Epigenetics: New tool for precision medicine

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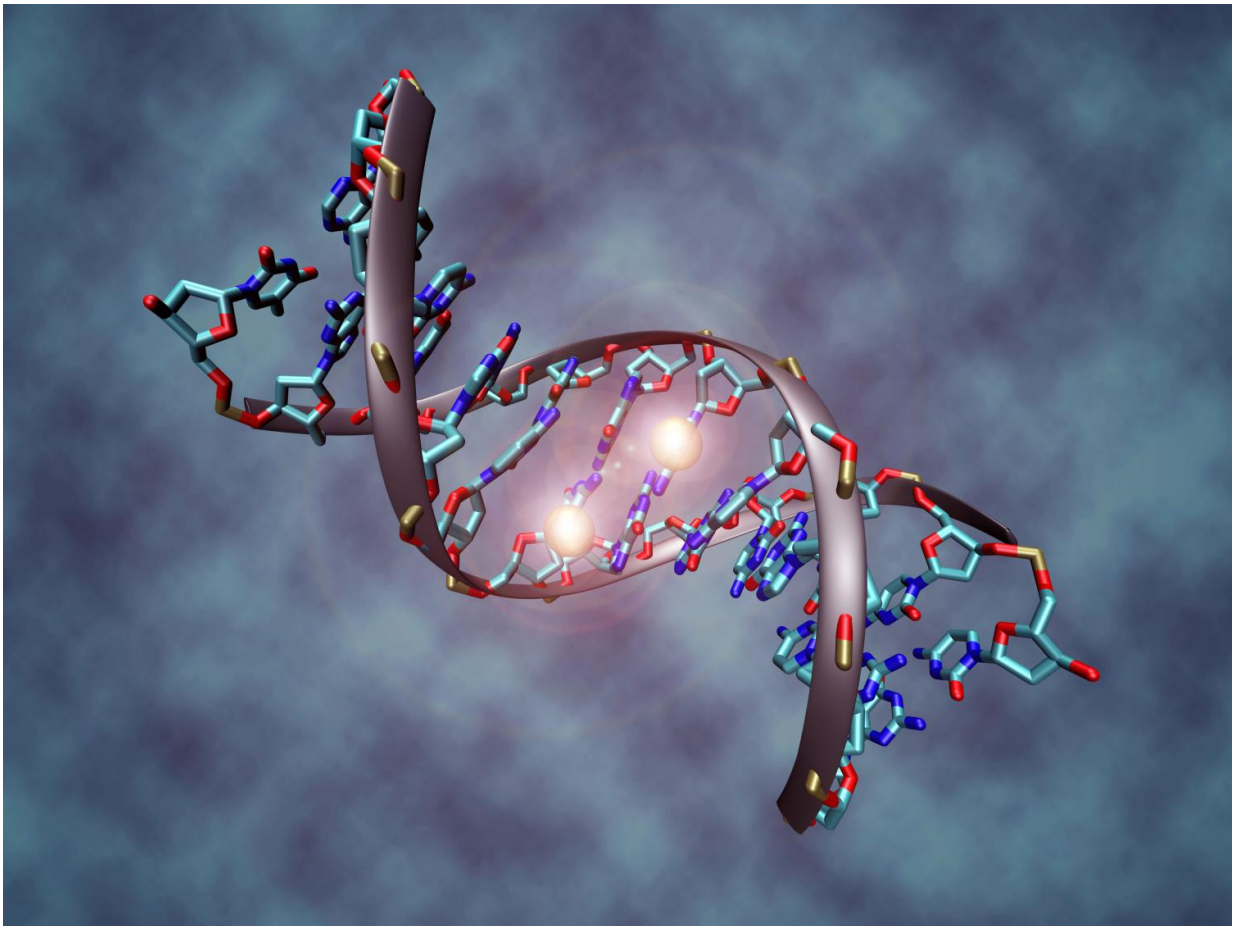


A DNA molecule that is methylated on both strands on the center cytosine. DNA methylation plays an important role for epigenetic gene regulation in development and cancer.[Details: The picture shows the crystal structure of a short DNA helix with sequence "accgcCGgcgcc", which is methylated on both strands at the center cytosine. The structure was taken from the Protein Data Bank (accession number 329D), rendering was performed with VMD and post-processing was done in Photoshop.] Credit: Christoph Bock/CeMM

Four new papers, co-published by an international consortium of biomedical researchers, mark the feasibility of epigenetic analysis for clinical diagnostics and precision medicine. Epigenetic analysis addresses key limitations of genetic testing, helping to ensure that patients are accurately diagnosed and treated with the right drug at the right time.

Epigenetic changes occur in all cancers, and in various other diseases. Measuring these changes provides unprecedented insights into the disease mechanisms at work in individual patients, which is important for better diagnosis and patient-specific treatment decisions.

In a series of four papers led by Christoph Bock (CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna) and Stephan Beck (University College London, UCL), an international group of scientists have validated the feasibility of epigenetic analysis for clinical applications.

Building upon years of technology development in laboratories around the world, this series of papers shows the accuracy and robustness of epigenetic tests. Going forward, clinical researchers will optimize and apply these methods for specific diseases, and it is expected that epigenetic tests will become widely used for selecting personalized treatments in cancer and other diseases.

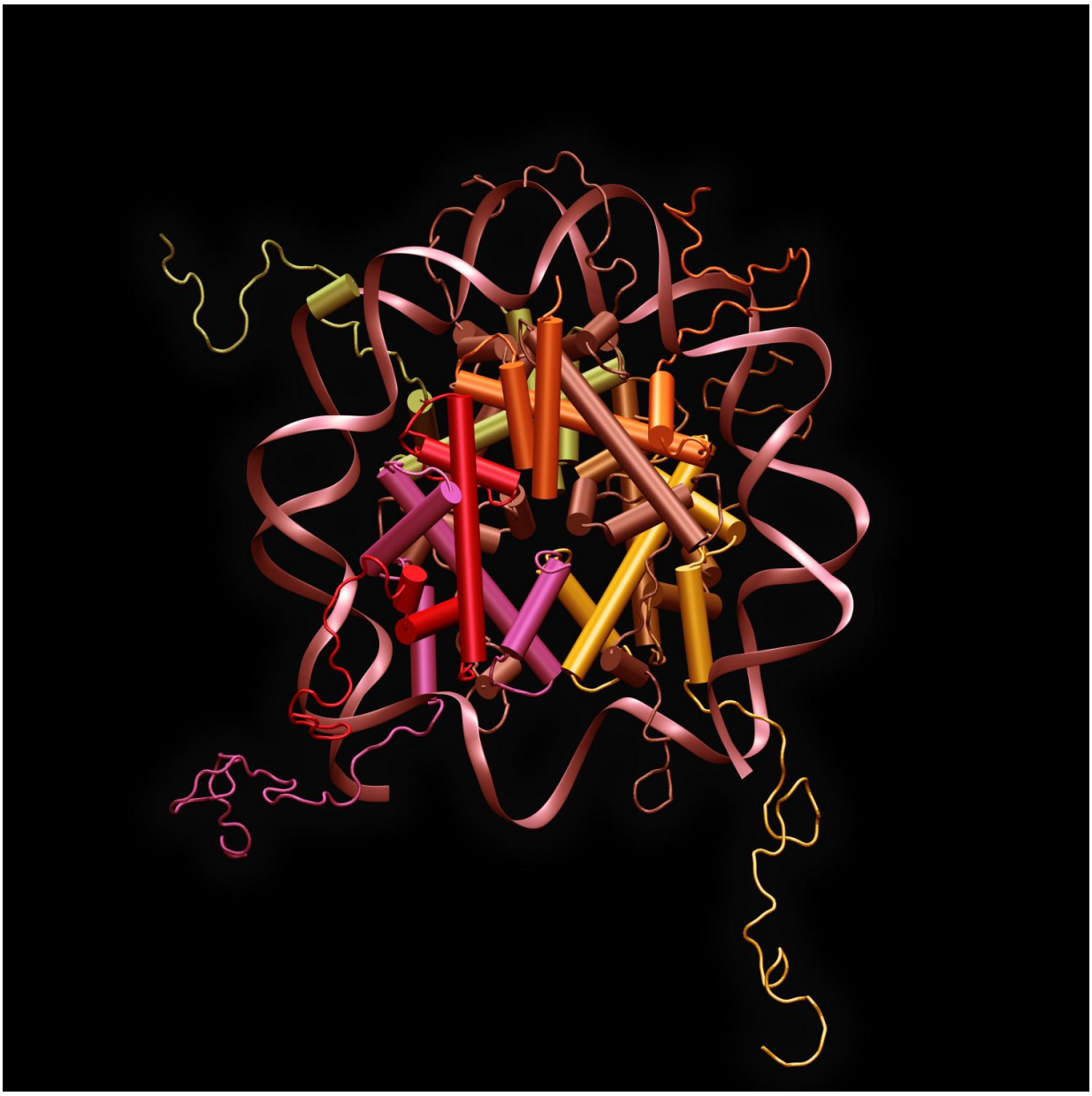
Epigenetics refers to chemical modifications of the DNA and its associated proteins that control gene activity independent of the genetic code. These epigenetic modifications define how two meters of DNA in each human cell are folded into tiny cell nuclei.

Epigenetic modifications can be inherited during cell division, which

helps maintain the ~200 cell types of the human body carrying the same genes. Moreover, epigenetic mechanisms provide an interface by which the environment influences gene activity.

In many diseases, including all cancers, the epigenetic control of the genome is heavily distorted. Measuring these alterations provides a detailed picture of the disease-specific changes, which is often informative for distinguishing disease subtypes or identifying suitable treatments. Therefore, epigenetics has much to offer for improving disease diagnosis and treatment choice.

The now published studies, which have been performed in the context of the European BLUEPRINT project and the International Human Epigenome Consortium, constitute a milestone for utilizing epigenetic information in clinical diagnostics and precision medicine.



A nucleosome -- the major carrier of epigenetic information -- in front of the DNA sequence of a typical gene promoter, which is highly enriched for the "CG" sequence pattern carrying DNA methylation in mammals.[Details: The nucleosome structure was taken from the Protein Data Bank (accession number 1KX5), with rendering using VMD and POV-Ray and postprocessing in Adobe Photoshop.] Credit: Christoph Bock/CeMM

The four papers in more detail

1. In a study published in *Nature Biotechnology* and coordinated by CeMM, 18 research groups from three continents compared all promising methods for analyzing DNA methylation in the clinic. This multicenter benchmarking study identifies the most accurate methods and shows that epigenetic tests based on DNA methylation are a mature technology ready for broad clinical use.http://doi.org/10.1038/nbt.3605

2. Also in *Nature Biotechnology*, the UCL team presents a computational validation of genome-wide DNA methylation sequencing technology, confirming its practical use for identifying DNA methylation differences between samples and disease subtypes.http://doi.org/10.1038/nbt.3524

3. The UCL team further extend their analysis in a paper published in *Nature Communications*, where they present new bioinformatic methods for discovering disease-specific DNA methylation patterns from cost-effective low-coverage DNA methylation sequencing data.http://doi.org/10.1038/ncomms11306

4. Finally, a *Nature Communications* paper by CeMM researchers - in collaboration with the clinicians at the University of Southampton and the Royal Bournemouth Hospital - demonstrates the utility of chromatin mapping for identifying disease subtypes and predicting prognosis in chronic lymphocytic leukemia. This study highlights the clinical utility of epigenetic biomarkers especially for diseases with widespread heterogeneity between individual patients.http://doi.org/10.1038/ncomms11938

Christoph Bock (Principal Investigator at CeMM) said: "Epigenetic tests have a key role to play for making precision medicine a clinical reality. Epigenetics captures part of each cell's individual history, and it can predict how cancer cells will react to drug treatment. This can be very

useful for personalized therapy."

More information: Quantitative comparison of DNA methylation assays for biomarker development and clinical applications, *Nature Biotechnology*, DOI: 10.1038/nbt.3605

Saturation analysis for whole-genome bisulfite sequencing data, *Nature Biotechnology*, DOI: 10.1038/nbt.3524

Nature Communications, 10.1038/ncomms11306

Nature Communications, 10.1038/ncomms11938

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