Nucleome Therapeutics founder Professor James Davies and Oxford University publish paper in prestigious journal *Cell*

- *Groundbreaking research using Nucleome MCC technology reveals complex structure of DNA inside living cells at base pair resolution for the first time, pioneering a new approach to identify new drug targets from human genetics*

Oxford, UK, 6 November 2025 – Nucleome Therapeutics ('Nucleome' or 'the Company'), an immunology company tackling the root causes of disease through a revolutionary new approach to solving human genetics, is delighted that its founder, Professor James Davies and his team at the Weatherall Institute of Molecular Medicine, Oxford University have published a paper in *Cell*. The paper, "Mapping chromatin structure at base-pair resolution unveils a unified model of cis-regulatory element interactions" demonstrates the most detailed view yet of how DNA folds and functions inside living cells. This reveals the intricate structure of the genome which can be used to decode the regulation of gene expression at scale to identify new drug targets.

Nucleome has an exclusive license from Oxford University to the technology known as Micro Capture-C (MCC). MCC physically identifies the contacts between regulatory elements in the non-coding genome and the genes they control. Regulatory elements are often at some distance along the chromosome sequence from their gene they regulate. The two come together in the folded 3D structure of chromatin in the cell nucleus. Nucleome has applied MCC to decipher the molecular basis of inflammatory diseases from thousands of non-coding disease-associated genetic variants in patients.

Dr. Mark Bodmer, CEO of Nucleome, commented: *"Congratulations to James and his team at Oxford on this groundbreaking work. Using MCC technology, for the first time it has been possible to see 3D interactions in the nucleus inside the cell at base pair resolution. This gives us a new way of looking at how genetic variation in the human genome causes disease. At Nucleome, we are applying this transformative technology to solve the molecular basis of inflammatory diseases. This has enabled us to discover hundreds of novel drug targets and to define molecular endotypes of complex diseases based on genetic variation in patients. We are using this knowledge to buid a pipeline of therapeutics to restore health in inflammatory diseases."*

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Full Press Release from Oxford University:

Oxford scientists capture genome's structure in unprecedented detail

Scientists at the MRC Weatherall Institute of Molecular Medicine, University of Oxford, have achieved the most detailed view yet of how DNA folds and functions inside living cells, revealing the physical structures that control when and how genes are switched on.

Using a new technique called MCC ultra, the team mapped the human genome down to a single base pair, unlocking how genes are controlled, or, how the body decides which genes to turn on or off at the right time, in the right cells. This breakthrough gives scientists a powerful new way to understand how genetic differences lead to disease and opens up fresh routes for drug discovery.

'For the first time, we can see how the genome's control switches are physically arranged inside cells, said Professor James Davies, lead author of the study.

‘This changes our understanding of how genes work and how things go wrong in disease. We can now see how changes in the intricate structure of DNA leads to conditions like heart disease, autoimmune disorders and cancer.’

For more than two decades, scientists have known the full sequence of the human genome — the three billion “letters” of DNA that make up our genetic code. But exactly how that code folds and functions inside the cell has remained largely hidden.

Each cell’s DNA, about two metres long, is tightly packed into a microscopic space one-hundredth of a millimetre across. Within this space, the DNA constantly bends and loops, bringing distant sections into contact. These 3D structures are crucial because they determine which genes are active or silent, much like how a circuit board determines which switches are connected and which are not.

Until now, researchers could only view these interactions at relatively low resolution. The new Oxford method captures them down to a single base pair - the smallest unit of DNA - offering a truly molecular view of gene control.

This level of detail matters because over 90% of genetic changes linked to common diseases lie not within genes themselves, but in the “switch” regions that regulate them. The ability to see how these switches are organised gives scientists a new framework for identifying where gene regulation goes wrong and how it might be corrected.

‘We now have a tool that lets us study how genes are controlled in exquisite detail,’ said Hangpeng Li, the doctoral researcher who led the experimental work. ‘That’s a critical step toward understanding what goes wrong in disease, and what might be done to fix it.’

The Oxford team also collaborated with Professor Rosana Collepardo-Guevara at the University of Cambridge, whose computer simulations confirmed that the folding patterns observed arise naturally from the physical properties of DNA and its packaging proteins.

Together, the scientists propose a new model of gene regulation in which cells use electromagnetic forces to bring DNA control sequences to the surface, where they cluster into “islands” of gene activity. These structures, which were previously invisible, appear to be a fundamental mechanism for how cells read their genetic instructions.

The research, published this week in Cell, represents a major advance in molecular genetics, providing a foundation for future studies into how changes in genome structure cause disease.

The work was funded by the Medical Research Council and the Lister Institute, with support for translation into new therapies from the Wellcome Trust and the NIHR Oxford Biomedical Research Centre. It forms part of a growing UK effort to move beyond sequencing the genome to truly understanding how it works in space and time.

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Notes to Editors

About Nucleome Therapeutics
Nucleome is using breakthrough genomics technologies to discover first-in-class antibody therapeutics for inflammatory diseases. The approach is based solely on human disease genetics and biology. Nucleome is able, for the first time, to reveal molecular mechanisms of disease and select drug targets using human genetic variants in the non-coding genome that alter gene expression. The Company's proprietary 3D genomics combines lab and machine learning technologies which can be applied to any set of disease-associated variants.

Lead program NTP464 is an antibody that activates an inflammation checkpoint. NTP464 stimulates natural cellular processes of inflammation resolution, a new principle in the treatment of inflammation with huge potential patient benefit. Other multiple targets based on the genetics of inflammatory diseases are in discovery.

Nucleome is backed by a world-class syndicate of investors: M Ventures, the venture capital arm of Merck KGaA; Johnson and Johnson Innovation - JJDC, Inc. ("JJDC"); Pfizer Ventures; British Business Bank and founding investor Oxford Science Enterprises.

Visit our website to find out more at: **www.nucleome.com**