

RSC Applied Interfaces

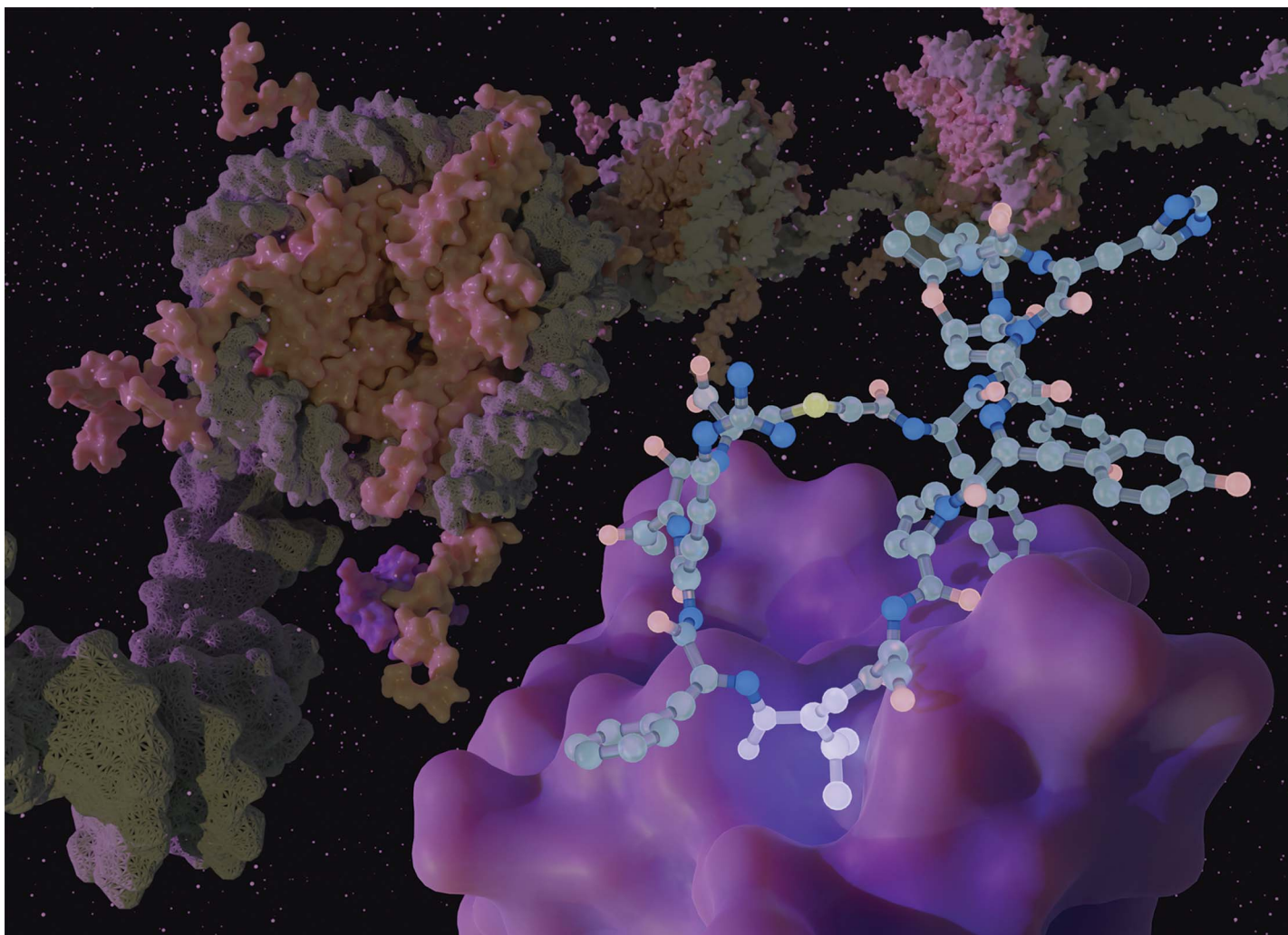
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**Interfacial and surface research
with an applied focus**

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**Fundamental questions
Elemental answers**



Showcasing research from Professor Akane Kawamura's laboratory, Chemistry - School of Natural & Environmental Sciences, Newcastle University, U.K.

Cyclic peptides target the aromatic cage of a PHD-finger reader domain to modulate epigenetic protein function

Plant homeodomain fingers (PHD-fingers) are chromatin reader domains that recruit epigenetic proteins to specific histone modification sites. We report a selective cyclic peptide inhibitor (OC9) targeting the N^{ϵ} -trimethyllysine-binding PHD fingers of KDM7 histone demethylases. OC9 disrupts PHD-finger interaction with histone H3K4me₃, engaging the N^{ϵ} -methyllysine-binding aromatic cage through a valine residue, revealing a non-lysine recognition motif for the PHD-fingers. PHD-finger inhibition leads to inhibition of KDM7B (PHF8) but stimulation of KDM7A (KIAA1718) histone demethylase activity, providing a new approach for selective allosteric modulation. Artwork by Tim Bell.

As featured in:



See Tim D. W. Claridge, Akane Kawamura *et al.*, *Chem. Sci.*, 2023, **14**, 7136.