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"Capture Technique" Enables Researchers to Study 49,000-Year-Old DNA to Study How Similar and Different Neandertals Were to Us

SANTA CLARA, Calif., LEIPZIG, Germany, and COLD SPRING HARBOR, N.Y., May 6, 2010 -- Researchers from the Max Planck Institute (MPI), Cold Spring Harbor Laboratory (CSHL), Agilent Technologies Inc. (NYSE:A), and other prestigious institutions worldwide have shown that DNA capture techniques can greatly enable the sequencing of ancient Neandertal DNA, providing new insight into the nature of these prehistoric hominids.

The method, published in the May 7, 2010 issue of the journal Science, uses two rounds of "target enrichment" procedure to enrich ancient DNA from rare and precious bone samples so it can be sequenced. The complete article, "Targeted Investigation of the Neandertal Genome by Array-Based Sequence Capture," is available at www.sciencemag.org.

“There is great interest in the relationship of Neandertals to people,” said senior author Svante Paabo of MPI. “Questions like, ‘Did our ancestors interbreed with Neandertals?’ are of interest, but also how our genome differs from that of Neandertals. Since Neandertals are our closest relatives, when we compare ourselves to them we can identify features in our genome that set us apart from all other organisms on the planet.”

“We were able to enrich Neandertal protein-coding regions where differences occurred on the human evolutionary lineage up to 190,000-fold using Agilent DNA array capture technology,” said Hernan Burbano of the MPI, one of the lead authors. “Ninety-six percent of all targeted positions were uncovered to an average sequencing depth of fivefold.”

“Attaining good coverage of the Neandertal genome had been a problem due to DNA contamination from microbes over the years,” Paabo added. “Simply sequencing, without first enriching for the genome, often didn’t work, especially where the contamination levels were high.”

Early in 2008, collaborators Emily Hodges and Greg Hannon of the Howard Hughes Medical Institute at CSHL were able to demonstrate through mock experiments that this problem could be resolved using target enrichment. Armed with this insight, the team began working on applying the technique to the contamination problem with ancient DNA. “Array hybridization capture technology” was originally reported by the CSHL group and is the subject of a longstanding collaboration with Agilent. The team recognized this as a promising method for recovering large regions of targeted sequence from Neandertal samples. “The method can also be used more widely with many other kinds of human remains,” Paabo observed.

“Working with ancient, sample-derived DNA is tough when compared with fresh samples,” said co-author Andy Bhattacharjee of Agilent’s Life Sciences Group. “Thirty to forty thousand years have passed since Neandertals walked on earth, and all that is left are ancient bones containing severely degraded DNA. The DNA itself has also undergone a sort of chemical aging (deamination).

“However, the worst offender is microbial contamination caused by colonization of microbes,” Bhattacharjee continued. “Therefore, removal of this contaminant DNA is of paramount importance, as this allows more coverage of the endogenous genome and therefore allows one to better decipher the genetic code. The capture methodology solves this big problem by enriching for Neandertal sequences and depleting contaminant DNA. It’s an elegant solution.”

“The methodology developed during this study can also be applied to other challenging studies in paleontology and archeology as well as in human forensics, which have been difficult to study systematically so far,” said co-author Leo Brizuela, also of Agilent. “This has been a very exciting and challenging project, and we appreciate the opportunity to work with this group.”

“These experiments were enabled by the flexibility and quality of the Agilent microarray platform on which the array capture technology is based,” Brizuela added. “In addition, our group has deep experience developed working on human exome sequencing, working with the Hannon group at CSHL and Jay Shendure of the University of Washington.”

About CSHL

Cold Spring Harbor Laboratory (CSHL) is a private, not-for-profit research and education institution at the forefront of efforts in molecular biology and genetics to generate knowledge that will yield better diagnostics and treatments for cancer, neurological diseases and other major causes of human suffering. For more information, visit www.cshl.edu.

About the Max Planck Institute for Evolutionary Anthropology

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