Ancient DNA reveals how a chicken virus evolved to become more deadly

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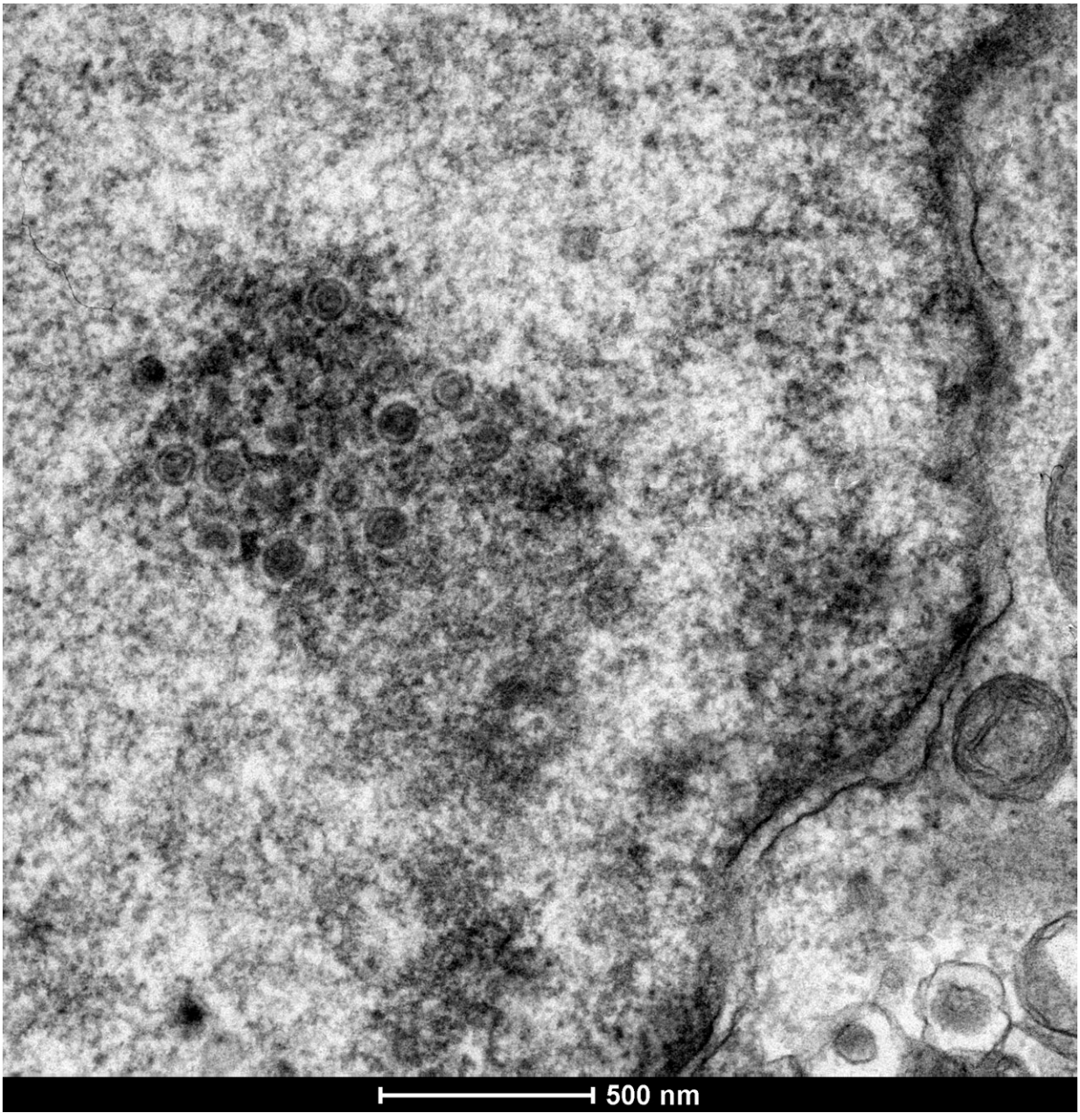

Electron Microscopy image of Marek's disease virus particles replicating in the nucleus of an infected cell. Credit: The Bioimaging group, Pirbright Institute

An international team of scientists led by geneticists and disease biologists from the University of Oxford and LMU Munich have used ancient DNA to trace the evolution of Marek's Disease Virus (MDV). This global pathogen causes fatal infections in unvaccinated chickens and costs the poultry industry over $1 billion per year.

The findings, published in the journal *Science* with the title "Ancient chicken remains reveal the origins of virulence in Marek's disease virus," show how viruses evolve to become more virulent and could lead to the development of better ways to treat viral infections.

The team, which includes archaeologists and biologists, recovered and reconstructed ancient MDV sequences from archaeological chickens spanning the past 1,000 years. By comparing viral genomes derived from both modern and ancient birds, they were able to pinpoint the genetic alterations responsible for the increased virulence of the modern virus.

Based on the ancient genetic sequences, they were also able to resurrect ancient biological processes using cellular assays, demonstrating that ancient strains were significantly milder than their modern counterparts.

This breakthrough not only sheds light on the evolutionary history of MDV, but also holds promise for the development of more effective therapies against this devastating poultry disease.

This new study is based on DNA isolated from chicken bones that were excavated from 140 archaeological sites in Europe and the Near East.

These ancient genomes revealed that MDV was widespread in European chickens at least 1,000 years before the disease was first described in 1907. This highlights the importance of preserving archaeological remains, especially given their power to reveal valuable insights into the evolution of virulence.

When first described, this disease only led to mild symptoms in older chickens. As chicken consumption dramatically increased in the 1950s and 1960s, MDV has continued to evolve and has become increasingly aggressive despite the development of several vaccines.

First author Dr. Steven Fiddaman (Department of Biology, University of Oxford) said, "Our findings not only unravel the evolutionary history of the Marek's Disease Virus but also provide a foundation for enhancing our current understanding of pathogen virulence. By combining ancient DNA techniques with modern genomics, we've opened a window into the past that can guide future strategies in managing viral diseases."

Professor Naomi Sykes (University of Exeter), lead archaeologist on the study, said, "This study underscores the profound significance of biological material preserved in archaeological and museum collections since we cannot foresee how their investigation might possess transformative applications in the future."

Professor Laurent Frantz (LMU Munich), co-senior author of the study added, "Our work highlights the power of interdisciplinary collaboration, bringing together paleogeneticists, virologists, archaeologists, and biologists to unravel the complex evolutionary history of a pathogen with significant economic and agricultural implications."

Professor Greger Larson (University of Oxford), co-senior author said, "We have seen how mitigating diseases often creates a selection pressure that increases the virulence of the virus. Being able to watch this process

take place by sequencing ancient virus genomes shows just how dramatically the virulence of MDV has increased in the past century."

Professor Adrian Smith (Department of Biology, University of Oxford), co-senior author said, "Ancient DNA has provided us with a unique perspective on the emergence of MDV as a deadly chicken virus and may teach us lessons that are applicable to the control of other viral infections of medical and veterinary importance."

Professor Venugopal Nair, Scientist Emeritus at The Pirbright Institute, said, "Findings from this paper on the origins of virulence, particularly associated with the genetic sequences of the ancient Marek's disease viruses, will provide great scientific opportunities to explore the molecular mechanisms of increasing virulence of this virus that coincided with the intensification of poultry farming from the 1960s."

More information: Steven R. Fiddaman et al, Ancient chicken remains reveal the origins of virulence in Marek's disease virus, *Science* (2023). DOI: 10.1126/science.adg2238. www.science.org/doi/10.1126/science.adg2238

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