

Metal complexes of ATCUN-like peptides for sequence-specific DNA cleavage

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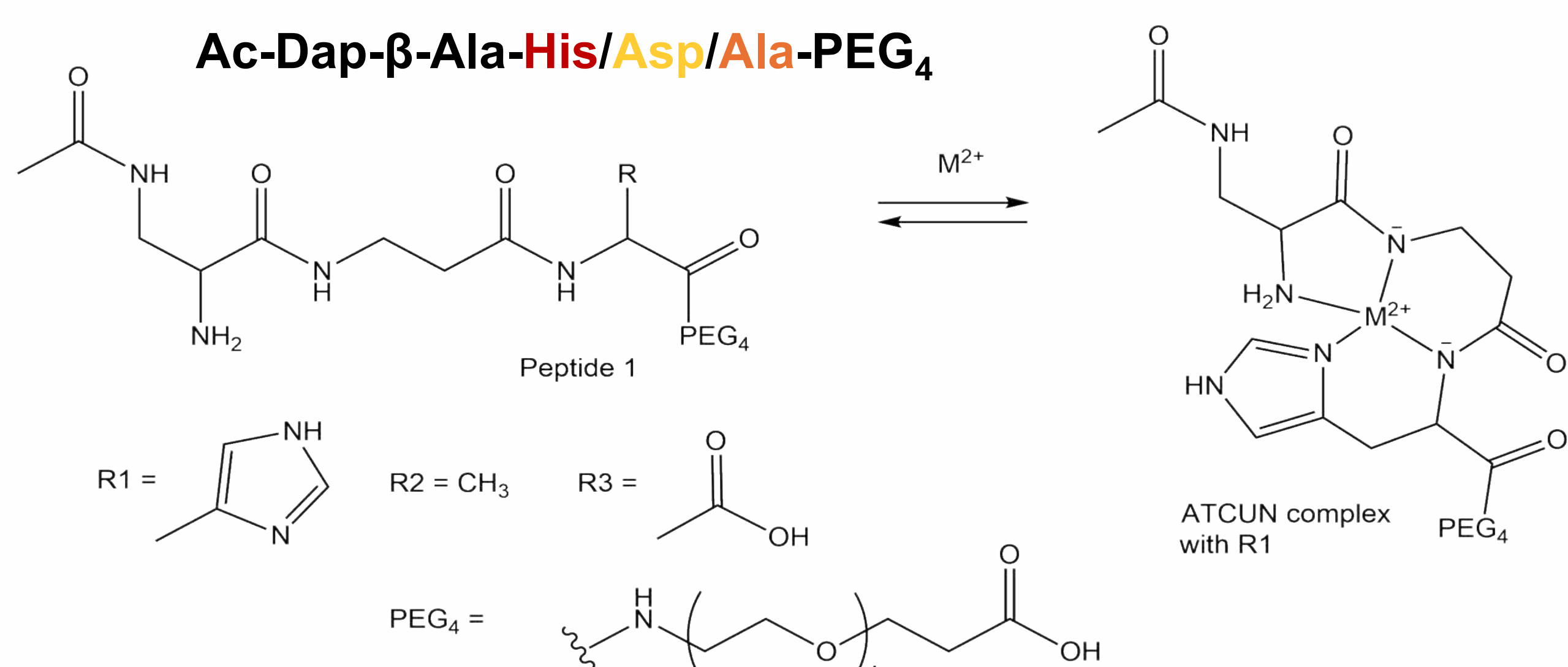


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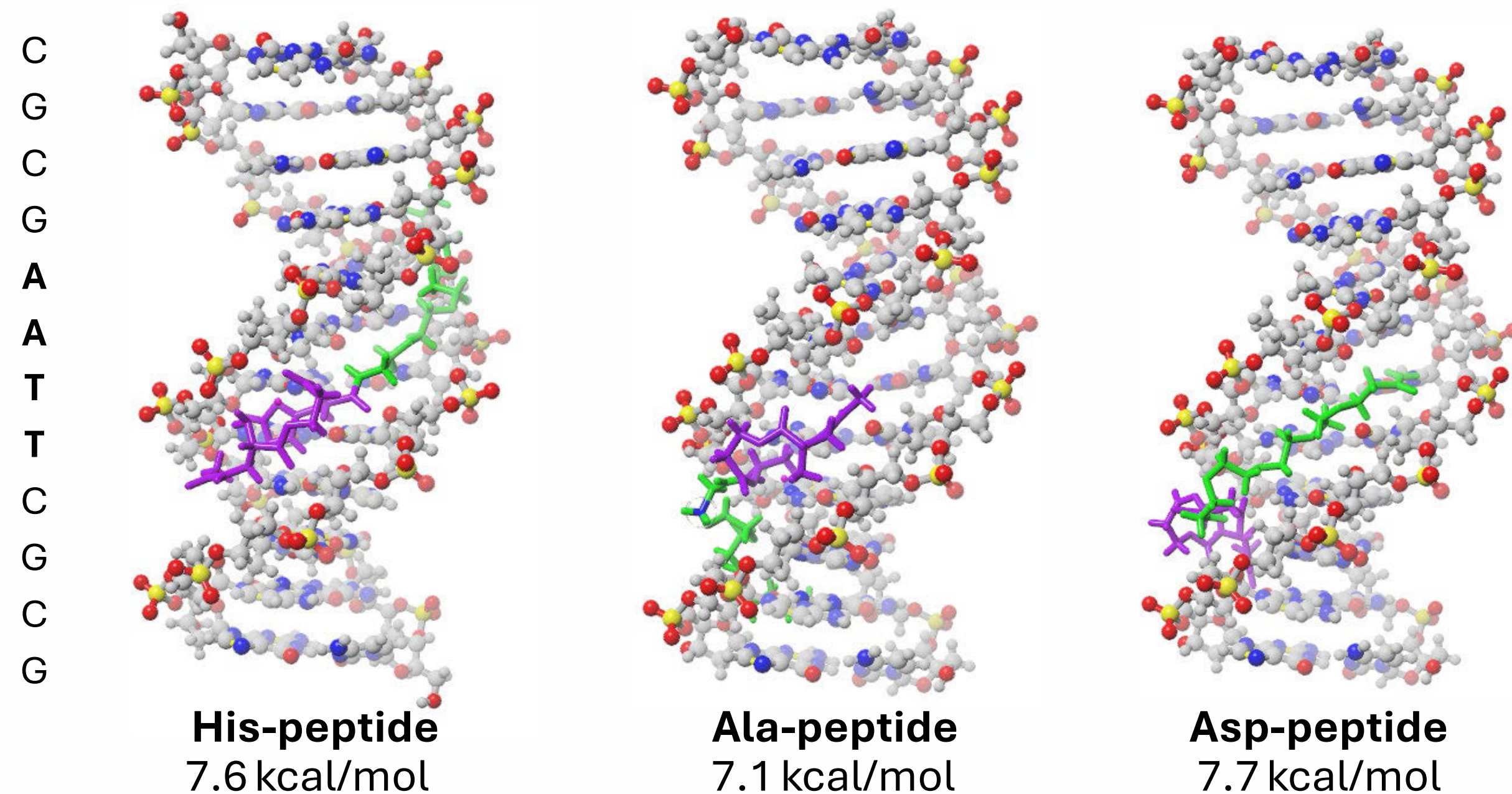
Peptides with Amino-Terminal Cu(II) and Ni(II) binding motif (ATCUN) motif are known to bind to the DNA minor groove and cleave the DNA, being promising for antimicrobial and antitumor activities. A typical ATCUN motif is Gly-Gly-His. We synthesized another His-containing peptide and two mutants where the His is substituted by Ala and Asp, and study whether these form complexes with Cu(II), bind to a DNA and exhibit cleavage activity.

ATCUN-like peptides can coordinate metals



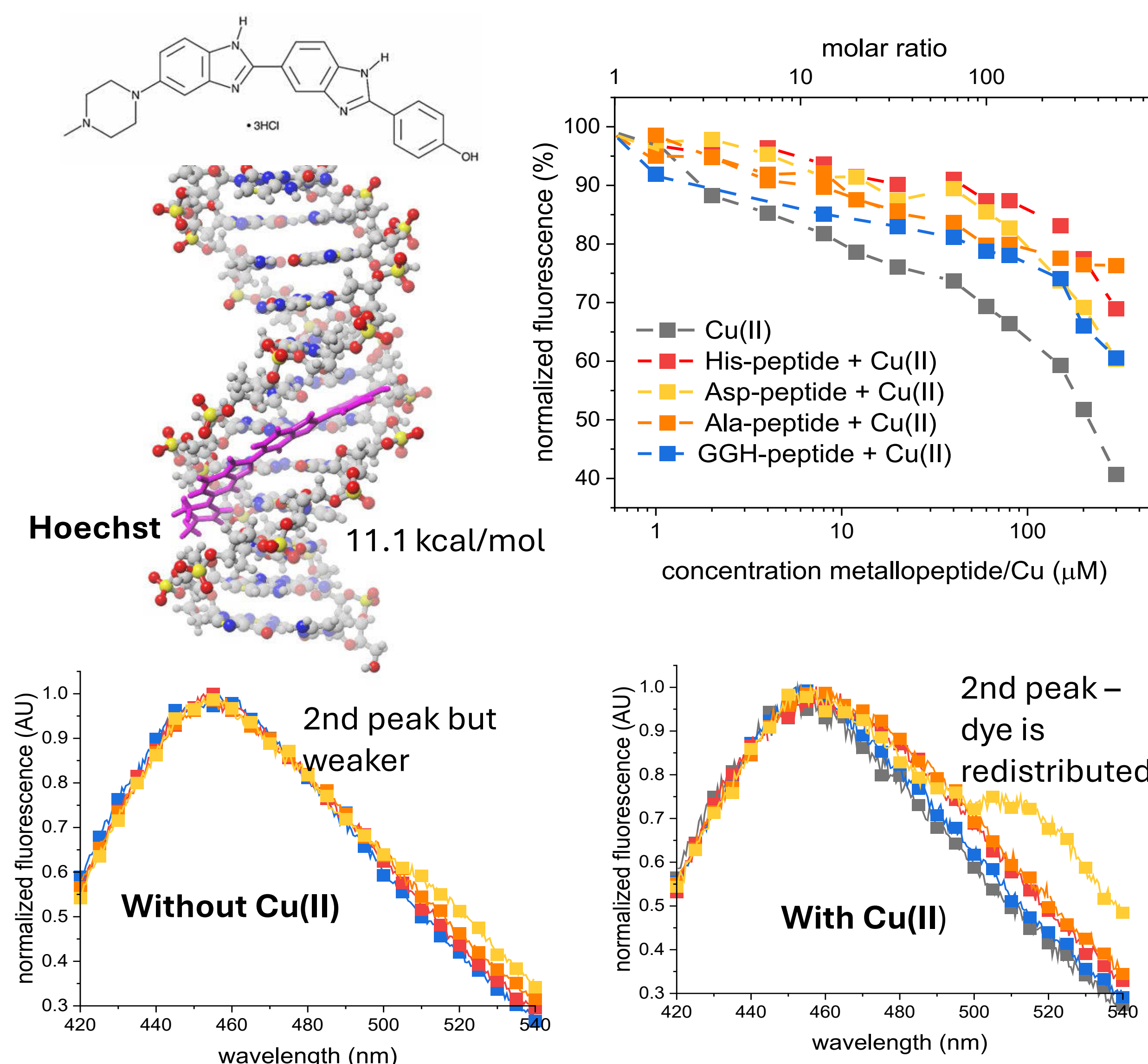
The peptides are simulated to bind to the DNA minor groove

Molecular docking shows binding for all three peptide complexes with Cu(II).

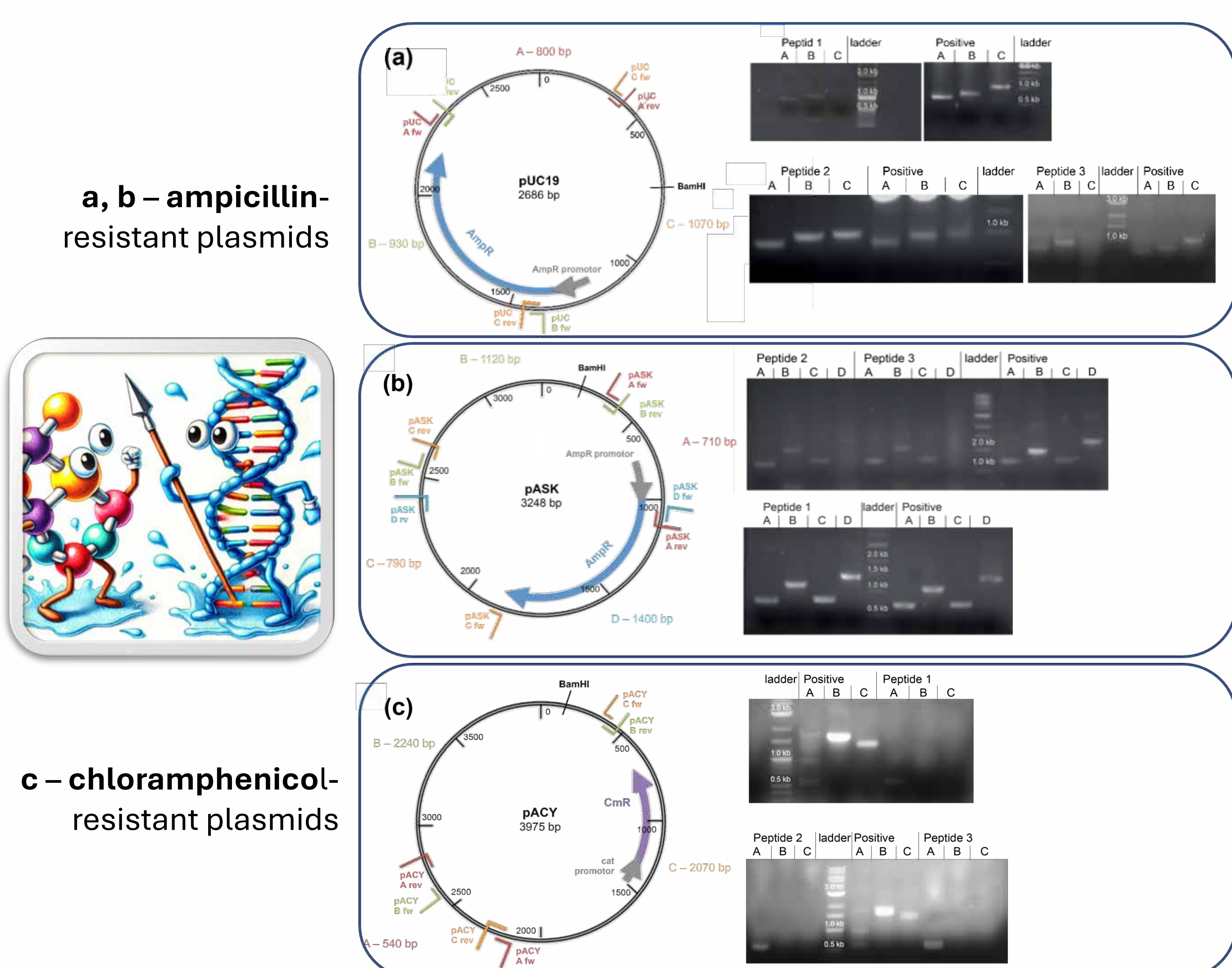


The peptides displace a dye from DNA minor groove

The Hoechst 33258 fluorescent dye binds to the minor groove with AT-specificity. Metallopeptides displace Hoechst and redistribute the dye from AT rich sites in the minor groove more prominently than a peptide with the classic Gly-Gly-His ATCUN motif.

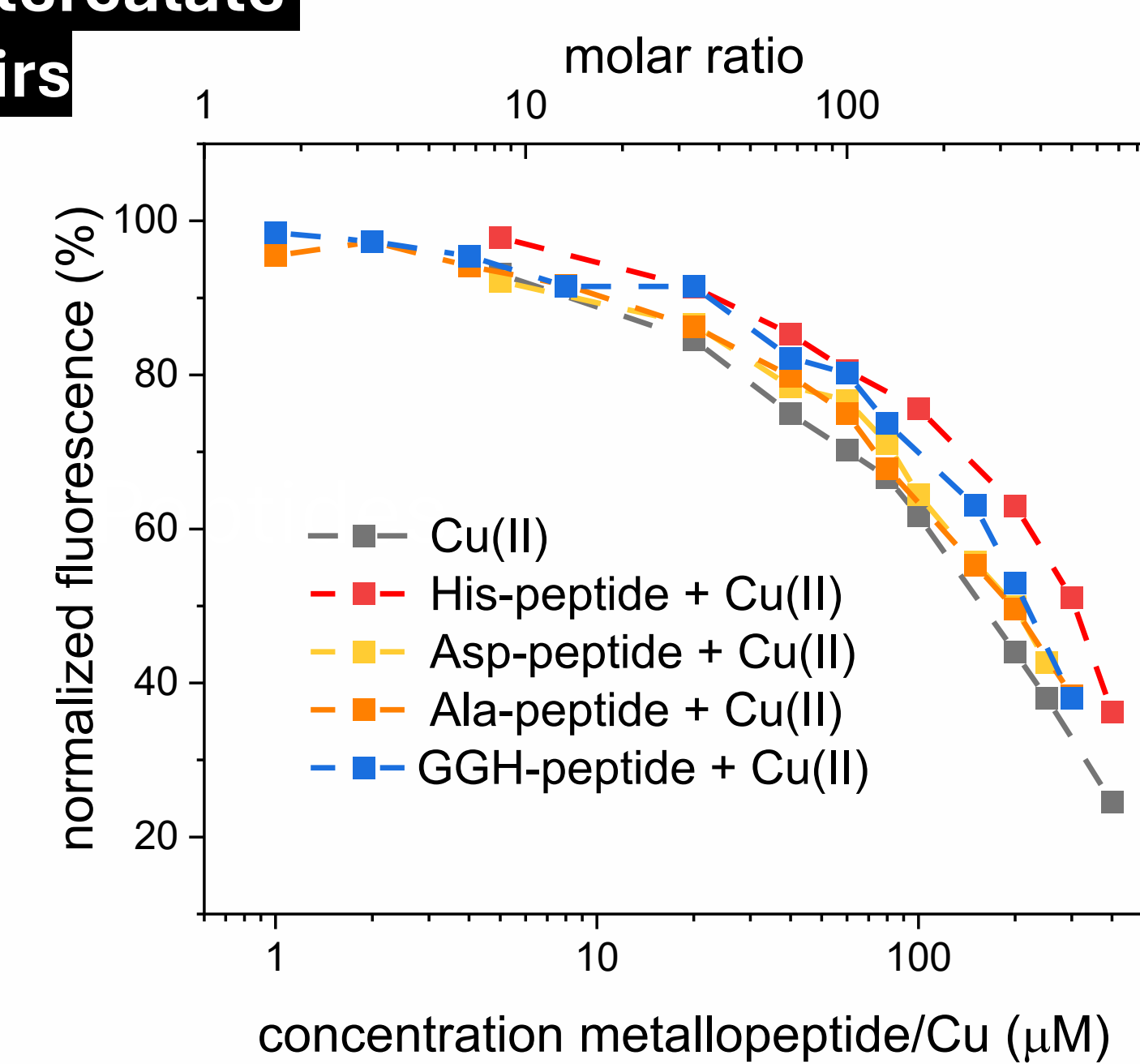
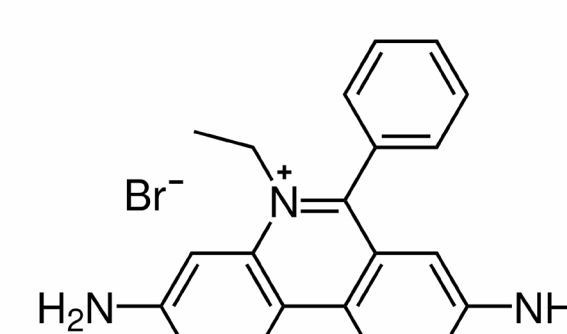


Antibiotic resistance plasmids are cleaved region-specifically



The peptides do not intercalate between DNA base pairs

Ethidium bromide is an intercalator dye but its fluorescence is not displaced or redistributed as compared to Cu(II) alone.



CONCLUSION

- All three peptides, even without His, bind to Cu(II).
- All our peptides, and especially the Asp-containing one, redistribute the fluorescent dye from the AT rich sites in the minor groove.
- All peptides linearize three studied plasmids.
- The Asp- and His-containing peptides cleave the DNA with specificity to AT-rich sites.
- These small metallopeptides are promising for drug design from anticancer to antimicrobial treatment.



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