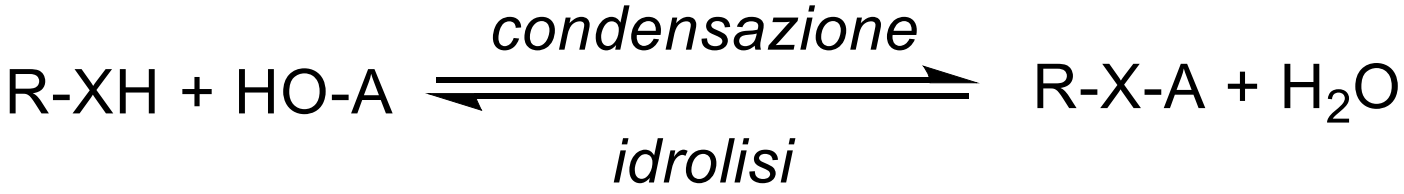
# $Zn^{2+}$ come acido di Lewis

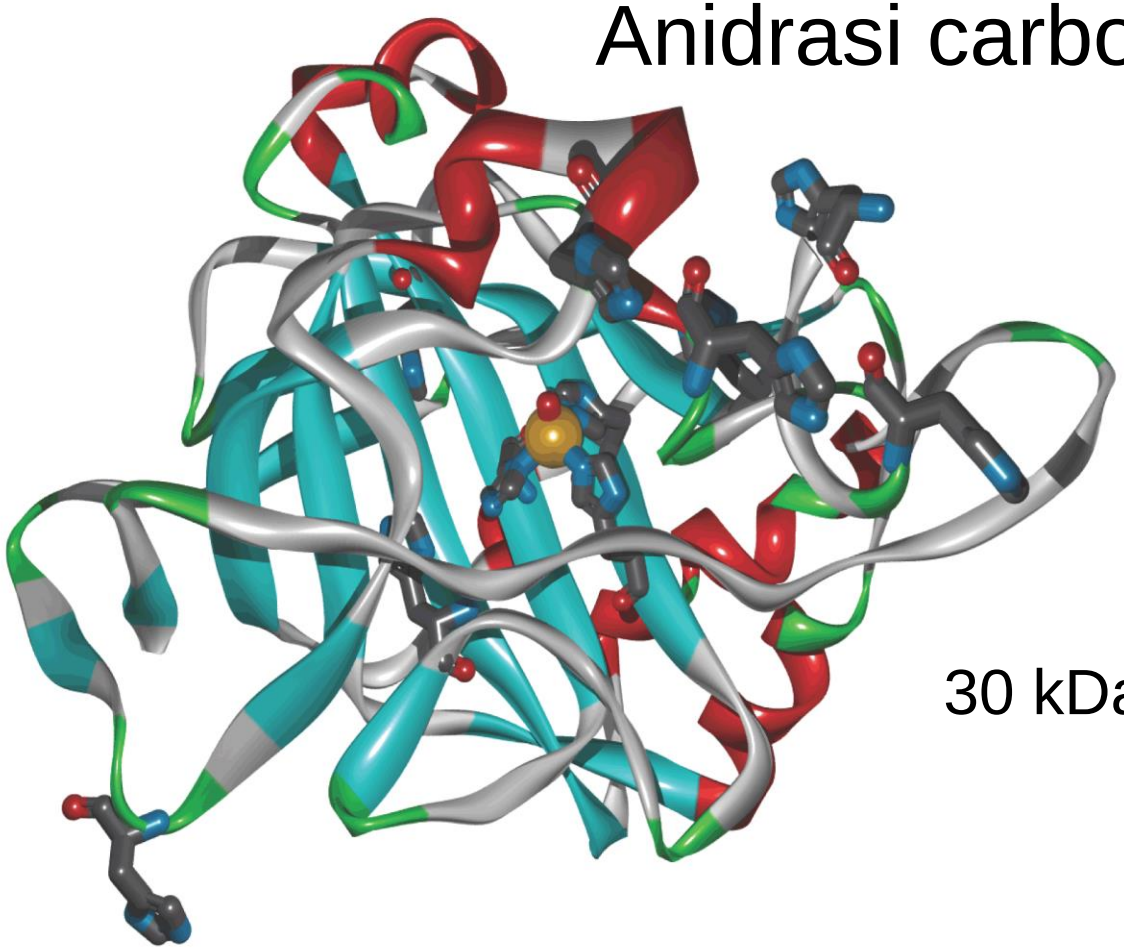

Lo ione idrosso coordinato allo zinco, $[Zn\text{-}OH]^+$, è meno nucleofilo di $OH^-$ libero, ma decisamente più nucleofilo di $H_2O$ e molto più abbondante di $OH^-$ a pH fisiologico.




| | |
|---|---|
| X = NH, A = -CO-R | *peptidasi, lattamasi, collagenasi* |
| X = O, A = -CO-R | *esterasi* |
| X = O, A = $PO_3^{2-}$ | *fosfatasi, nucleasi* |

- Esclusivamente $Zn^{2+}$
- $d^{10}$ (no LFSE)
- Numeri di coordinazione e geometria flessibili
- Ruolo catalitico (acido di Lewis) o strutturale
- Più di 200 Zn-proteine (*zincosoma*)

# Anidrasi carbonica

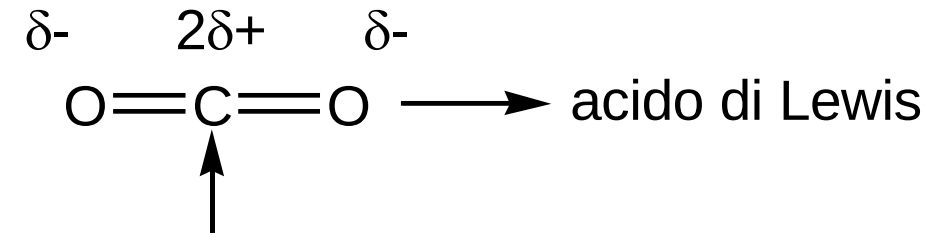


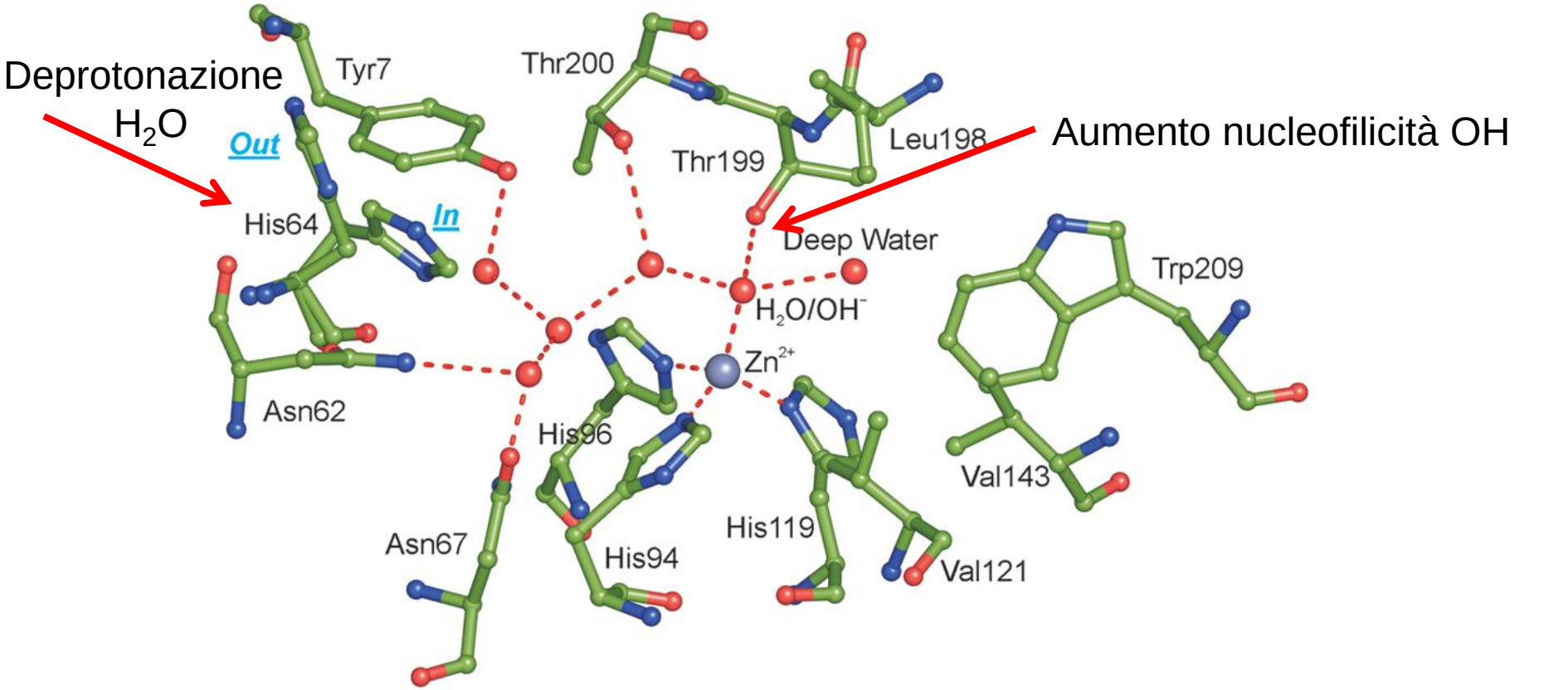
30 kDa, 259 a.a.

$$H_2O + CO_2 \rightleftharpoons HCO_3^- + H^+$$

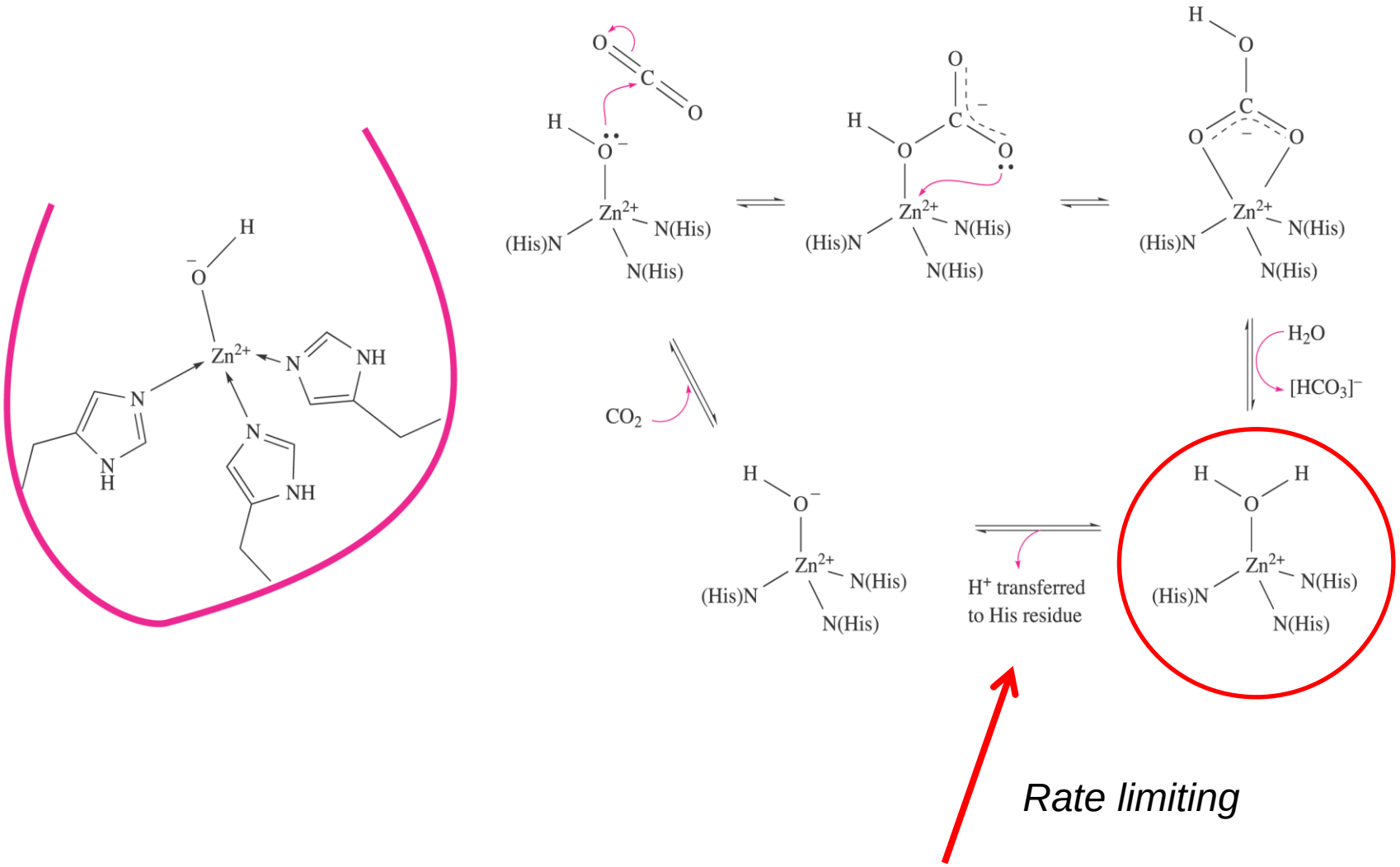
$k \approx 10^{-1}\ s^{-1} \rightarrow 10^{6}\ s^{-1}$

# Sito catalitico della anidrasi carbonica



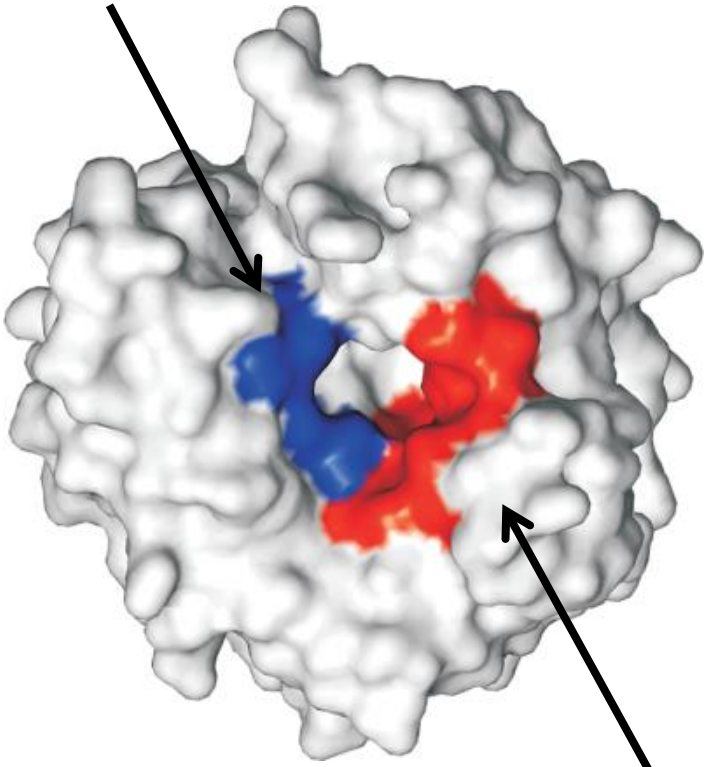



# Ciclo catalitico della anidrasi carbonica

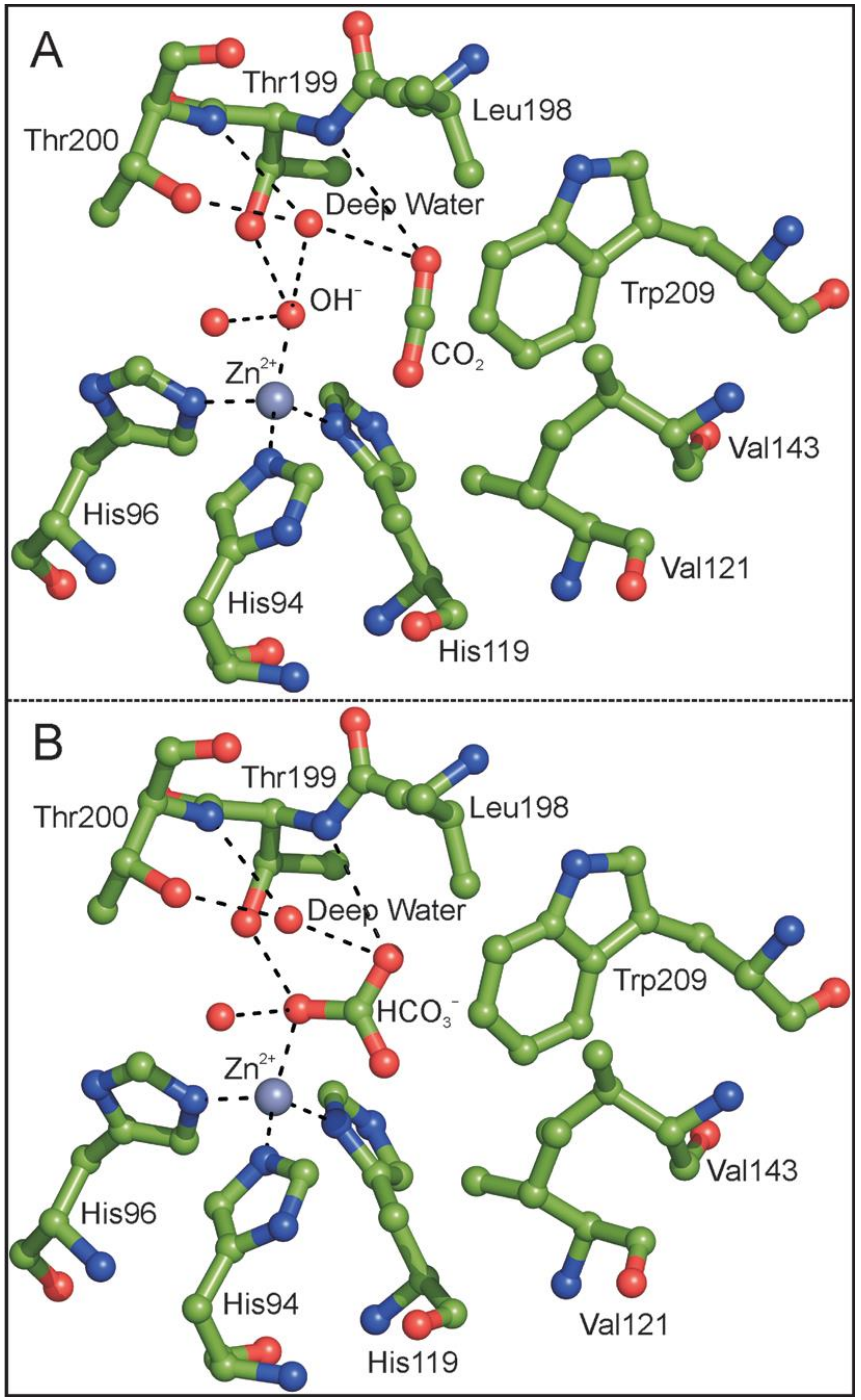


# Cavità del sito catalitico nelle CA

Regione idrofilica

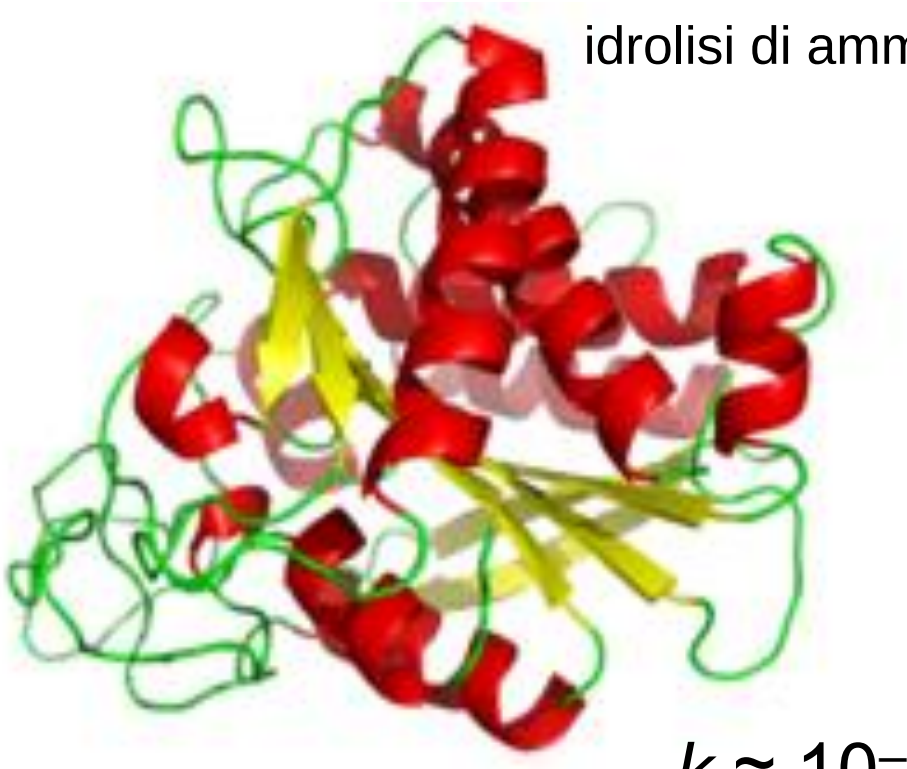


Regione idrofobica



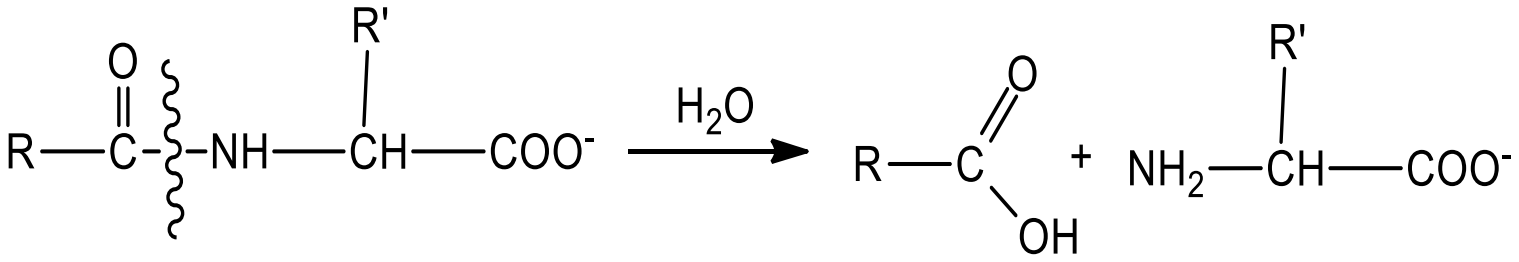
# Carbossipeptidasi A (CPD A)

idrolisi di amminoacidi C-terminali

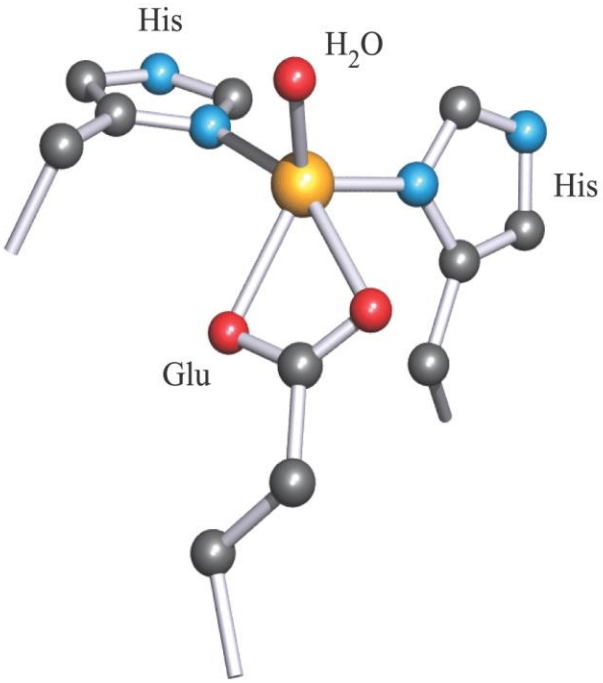


34 kDa, 300 a.a.

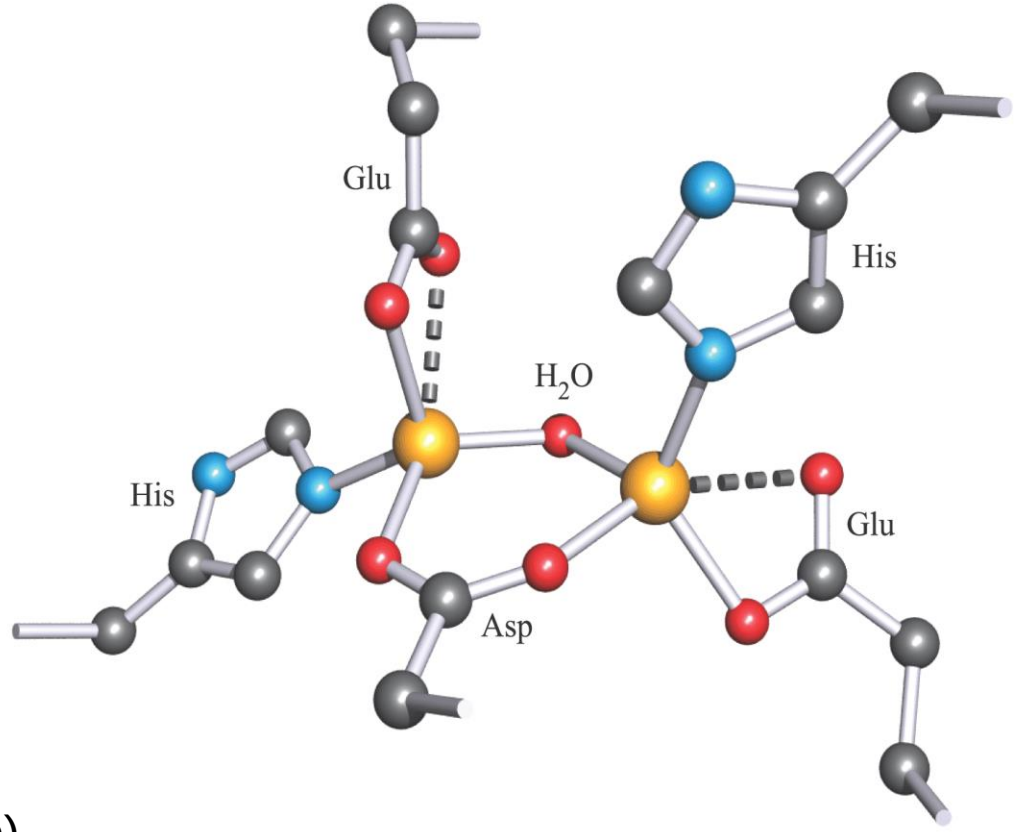
$k \approx 10^{-11}\ s^{-1} \rightarrow 10^{4}\ s^{-1}$



# Siti attivi di carbossipeptidasi

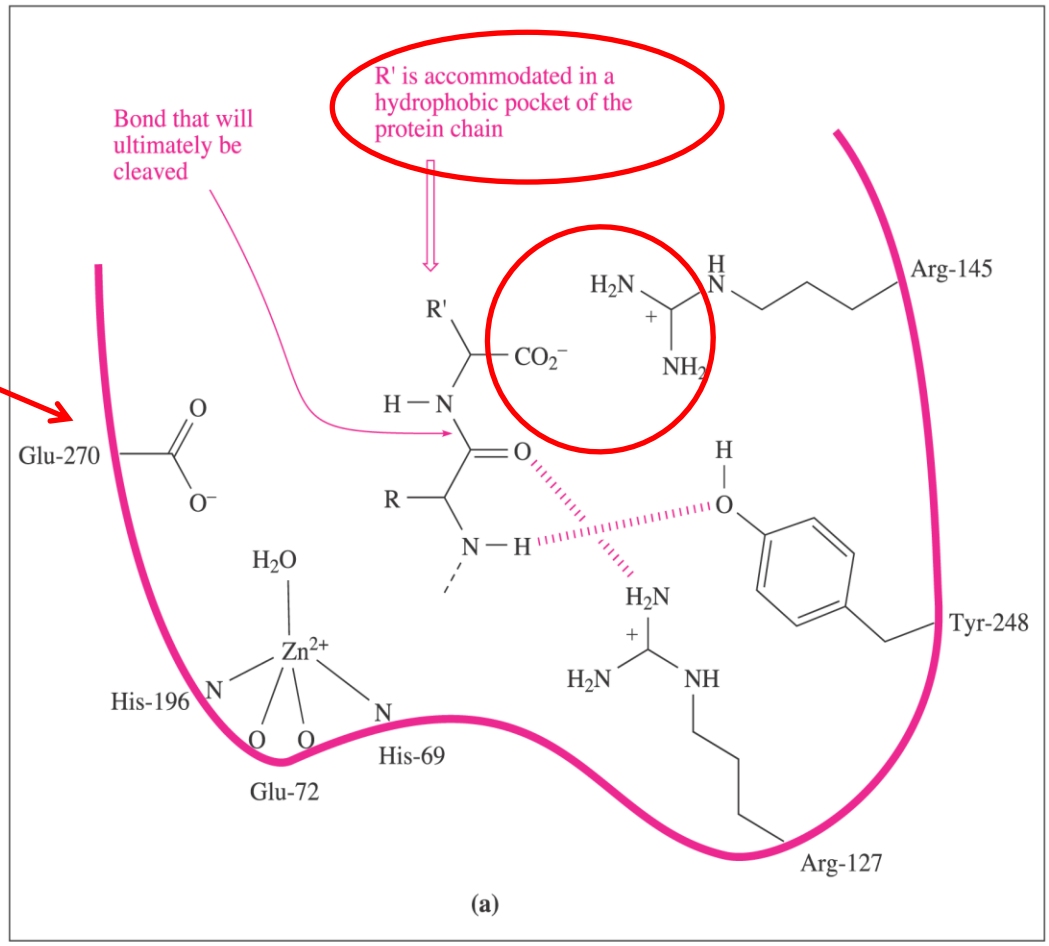



Carbossipeptidasi A (CPD A, bovino)

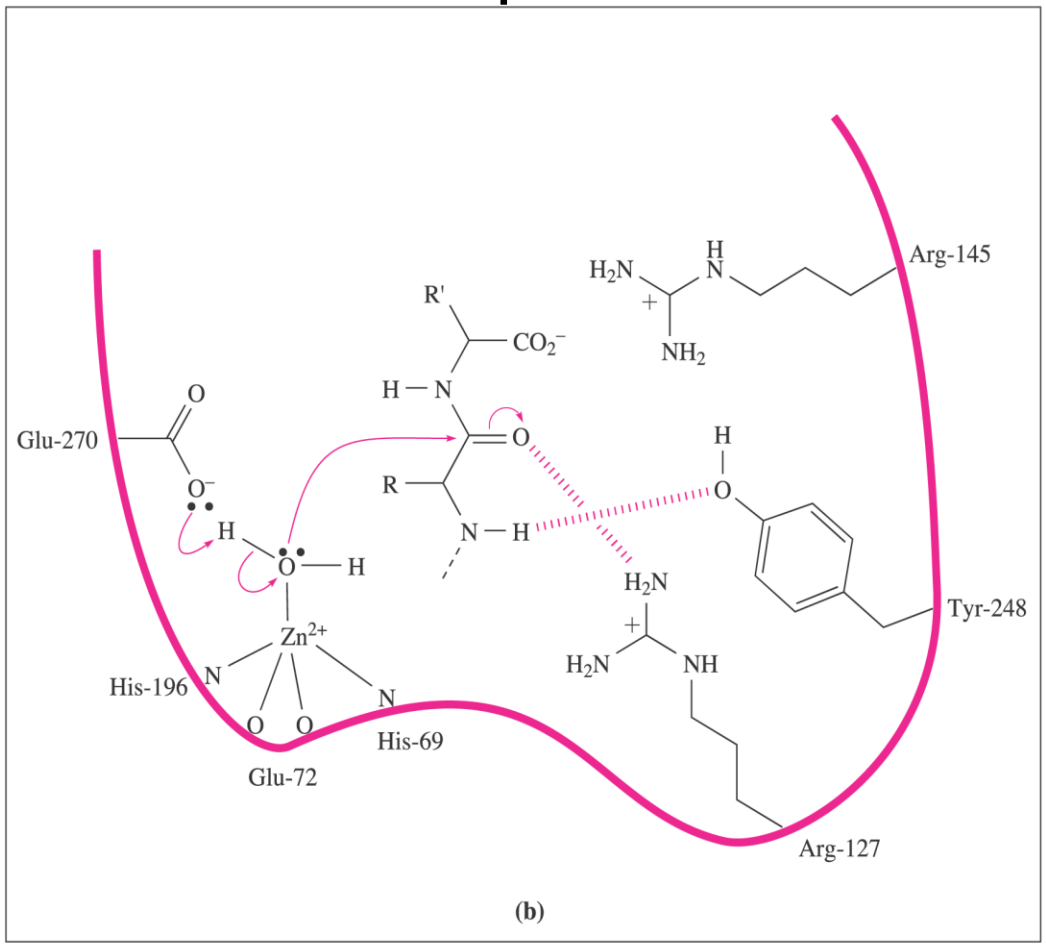



Carbossipeptidasi G2 (CPG2, batterio)

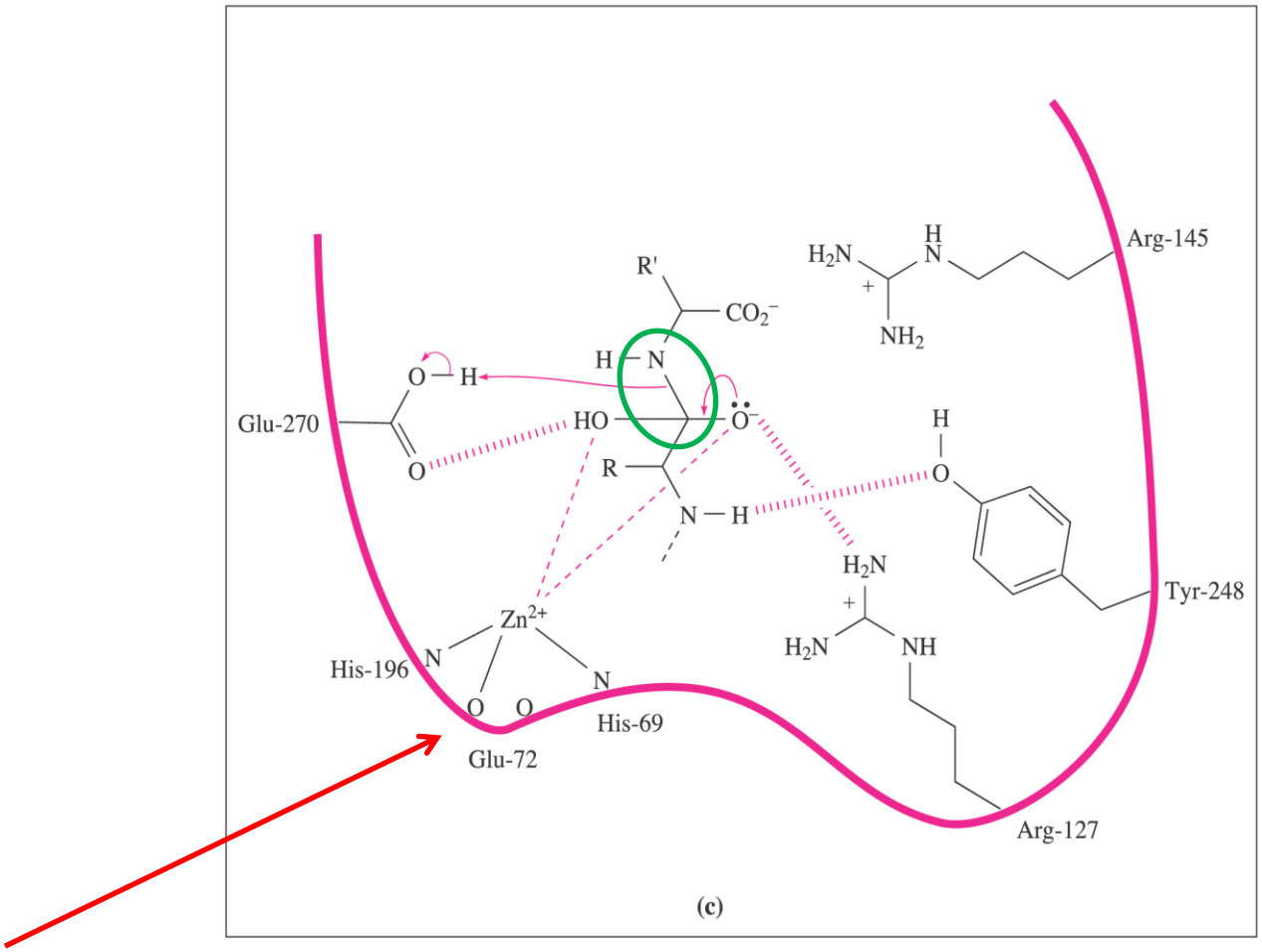
# Posizionamento del substrato vicino al sito attivo della CPA



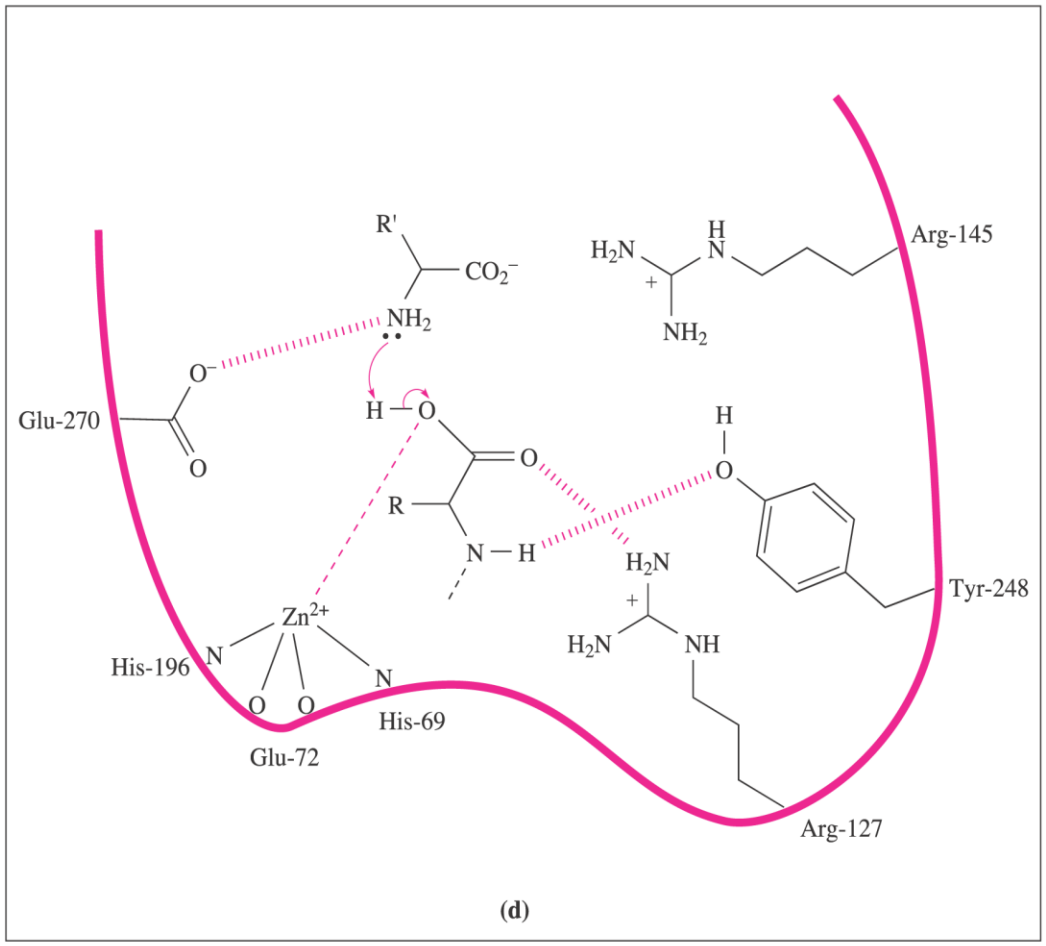
# Deprotonazione dell'acqua e attacco nucleofilo



# Rottura del legame peptidico C–N

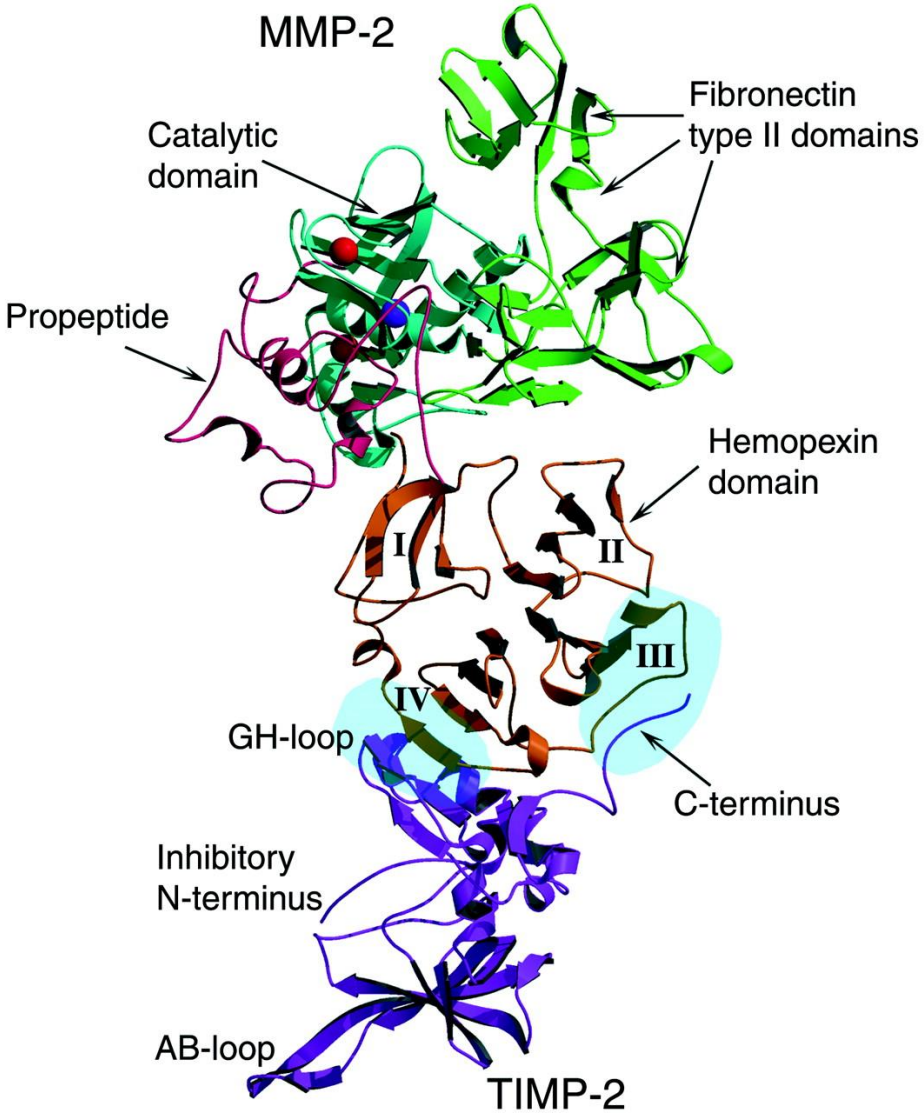


# Trasferimento di un protone con formazione di $NH_3^+$ e del carbossilato




(d)

# Matrix MetalloProteinases (MMPs) + Tissue Inhibitors of MetalloProteinases (TIMPs)

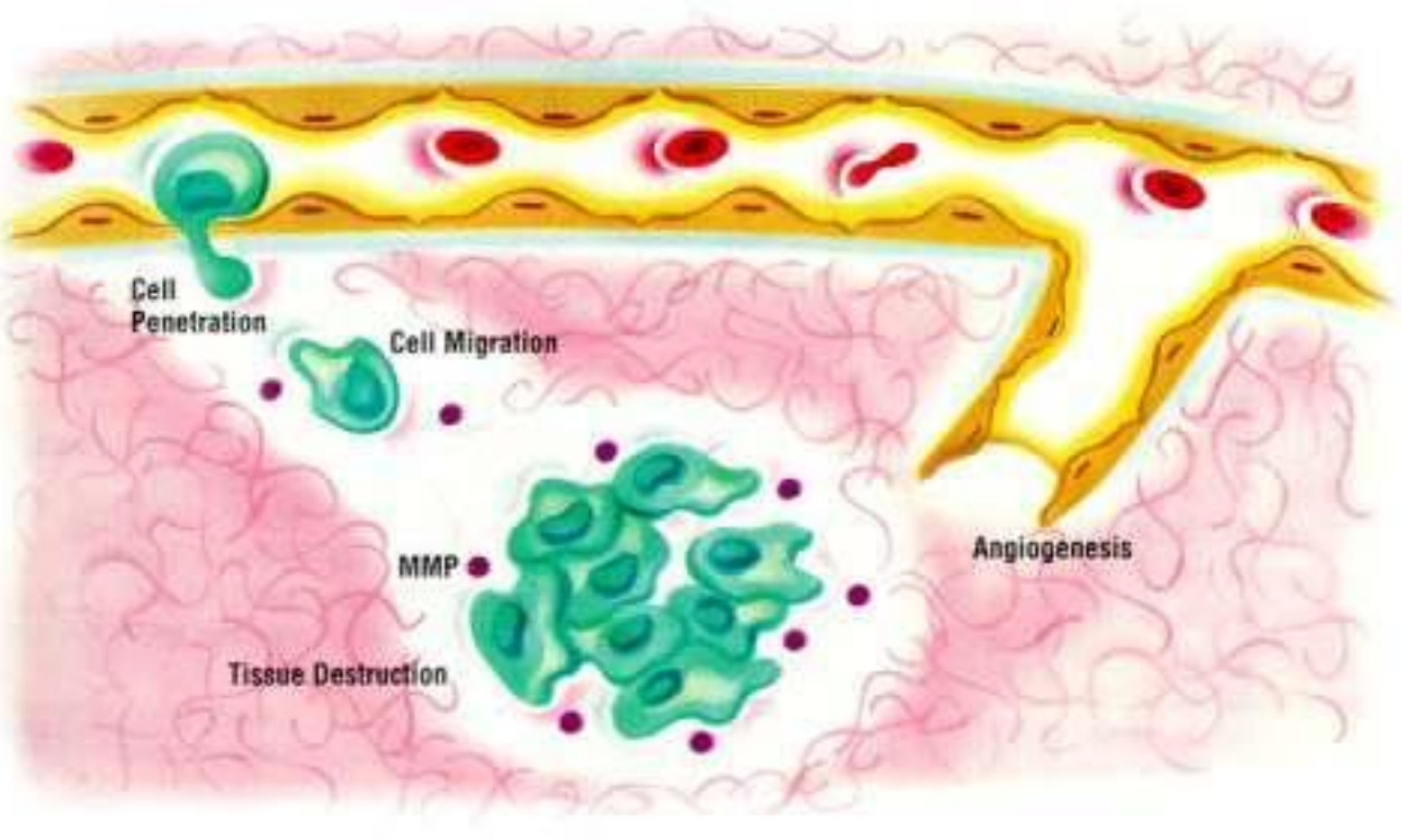



= Zn

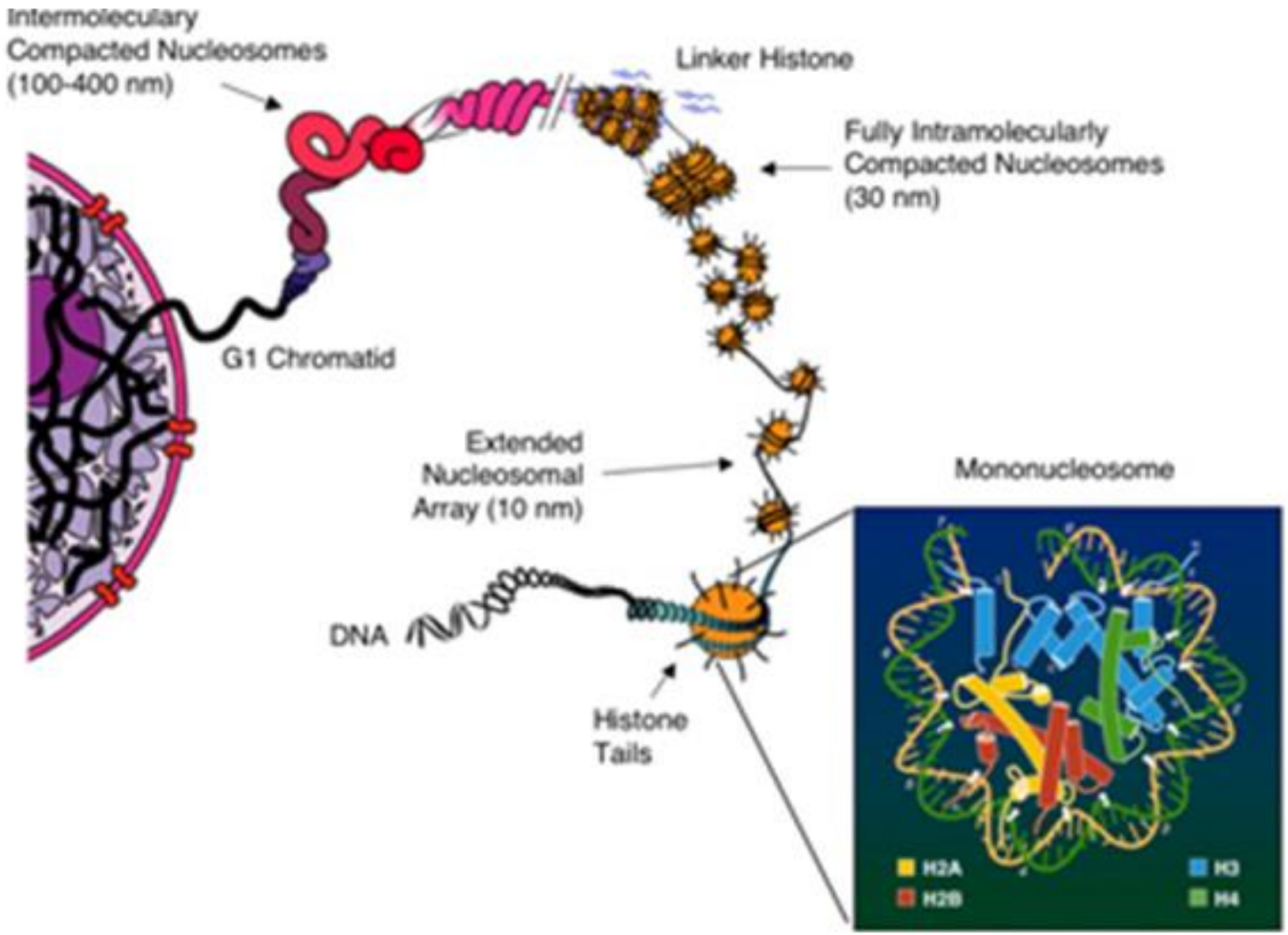
= Ca

Zinco-endopeptidasi, degradano le proteine che costituiscono le matrici extracellulari (e.g. il collagene)

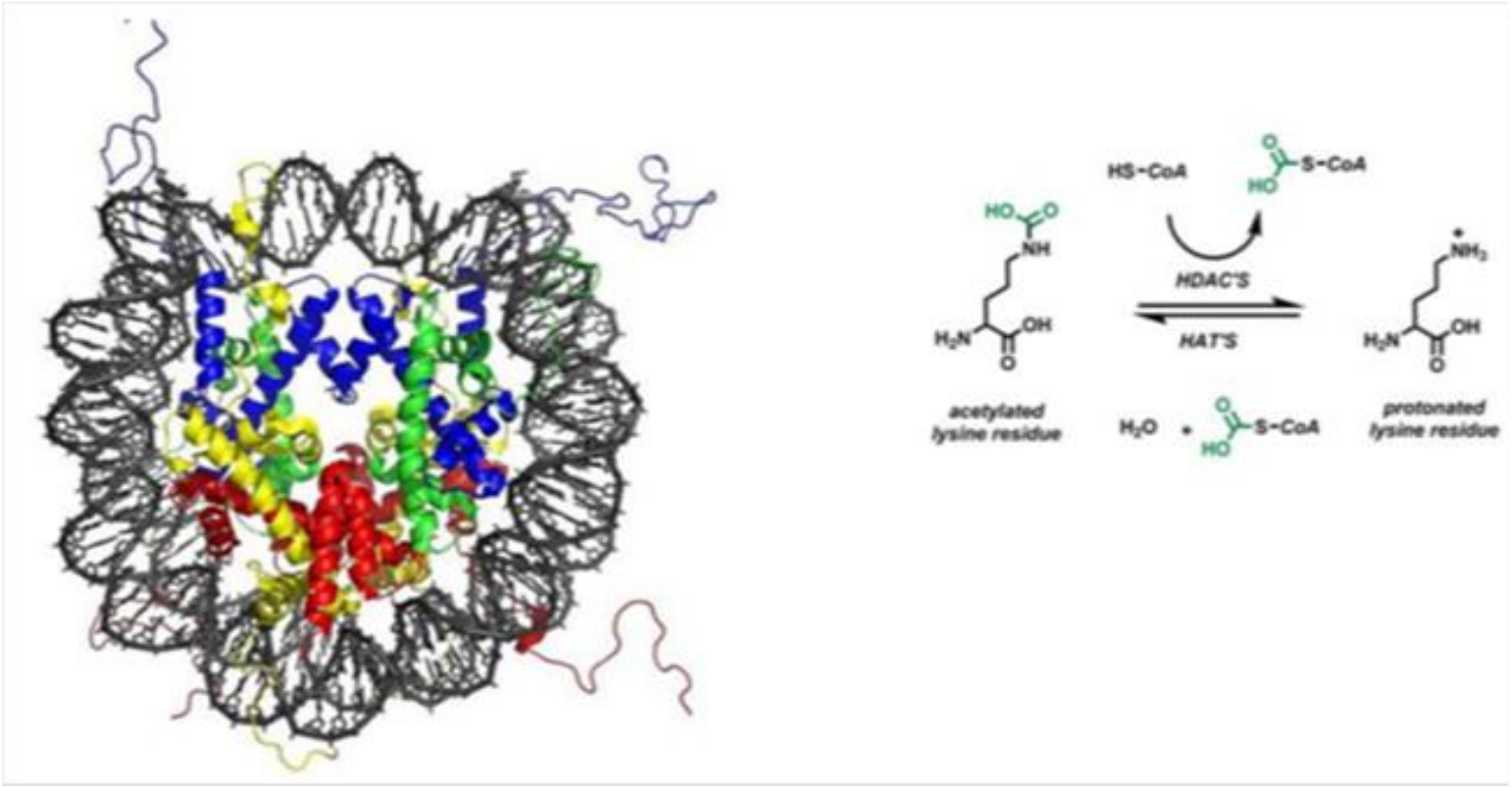
# Processo metastatico favorito da MMP



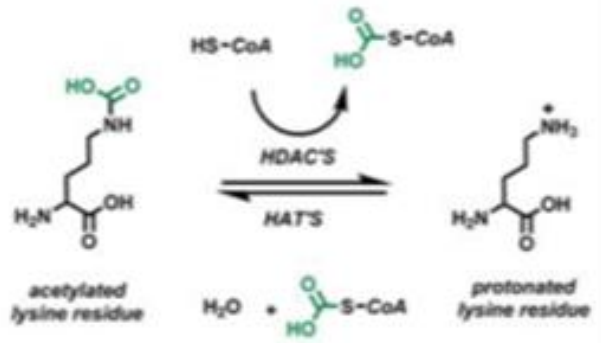
# Cromatina, Nucleosomi e Istoni



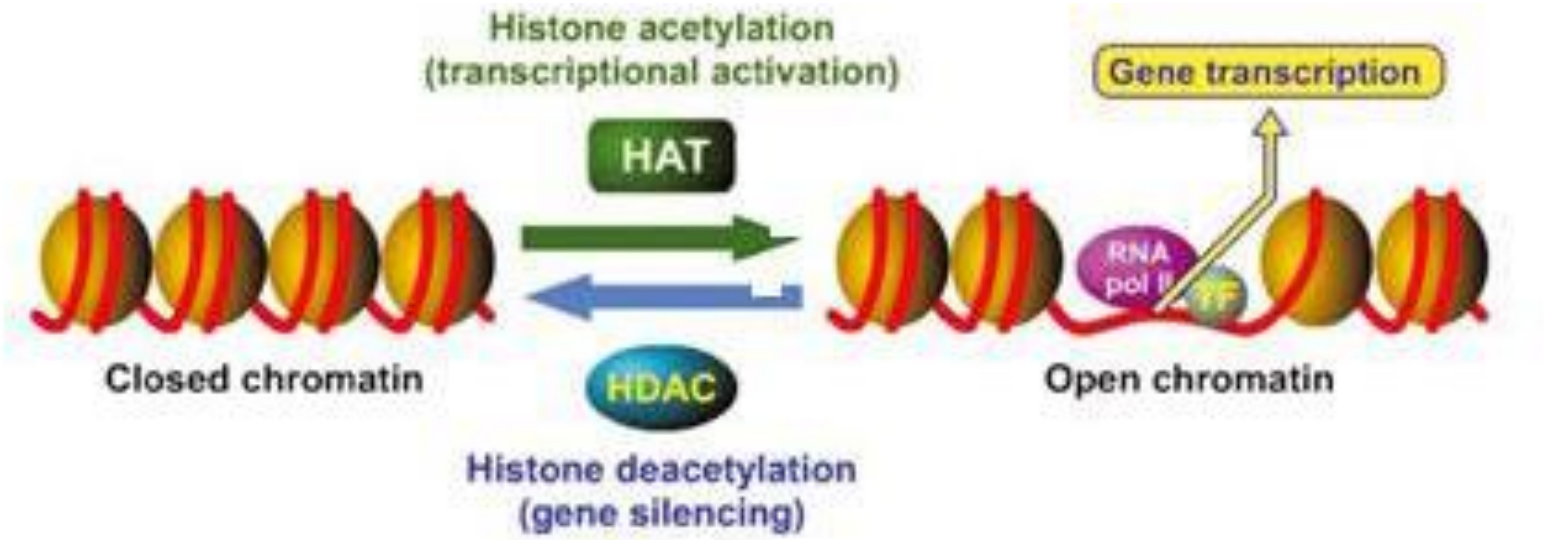
# Istone deacetilasi (HDAC)
# e
# Istone acetiltrasferasi (HAT)




Nucleosoma e Istoni

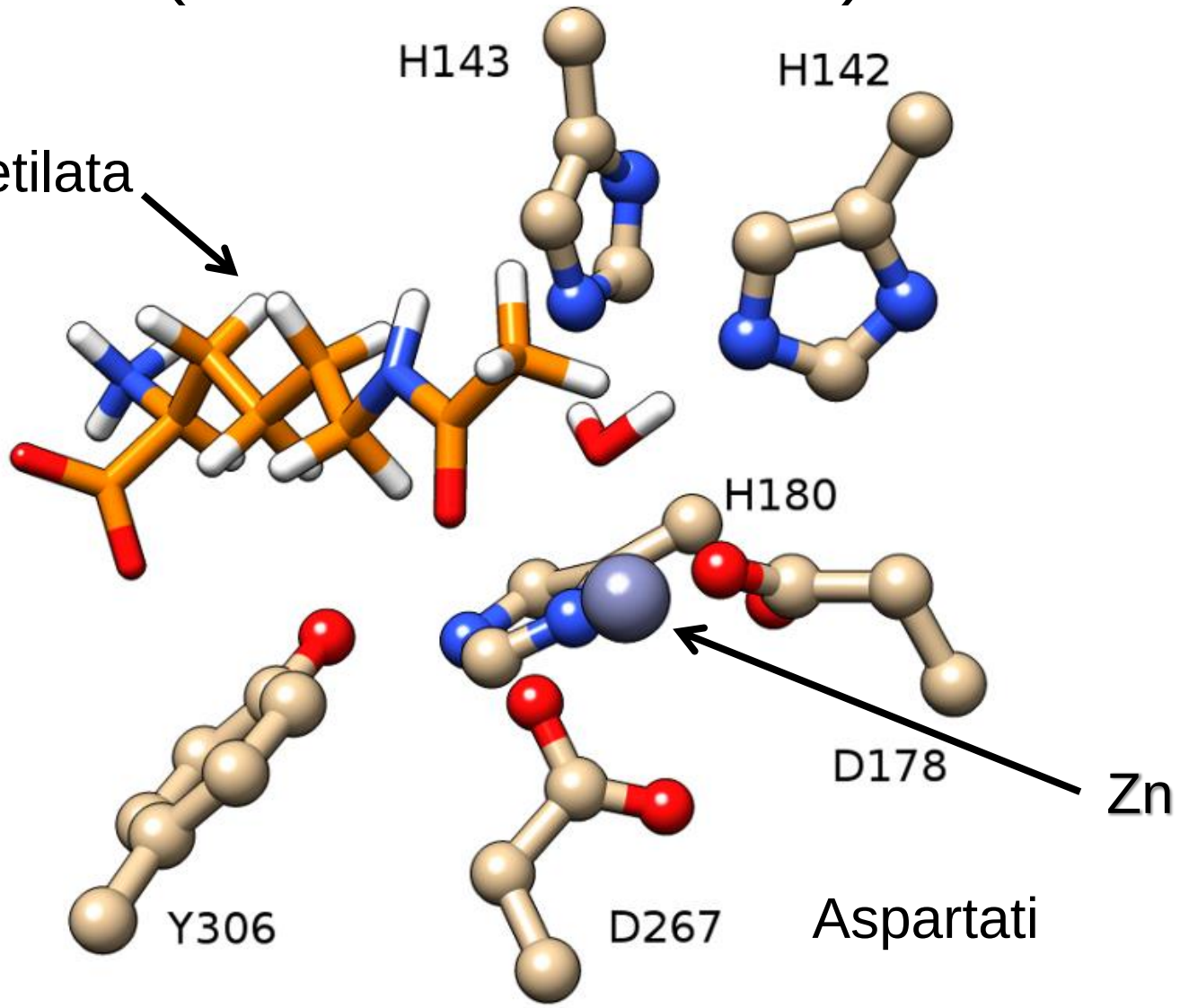



acetilazione e deacetilazione
delle lisine degli istoni

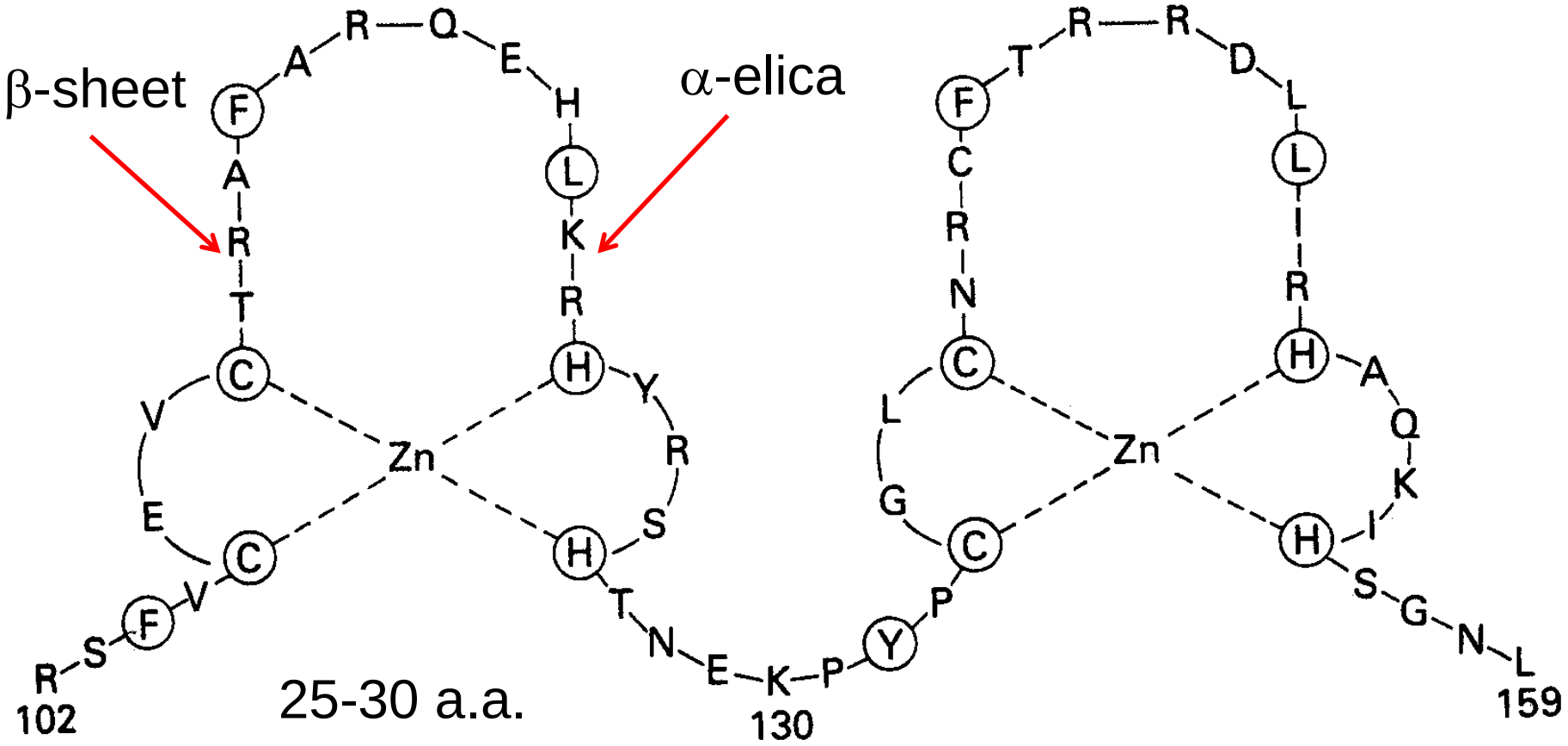



*Modulazione epigenetica*

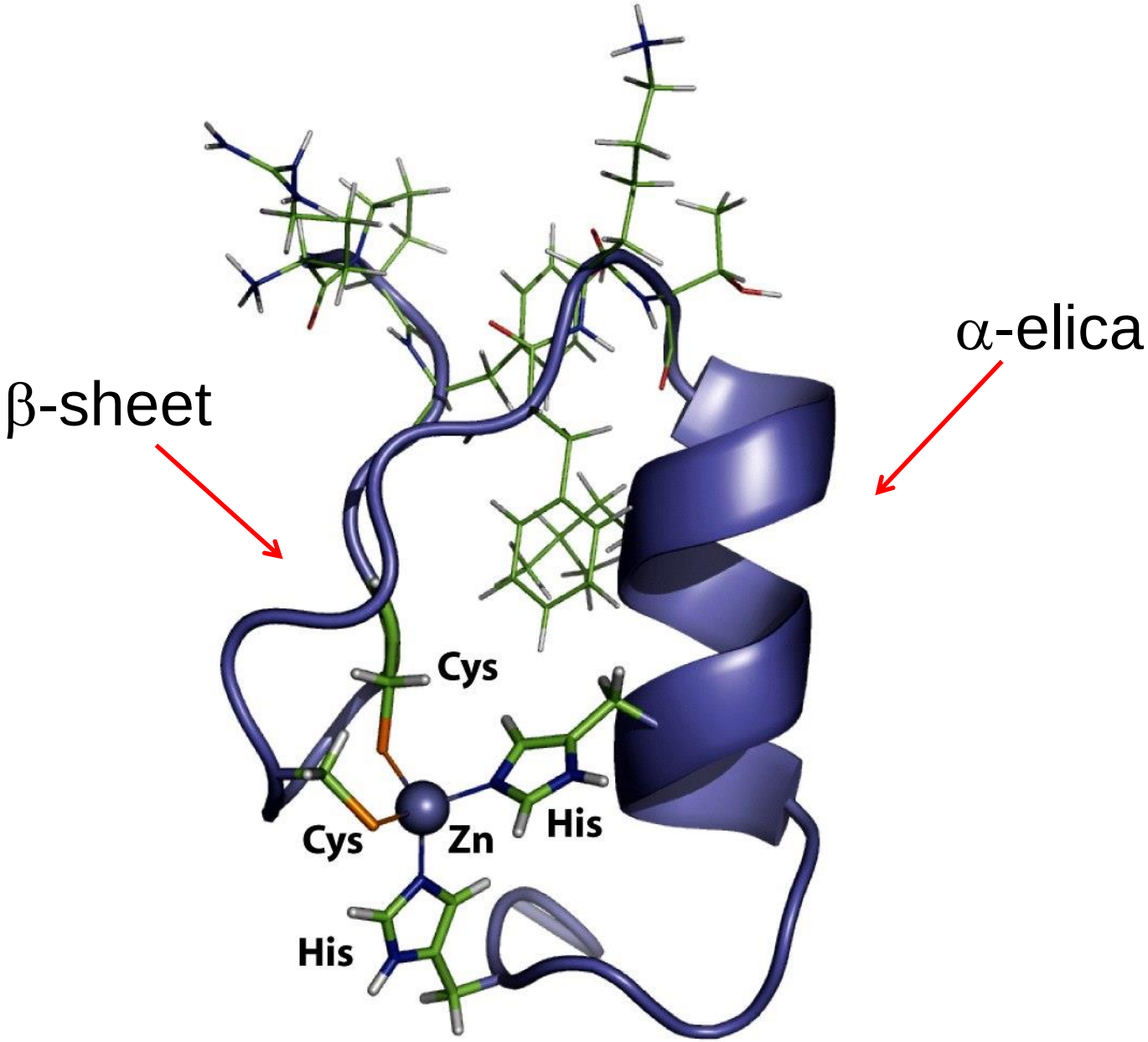
# Sito attivo di HDAC8 (istone-deacetilasi 8)

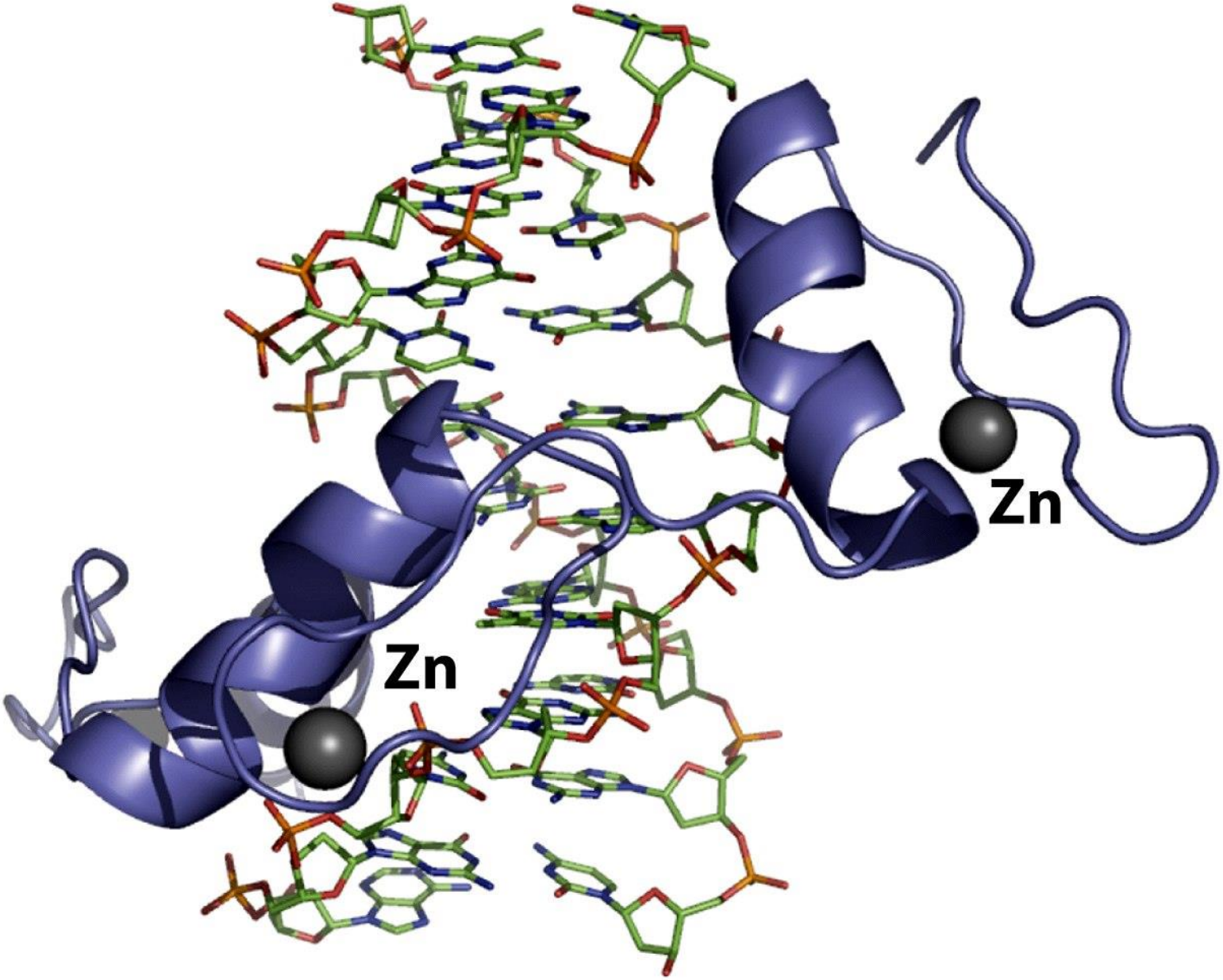


# Zinc fingers




*gene regulatory proteins* e *transcription factors*


β-sheet
α-elica
Cys
Cys
Zn
His
His




Interazione di zinc-fingers con DNA