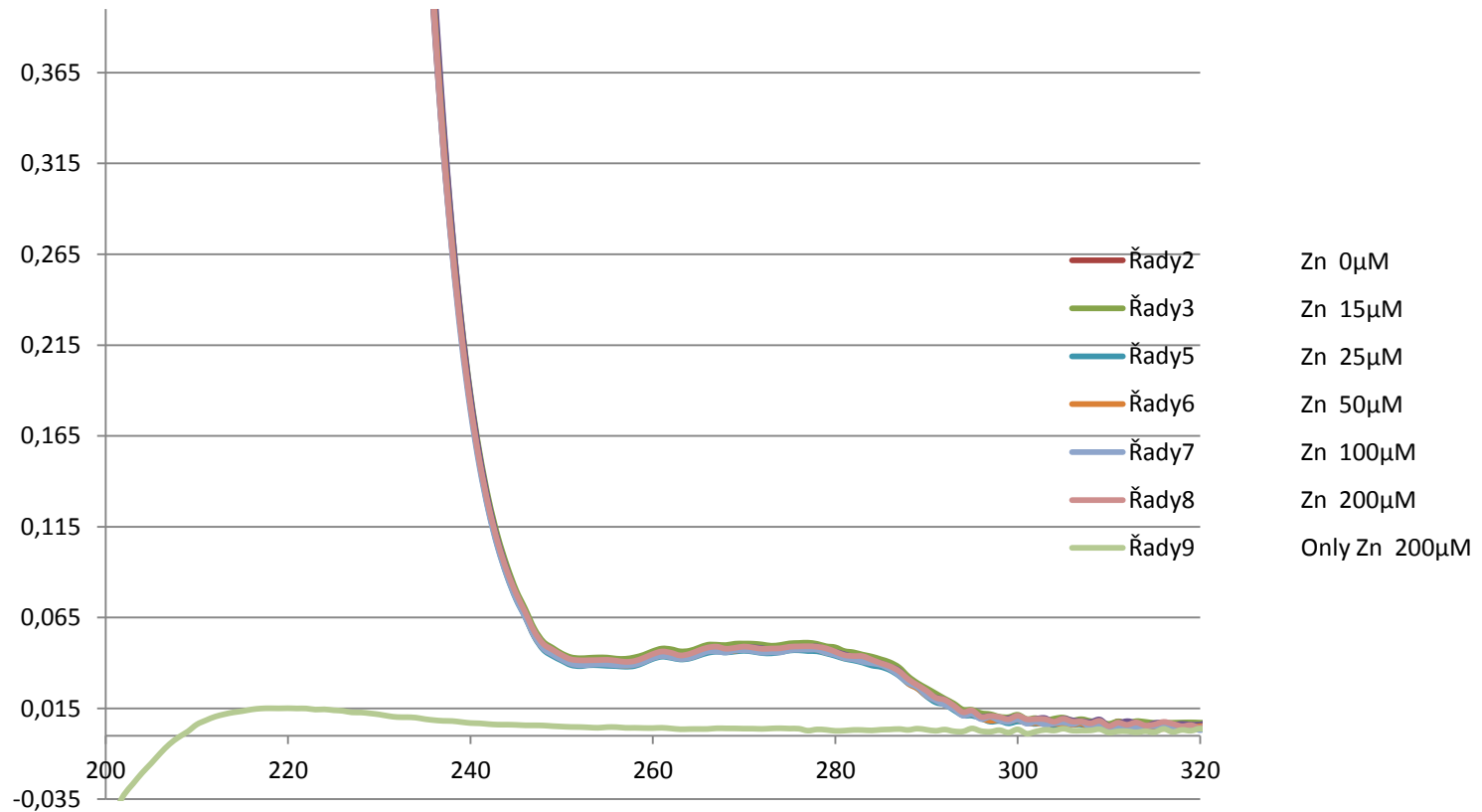
# MT and SOD on Brdicka reaction



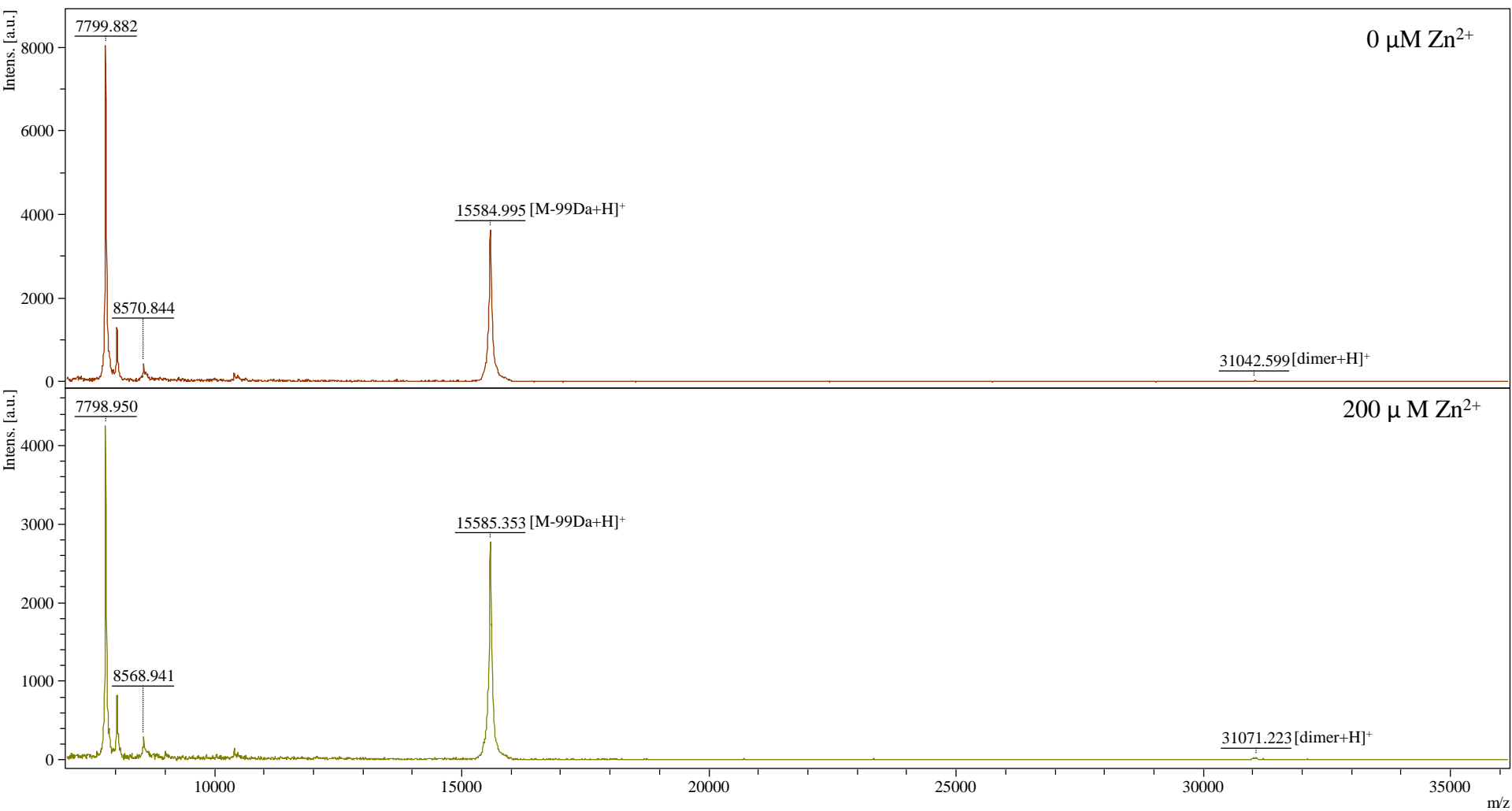
# Binding of Zn<sup>2+</sup> (ZnCl<sub>2</sub>) by MT1/2



# Binding of Zn<sup>2+</sup> (ZnCl<sub>2</sub>) by SOD



Mass spectra of SOD1 with and without 200  $\mu\text{M}$   $\text{Zn}^{2+}$ ;  $M = 15683$  Da;  
linear positive mode; HCCA matrix; laser 40 %.

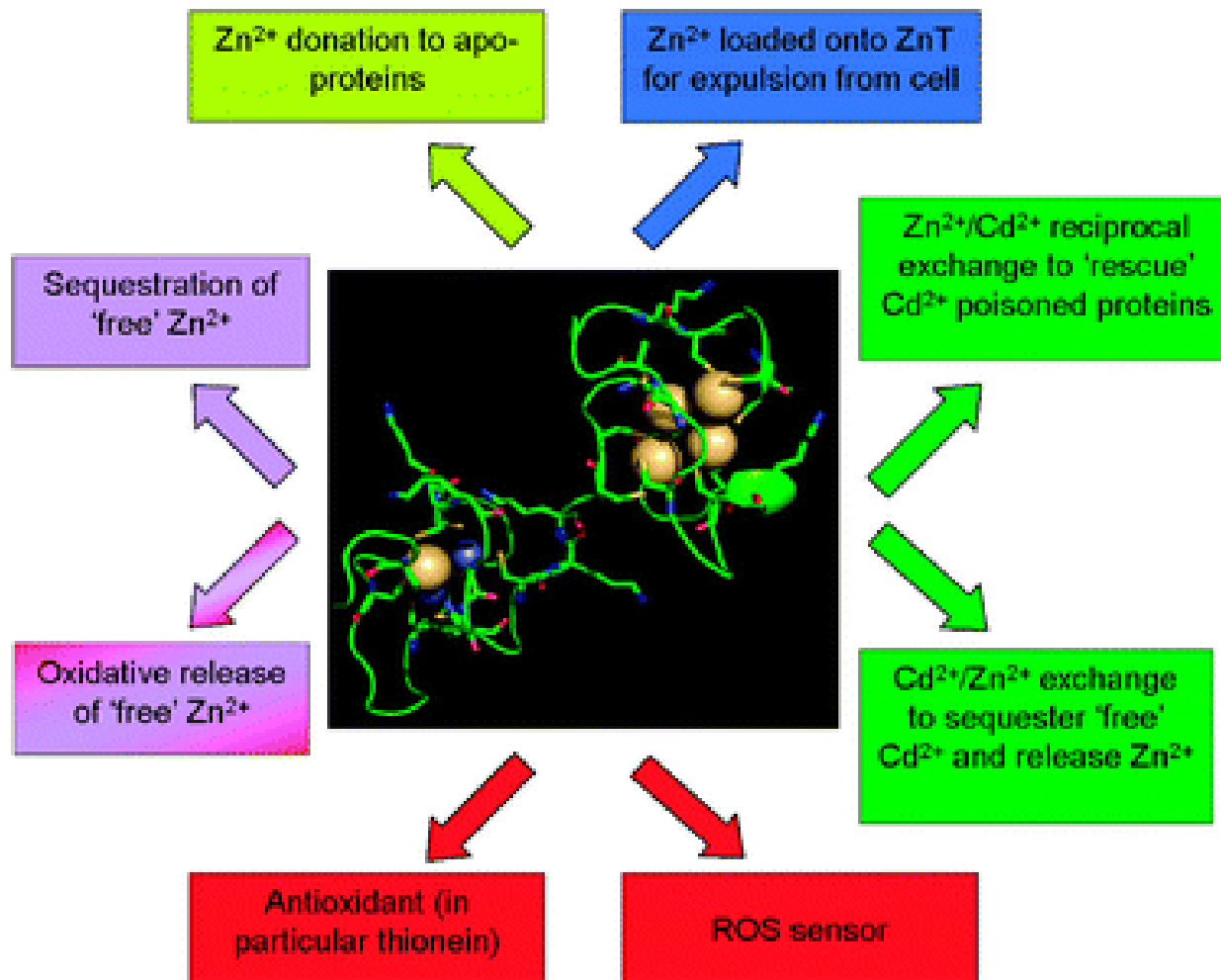


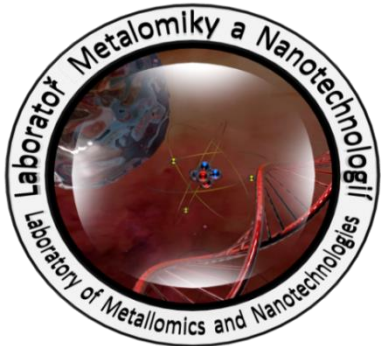
Thank you for your attention

Děkuji za pozornost



# Roles of MT in Zn<sup>2+</sup> trafficking





Mendel  
University  
in Brno



WROCLAW  
MEDICAL UNIVERSITY



Thank you for your attention!



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MLÁDEŽE A TĚLOVÝCHOVY



OP Vzdělávání  
pro konkurenceschopnost

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ