

**Aggregate sample of press clippings reporting Dr. Corthals's scientific publications**

**Period: 2009 - 2016**

**Press about Coca Article:**

**2011 - Dávalos, L. M., A. C. Bejarano, M. Hall, H. L. Correa, A. Corthals, O. J. Espejo. Forests and drugs: coca-driven deforestation in global biodiversity. Environmental Science and Technology**

## Cocaine production increases destruction of Colombia's rainforests

*Date:* January 29, 2011

*Source:* Stony Brook University

*Summary:* Scientists are reporting new evidence that cultivating coca bushes, the source of cocaine, is speeding up destruction of rainforests in Colombia and threatening the region's "hotspots" of plant and animal diversity. The findings underscore the need for establishing larger protected areas to help preserve biodiversity.

### FULL STORY

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Image from Nariño in southern Colombia featuring recent clearings, abandoned clearings, and coca plants (center). (The picture was taken from low-flying aircraft.)

*Credit: María Ximena Gualdrón / SIMCI*

Scientists from Stony Brook University are reporting new evidence that cultivating coca bushes, the source of cocaine, is speeding up destruction of rainforests in Colombia and threatening the region's "hotspots" of plant and animal diversity. The findings, which they say underscore the need for establishing larger protected areas to help preserve biodiversity, appear in ACS' journal *Environmental Science & Technology*.

Dr. Liliana M. Dávalos, professor in the Department of Ecology and Evolution at Stony Brook, and her colleagues note that the pace of deforestation in Colombia has accelerated over the past 20 years, even as population growth has slowed and the economy has shifted from agriculture to other revenue sources. This increase in deforestation overlaps with an increase in the cultivation of coca for cocaine production, and the country accounted for 75 per cent of the world's coca in 2000.

Earlier reports found that direct deforestation from coca was surprisingly small, with as little as 150 km<sup>2</sup> of forests replaced by coca each year by 2005. Since rainforests contain about 10 percent of the world's plant and animal species -- some of which become the basis of new medicines -- deforestation

represents a serious threat to global biodiversity. With studies suggesting that coca cultivation contributes indirectly to deforestation, the scientists set out to further document this impact.

Their analysis of data from 2002-2007 on the effects of coca cultivation on deforestation of rainforests in Colombia identified several factors that boosted the likelihood that rainforests would be destroyed. In southern Colombia, a forest close to newly developed coca farms, for instance, was likely to be cut, as was land in areas where much of the farmland was devoted to coca.

This is the first time the indirect impact on deforestation from cultivation destined for the global cocaine market has been quantified across South America's biodiversity hotspots.

The Stony Brook University scientists also showed that designating protected areas, regions that are set-aside for special protection for environmental reasons, reduced forest destruction in coca-growing areas. Establishing larger protected areas in the region could help control deforestation and preserve biodiversity, the report suggests.

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### Story Source:

The above post is reprinted from materials provided by **Stony Brook University**. *Note: Content may be edited for style and length.*

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### Journal Reference:

1. Liliana M. Dávalos, Adriana C. Bejarano, Mark A. Hall, H. Leonardo Correa, Angelique Corthals, Oscar J. Espejo. **Forests and Drugs: Coca-Driven Deforestation in Tropical Biodiversity Hotspots**. *Environmental Science & Technology*, 2011; 110111122451071 DOI: 10.1021/es102373d

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### Cite This Page:

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GenomeWeb, 2015

Genetically modified crops and developing countries.

**Press about the articles on Multiple Sclerosis:**

**2011 - Corthals, A. Multiple Sclerosis is not a disease of the Immune System. A New Framework for MS. Quarterly Review of Biology, 86, 4 (December Issue)**

**Includes:**

- Washington Post
- Eureka Alert
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# Is multiple sclerosis really an immune system disease?

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By **Jennifer LaRue Huget** January 2, 2012

Multiple sclerosis has long been understood to be an autoimmune disease in which the body's immune system, for reasons poorly understood, responds destructively to antigens in the central nervous system.

But research published in December in *The Quarterly Review of Biology* posits a different way of looking at MS. Angelique Corthals, a forensic anthropologist at the John Jay College of Criminal Justice in New York, suggests that MS may result from problems with the way the body metabolizes lipids, or fats in the blood, which in turn cause inflammation and spark a series of damaging events.

Corthals, in her lengthy review and analysis of existing research, notes that MS shares that underlying mechanism with atherosclerosis. ("Sclerosis" refers to hardening or scarring such as the build-up of plaque in arteries and the development of plaques in the brain associated with MS.)

She concludes that viewing MS in this light helps explain many mysteries that the autoimmune model leaves unanswered, including the role genetics play in MS risk, the environmental elements or pathogens that may trigger disease onset, and the reasons MS strikes twice as many women as men. (Atherosclerosis affects men more commonly than women; Carthals suggests gender differences in lipid metabolism may play a big role in determining who gets which condition.)

Because anti-inflammatory drugs such as statins commonly used to fight cardiovascular disease have also been used to treat symptoms of MS, she writes, such drugs may become part of more comprehensive and effective MS treatments than currently exist.

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I contacted the [National Multiple Sclerosis Society](#) for a response to the Corthals research, which that organization did not fund. Here's a shortened version of the MS Society's prepared statement:

"This paper puts forth a hypothesis about biological activities, and in particular lipids, which may lead to multiple sclerosis. Dr. Corthals's paper adds to ongoing discussion about what causes MS, but since it is a review of published research, rather than

Is multiple sclerosis really an immune system disease? - The Wa...  
results from original studies, the report carefully notes the need for more research.

<https://www.washingtonpost.com/blogs/the-checkup/post/is-mul...>

The National MS Society welcomes the ideas of thoughtful people who want to end MS, and fully agrees that we need to pursue all promising leads to do so.”

The statement goes on to list related research funded by the MS Society before concluding, “It’s a great sign that so many people from multi-research specialties are focusing efforts to unravel the mysteries that have always surrounded the disease multiple sclerosis.”

I couldn’t agree more. What do you think of this different approach to understanding MS?

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PUBLIC RELEASE: 22-DEC-2011

# Researcher contends multiple sclerosis is not a disease of the immune system

UNIVERSITY OF CHICAGO PRESS JOURNALS

An article forthcoming in the December 2011 issue of *The Quarterly Review of Biology* argues that multiple sclerosis, long viewed as primarily an autoimmune disease, is not actually a disease of the immune system. Dr. Angeliqe Corthals, a forensic anthropologist and professor at the John Jay College of Criminal Justice in New York, suggests instead that MS is caused by faulty lipid metabolism, in many ways more similar to coronary atherosclerosis (hardening of the arteries) than to other autoimmune diseases.

Framing MS as a metabolic disorder helps to explain many puzzling aspects of the disease, particularly why it strikes women more than men and why cases are on the rise worldwide, Corthals says. She believes this new framework could help guide researchers toward new treatments and ultimately a cure for the disease.

Multiple sclerosis affects at least 1.3 million people worldwide. Its main characteristic is inflammation followed by scarring of tissue called myelin, which insulates nerve tissue in the brain and spinal cord. Over time, this scarring can lead to profound neurological damage. Medical researchers have theorized that a runaway immune system is at fault, but no one has been able to fully explain what triggers the onset of the disease. Genes, diet, pathogens, and vitamin D deficiency have all been linked to MS, but evidence for these risk factors is inconsistent and even contradictory, frustrating researchers in their search for effective treatment.

"Each time a genetic risk factor has shown a significant increase in MS risk in one population, it has been found to be unimportant in another," Corthals said. "Pathogens like Epstein-Barr virus have been implicated, but there's no explanation for why genetically similar populations with similar pathogen loads have drastically different rates of disease. The search for MS triggers in the context of autoimmunity simply hasn't led to any unifying conclusions about the etiology of the disease."

However, understanding MS as metabolic rather than an autoimmune begins to bring the disease and its causes into focus.

## THE LIPID HYPOTHESIS

Corthals believes that the primary cause of MS can be traced to transcription factors in cell nuclei that control the uptake, breakdown, and release of lipids (fats and similar compounds) throughout the body. Disruption of these proteins, known as peroxisome proliferator-activated receptors (PPARs), causes a toxic byproduct of "bad" cholesterol called oxidized LDL to form plaques on the affected tissue. The accumulation of plaque in turn triggers an immune response, which ultimately leads to scarring. This is essentially the same mechanism involved in atherosclerosis, in which PPAR failure causes plaque accumulation, immune response, and scarring in coronary arteries.

"When lipid metabolism fails in the arteries, you get atherosclerosis," Corthals explains. "When it happens in the central nervous system, you get MS. But the underlying etiology is the same."

A major risk factor for disruption of lipid homeostasis is having high LDL cholesterol. So if PPARs are at the root of MS, it would explain why cases of the disease have been on the rise in recent decades. "In general



people around the world are increasing their intake of sugars and animal fats, which often leads to high LDL cholesterol," Corthals said. "So we would expect to see higher rates of disease related to lipid metabolism--like heart disease and, in this case, MS." This also explains why statin drugs, which are used to treat high cholesterol, have shown promise as an MS treatment.

The lipid hypothesis also sheds light on the link between MS and vitamin D deficiency. Vitamin D helps to lower LDL cholesterol, so it makes sense that a lack of vitamin D increases the likelihood of the disease--especially in the context of a diet high in fats and carbohydrates.

Corthals's framework also explains why MS is more prevalent in women.

"Men and women metabolize fats differently," Corthals said. "In men, PPAR problems are more likely to occur in vascular tissue, which is why atherosclerosis is more prevalent in men. But women metabolize fat differently in relation to their reproductive role. Disruption of lipid metabolism in women is more likely to affect the production of myelin and the central nervous system. In this way, MS is to women what atherosclerosis is to men, while excluding neither sex from developing the other disease."

In addition to high cholesterol, there are several other risk factors for reduced PPAR function, including pathogens like Epstein-Barr virus, trauma that requires massive cell repair, and certain genetic profiles. In many cases, Corthals says, having just one of these risk factors isn't enough to trigger a collapse of lipid metabolism. But more than one risk factor could cause problems. For example, a genetically weakened PPAR system on its own might not cause disease, but combining that with a pathogen or with a poor diet can cause disease. This helps to explain why different MS triggers seem to be important for some people and populations but not others.

"In the context of autoimmunity, the various risk factors for MS are frustratingly incoherent," Corthals said. "But in the context of lipid metabolism, they make perfect sense."

Much more research is necessary to fully understand the role of PPARs in MS, but Corthals hopes that this new understanding of the disease could eventually lead to new treatments and prevention measures.

"This new framework makes a cure for MS closer than ever," Corthals said.

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Angelique Corthals, "Multiple Sclerosis (MS) is not a disease of the immune system," *The Quarterly Review of Biology* 86:4 (December 2011).

The premier review journal in biology since 1926, *The Quarterly Review of Biology* publishes articles in all areas of biology but with a traditional emphasis on evolution, ecology, and organismal biology. QRB papers do not merely summarize a topic, but offer important new ideas, concepts, and syntheses. They often shape the course of future research within a field. In addition, the book review section of the QRB is the most comprehensive in biology.

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[Newsroom](#) > Professor Angelique Corthals' Groundbreaking Research on Multiple Sclerosis Published in the Quarterly Review of Biology

## Newsroom Archive

### Professor Angelique Corthals' Groundbreaking Research on Multiple Sclerosis Published in the Quarterly Review of Biology

*December 21, 2011* – Multiple sclerosis, long viewed as an autoimmune disease, may in fact be a metabolic disorder, according to Assistant Professor Angelique Corthals of the Department of Sciences at John Jay College of Criminal Justice, whose findings appear in the December 2011 issue of the *Quarterly Review of Biology*.

In Corthals' article, "Multiple Sclerosis Not a Disease of the Immune System", the forensic anthropologist, suggests that MS is caused by faulty lipid metabolism, in many ways more similar to coronary atherosclerosis (hardening of the arteries). Framing MS as a metabolic disorder helps to explain many puzzling aspects of the disease, particularly why it strikes women more than men and why cases are on the rise worldwide, Corthals says. She believes this new framework could help guide researchers toward new treatments and ultimately lead to a cure for the dreaded disease.

Multiple sclerosis affects at least 1.3 million people worldwide. Its main characteristic is inflammation followed by scarring of tissue called myelin, which insulates nerve tissue in the brain and spinal cord. Over time, this scarring can lead to profound neurological damage. Medical researchers have theorized that a runaway immune system is at fault, but no one has been able to fully explain what triggers the onset of the disease. Genes, diet, pathogens and vitamin D deficiency have all been linked to MS, but evidence for these risk factors is inconsistent and even contradictory in some populations, frustrating researchers in their search for effective treatment.

"Each time a genetic risk factor has shows a significant increase in MS in one population, it has been found to be unimportant in another," Corthals said. "Pathogens like Epstein-Barr virus have been implicated, but there's no explanation for why genetically similar populations with similar pathogen loads have drastically different rates of disease. The search for MS triggers in the context of autoimmunity simply hasn't led to any unifying conclusions about the etiology of the disease."

However, understanding the nature of MS as metabolic rather than autoimmune begins to bring the disease and its causes into focus.

"When lipid metabolism fails in the arteries, you get atherosclerosis," Corthals explains. "When it happens in the central nervous system, you get MS. But the underlying etiology is the same." The body is "primed" for the disease which is triggered by a pathogen or trauma or any event causing inflammation.

Corthals hopes that this new understanding of the disease could eventually lead to new treatments and prevention measures.

"This new framework makes a cure for MS closer than ever," she said.

Professor Angelique Corthals is a biological/forensic anthropologist. She earned her DPhil (PhD) at the University of Oxford and has over ten years of scientific research and teaching experience in the fields of pathology, forensic, biomedical and physical anthropology, phylogenetics and evolutionary biology, genetic resources and epidemiology.

To review the article, [click here](#).

**The Quarterly Review of Biology**, or QRB, is a scientific review of current and historical topics in biology as well as a source of book reviews. It was begun in 1926 by Raymond Pearl. It is currently published by the University of Chicago Press.

**About John Jay College of Criminal Justice:** An international leader in educating for justice, John Jay College of Criminal Justice of The City University of New York offers a rich liberal arts and professional studies curriculum to upwards of 15,000 undergraduate and graduate students from more than 135 nations. In teaching, scholarship and research, the College approaches justice as an applied art and science in service to society and as an ongoing conversation about fundamental human desires for fairness, equality and the rule of law. For more information, visit [www.jjay.cuny.edu](http://www.jjay.cuny.edu).

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## PROFESSOR ANGELIQUE CORTHALS' GROUNDBREAKING RESEARCH ON MULTIPLE SCLEROSIS PUBLISHED IN THE QUARTERLY REVIEW OF BIOLOGY

January 3, 2012 | [John Jay College of Criminal Justice](#)



Multiple sclerosis, long viewed as an autoimmune disease, may in fact be a metabolic disorder, according to Assistant Professor Angelique Corthals of the Department of Sciences at John Jay College of Criminal Justice, whose findings appear in the December 2011 issue of the *Quarterly Review of Biology*.

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For more information, call:

Doreen Vifias-Pineda 212-237-8645



# Have we been looking at Multiple Sclerosis all wrong?



Tim Barribeau

1/27/12 7:20pm · Filed to: MEDICINE



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Multiple sclerosis is a confusing disease. Widely regarded as an autoimmune problem, it affects millions of sufferers, and we still don't have a complete grasp of what causes it. Part of this problem is due to the fact that every time we find something that seems to be a factor in how it works, that factor doesn't seem universal.

But now there's a new theory of MS that could lead to a radically different treatment for the disease.

*Top image: Random 42 Medical Animation.*

A new meta-analysis by Dr. Angélique Corthals proposes that much of the difficulty we have with understanding the causes of MS may be because we're wrong about its basic mechanism. In a publication in *The Quarterly Review of Biology*, she proposes that rather than an autoimmune disease like previously supposed, MS might in fact be a metabolic one with an immune component.

It's a bold assertion to be sure, and one without original data to back it up (at this point, anyway). With MS, the myelin which protects and insulated the nerve tissue on your brain and spinal cord swells, and then scars, leading to neuronal damage. Corthals' theory gives another framework to approach this damage, and one with links to a disease we do understand — atherosclerosis.

This is where things get a bit dense, so bear with me.

There are certain environmental and genetic factors which can impair PPARs (peroxisome proliferator-activated receptors), which is part of the system that controls the metabolism of fat as well as immune response. When it's running at partial power, the PPARs can't properly control the levels of LDL — the infamous bad cholesterol — which leads to a build up of an oxidized toxic derivative of LDL called oxLDL in the blood. Once these are in the system, Corthals believes the body is "primed" for MS, and it can be triggered by a number of causes, including Epstein-Barr Virus, which is linked to MS in its own right.

Once triggered, an immune system chain reaction starts. The body sends out macrophages to deal with a pathogen, but the macrophages incorrectly gorge themselves on oxLDL. This puts them in a "zombie state", where they don't die and can't empty their contents, instead just building up plaques which damage the myelin sheath, and cause the symptoms of MS.

*Edited to clarify:* At this point, the disease triggers the immune problems we know of as MS. The theory isn't discarding the immunological side of the disease, just citing metabolism as a root trigger, which leads to the problems of the immune response.

Said Corthals:

Eventually, the toxic macrophages are cleared, leading to the remission part of the RRMS (relapsing-remitting MS) cycle. But this detente holds only until the next trigger comes along. Dysfunction of the PPAR is further implicated in MS because it slows the repair mechanism of the central nervous system to a crawl, preventing the efficient renewal and synthesis of myelin.

It's a novel theory, and while Corthals is working on pulling together some empirical data to back it up, it does answer some of the issues with how MS manifests. The disease has been linked previously to low levels of vitamin D, and is on the uptick in recent decades. Low vitamin D and a diet high in both saturated fat and carbohydrates (which is likewise on the rise) both contribute to the impairment of PPARs.

The mechanism that Corthals suggests is also interesting because it's incredibly similar to that of atherosclerosis. Atherosclerosis is when PPAR failure causes plaque buildup and scarring in arteries, which is the equivalent to what's being described happening to myelin. Also interestingly, men are far more likely to have atherosclerosis and women to have MS, which Corthals suggests may be because of the different way sexes metabolize fats. In the paper, she recommends "multiple sclerosis should be thought of as a metabolic disease, the female equivalent of atherosclerosis, not as a disease of the immune system."

If the raw data bears out this theory, it would mean a radically different approach to the treatment of a major chronic disease. One based on lipid metabolism (and potentially diet) rather than targeting the immune system directly. If it holds up, it would be a major paradigm shift in the way MS is handled — but first we need to see if the data

For further reading, Corthals has been weighing in on this discussion, and if we're lucky, she may even pop up here.



# MS may not be autoimmune disease

Published: Jan. 1, 2012 at 12:29 AM

NEW YORK, Jan. 1 (UPI) --

NEW YORK, Jan. 1 (UPI) -- Multiple sclerosis, long viewed as primarily an autoimmune disease, is not actually a disease of the immune system, a U.S. researcher says.

Dr. Angelique of the John Jay College of Criminal Justice in New York suggests instead that MS is caused by faulty lipid metabolism -- in many ways more similar to coronary atherosclerosis -- hardening of the arteries -- than to other autoimmune diseases.

Considering MS as a metabolic disorder helps to explain many puzzling aspects of the disease, particularly why it strikes women more than men and why cases are on the rise worldwide, Corthals said.

Multiple sclerosis is mainly characterized by inflammation followed by scarring of tissue called myelin, which insulates nerve tissue in the brain and spinal cord.

Over time, this scarring can lead to profound neurological damage, but medical researchers have theorized that a runaway immune system is at fault, but no one has been able to fully explain what triggers the onset of the disease.

Corthals said the primary cause of MS can be traced to transcription factors in cell nuclei that control the uptake, breakdown, and release of lipids -- fats and similar compounds -- throughout the body. Disruption of these proteins, known as peroxisome proliferator-activated receptors, causes a toxic byproduct of "bad" low-density lipoprotein cholesterol to form plaque on the affected tissue. The accumulation of plaque in turn triggers an immune response, which ultimately leads to scarring.

Corthals' framework explains why MS is more prevalent in women.

"Men and women metabolize fats differently," Corthals said. "In men, problems are more likely to occur in vascular tissue, which is why atherosclerosis is more prevalent in men. But women metabolize fat differently in relation to their reproductive role."

The findings are published in The Quarterly Review of Biology.

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Multiple Sclerosis   Immune System / Vaccines

# Researcher Contends Multiple Sclerosis Is Not A Disease Of The Immune System

Adapted Media Release

**Published:** Tuesday 3 January 2012

An article published Friday Dec. 23 in the December 2011 issue of The Quarterly Review of Biology argues that [multiple sclerosis](#), long viewed as primarily an autoimmune disease, is not actually a disease of the immune system. Dr. Angelique Corthals, a forensic anthropologist and professor at the John Jay College of Criminal Justice in New York, suggests instead that MS is caused by faulty lipid metabolism, in many ways more similar to coronary [atherosclerosis](#) (hardening of the arteries) than to other autoimmune diseases.

Framing MS as a metabolic disorder helps to explain many puzzling aspects of the disease, particularly why it strikes women more than men and why cases are on the rise worldwide, Corthals says. She believes this new framework could help guide researchers toward new treatments and ultimately a cure for the disease.

Multiple sclerosis affects at least 1.3 million people worldwide. Its main characteristic is [inflammation](#) followed by scarring of tissue called myelin, which insulates nerve tissue in the brain and spinal cord. Over time, this scarring can lead to profound neurological damage. Medical researchers have theorized that a runaway immune system is at fault, but no one has been able to fully explain what triggers the onset of the disease. Genes, diet, pathogens, and [vitamin D](#) deficiency have all been linked to MS, but evidence for these risk factors is inconsistent and even contradictory, frustrating researchers in their search for effective treatment.

"Each time a genetic risk factor has shown a significant increase in MS risk in one population, it has been found to be unimportant in another," Corthals said. "Pathogens like Epstein-Barr virus have been implicated, but there's no explanation for why genetically similar populations with similar pathogen loads have drastically different rates of disease. The search for MS triggers in the context of autoimmunity simply hasn't led to any unifying conclusions about the etiology of the disease."

However, understanding MS as metabolic rather than an autoimmune begins to bring the disease and its causes into focus.

## THE LIPID HYPOTHESIS

Corthals believes that the primary cause of MS can be traced to transcription factors in cell nuclei that control the

uptake, breakdown, and release of lipids (fats and similar compounds) throughout the body. Disruption of these proteins, known as peroxisome proliferator-activated receptors (PPARs), causes a toxic byproduct of "bad" [cholesterol](#) called oxidized LDL to form plaques on the affected tissue. The accumulation of plaque in turn triggers an immune response, which ultimately leads to scarring. This is essentially the same mechanism involved in atherosclerosis, in which PPAR failure causes plaque accumulation, immune response, and scarring in coronary arteries.

"When lipid metabolism fails in the arteries, you get atherosclerosis," Corthals explains. "When it happens in the [central nervous system](#), you get MS. But the underlying etiology is the same."

A major risk factor for disruption of lipid homeostasis is having high LDL cholesterol. So if PPARs are at the root of MS, it would explain why cases of the disease have been on the rise in recent decades. "In general people around the world are increasing their intake of sugars and animal fats, which often leads to high LDL cholesterol," Corthals said. "So we would expect to see higher rates of disease related to lipid metabolism - like [heart disease](#) and, in this case, MS." This also explains why statin drugs, which are used to treat high cholesterol, have shown promise as an MS treatment.

The lipid hypothesis also sheds light on the link between MS and [vitamin D](#) deficiency. Vitamin D helps to lower LDL cholesterol, so it makes sense that a lack of vitamin D increases the likelihood of the disease - especially in the context of a diet high in fats and [carbohydrates](#).

Corthals's framework also explains why MS is more prevalent in women.

"Men and women metabolize fats differently," Corthals said. "In men, PPAR problems are more likely to occur in vascular tissue, which is why atherosclerosis is more prevalent in men. But women metabolize fat differently in relation to their reproductive role. Disruption of lipid metabolism in women is more likely to affect the production of myelin and the central nervous system. In this way, MS is to women what atherosclerosis is to men, while excluding neither sex from developing the other disease."

In addition to high cholesterol, there are several other risk factors for reduced PPAR function, including pathogens like Epstein-Barr virus, trauma that requires massive cell repair, and certain genetic profiles. In many cases, Corthals says, having just one of these risk factors isn't enough to trigger a collapse of lipid metabolism. But more than one risk factor could cause problems. For example, a genetically weakened PPAR system on its own might not cause disease, but combining that with a pathogen or with a poor diet can cause disease. This helps to explain why different MS triggers seem to be important for some people and populations but not others.

"In the context of autoimmunity, the various risk factors for MS are frustratingly incoherent," Corthals said. "But in the context of lipid metabolism, they make perfect sense."

Much more research is necessary to fully understand the role of PPARs in MS, but Corthals hopes that this new understanding of the disease could eventually lead to new treatments and prevention measures.

"This new framework makes a cure for MS closer than ever," Corthals said.

Angelique Corthals, "Multiple Sclerosis (MS) is not a disease of the immune system," *The Quarterly Review of Biology*

86:4 (December 2011).

#### References

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## Multiple Sclerosis Not Disease Of Immune System?

BY EURASIA REVIEW DECEMBER 23, 2011

An

article to be published Friday (Dec. 23) in the December 2011 issue of The Quarterly Review of Biology argues that multiple sclerosis, long viewed as

primarily an autoimmune disease, is not actually a disease of the immune system. Dr. Angelique Corthals, a forensic anthropologist and professor at the John Jay College of Criminal Justice in New York, suggests instead that MS is caused by faulty lipid metabolism, in many ways more similar to coronary atherosclerosis (hardening of the arteries) than to other autoimmune diseases.

Framing MS as a metabolic disorder helps to explain many puzzling aspects of the disease, particularly why it strikes women more than men and why cases are on the rise worldwide, Corthals says. She believes this new framework could help guide researchers toward new treatments and ultimately a cure for the disease.

Multiple sclerosis affects at least 1.3 million people worldwide. Its main characteristic is inflammation followed by scarring of tissue called myelin, which insulates nerve tissue in the brain and spinal cord. Over time, this scarring can lead to profound neurological damage. Medical researchers have theorized that a runaway immune system is at fault, but no one has been able to fully explain what triggers the onset of the disease. Genes, diet, pathogens, and vitamin D deficiency have all been linked to MS, but evidence for these risk factors is inconsistent and even contradictory, frustrating researchers in their search for effective treatment.

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“Each time a genetic risk factor has shown a significant increase in MS risk in one population, it has been found to be unimportant in another,” Corthals said. “Pathogens like Epstein-Barr virus have been implicated, but there’s no explanation for why genetically similar populations with similar pathogen loads have drastically different rates of disease. The search for MS triggers in the context of

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autoimmunity simply hasn't led to any unifying conclusions about the etiology of the disease.”

However, understanding MS as metabolic rather than an autoimmune begins to bring the disease and its causes into focus.

## THE LIPID HYPOTHESIS

Corthals believes that the primary cause of MS can be traced to transcription factors in cell nuclei that control the uptake, breakdown, and release of lipids (fats and similar compounds) throughout the body. Disruption of these proteins, known as peroxisome proliferator-activated receptors (PPARs), causes a toxic byproduct of “bad” cholesterol called oxidized LDL to form plaques on the affected tissue. The accumulation of plaque in turn triggers an immune response, which ultimately leads to scarring. This is essentially the same mechanism involved in atherosclerosis, in which PPAR failure causes plaque accumulation, immune response, and scarring in coronary arteries.

“When lipid metabolism fails in the arteries, you get atherosclerosis,” Corthals explains. “When it happens in the central nervous system, you get MS. But the underlying etiology is the same.”

A major risk factor for disruption of lipid homeostasis is having high LDL cholesterol. So if PPARs are at the root of MS, it would explain why cases of the disease have been on the rise in recent decades. “In general people around the world are increasing their intake of sugars and animal fats, which often leads to high LDL cholesterol,” Corthals said. “So we would expect to see higher rates of disease related to lipid metabolism—like heart disease and, in this case, MS.” This also explains why



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statin drugs, which are used to treat high cholesterol, have shown promise as an MS treatment.

The lipid hypothesis also sheds light on the link between MS and vitamin D deficiency. Vitamin D helps to lower LDL cholesterol, so it makes sense that a lack of vitamin D increases the likelihood of the disease—especially in the context of a diet high in fats and carbohydrates.

Corthals's framework also explains why MS is more prevalent in women.

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“Men and women metabolize fats differently,” Corthals said. “In men, PPAR problems are more likely to occur in vascular tissue, which is why atherosclerosis is more prevalent in men. But women metabolize fat differently in relation to their reproductive role. Disruption of lipid metabolism in women is more likely to affect the production of myelin and the central nervous system. In this way, MS is to women what atherosclerosis is to men, while excluding neither sex from developing the other disease.”

In addition to high cholesterol, there are several other risk factors for reduced PPAR function, including pathogens like Epstein-Barr virus, trauma that requires massive cell repair, and certain genetic profiles. In many cases, Corthals says, having just one of these risk factors isn't enough to trigger a collapse of lipid metabolism. But more than one risk factor could cause problems. For example, a genetically weakened PPAR system on its own might not cause disease, but combining that with a pathogen or with a poor diet can cause disease. This helps to explain why different MS triggers seem to be important for some people and populations but not others.

EURASIA REVIEW

## NEWSLETTER



“In the context of autoimmunity, the various risk factors for MS are frustratingly incoherent,” Corthals said. “But in the context of lipid metabolism, they make perfect sense.”

Much more research is necessary to fully understand the role of PPARs in MS, but Corthals hopes that this new understanding of the disease could eventually lead to new treatments and prevention measures.

“This new framework makes a cure for MS closer than ever,” Corthals said.

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ON "MULTIPLE SCLEROSIS NOT DISEASE OF IMMUNE SYSTEM?"

bluridgelvr | December 23, 2011  
at 1:39 pm | Reply

Actually this study goes against the evidenced-challenged but social media-driven CCSVI theory. I predict however that their ignorant activists will argue that this study supports their cause.

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Nebby | December 23, 2011 at  
7:23 pm | Reply



## Sclerosi multipla: non sarebbe una malattia autoimmune. Lo sostiene una ricercatrice

23 DICEMBRE 2011 / NO COMMENTS / 283 VIEWS

In un articolo pubblicato nel numero di dicembre della rivista medica "The Quarterly Review of Biology" si sostiene che la sclerosi multipla (SM), a lungo considerata principalmente come una malattia autoimmune, in realtà non sarebbe una malattia del sistema immunitario. La prof.ssa Angelique Corthals, un antropologa forense e docente presso il John Jay College of Criminal Justice di New York, suggerisce invece che la sclerosi multipla potrebbe essere causata dal metabolismo difettoso dei lipidi, per molti versi più simile all'aterosclerosi coronarica (indurimento delle arterie) rispetto ad altre malattie autoimmuni.

Definire la SM come un disordine metabolico aiuterebbe a spiegare molti aspetti sconcertanti della malattia, in particolare perché colpisca le donne più degli uomini, e perché i casi siano in aumento in tutto il mondo, spiega la Corthals. Crede che questo nuovo quadro potrebbe aiutare i ricercatori verso nuovi trattamenti e, infine, una cura per la malattia.

La sclerosi multipla colpisce almeno 1,3 milioni di persone in tutto il mondo. La sua caratteristica principale è l'infiammazione seguita dalla cicatrizzazione del tessuto chiamato mielina, che isola il tessuto nervoso del cervello e del midollo spinale. Nel tempo queste cicatrici possono portare ad importanti danni neurologici. I ricercatori hanno teorizzato che un sistema immunitario impazzito ne sia la causa, ma nessuno è stato in grado di spiegare pienamente ciò che innesci l'insorgenza della malattia. I geni, la dieta, gli agenti patogeni e deficit di vitamina D sono stati tutti legati alla SM, ma le evidenze di questi fattori di rischio sono inconsistenti e addirittura contrastanti, frustrando i ricercatori nella loro ricerca per una terapia efficace.

"Ogni volta che un fattore di rischio genetico ha mostrato un aumento significativo del rischio di SM in una popolazione, è stato trovato essere irrilevante in un'altra", ha spiegato la Corthals. "Sono stati implicati gli agenti patogeni come il virus di Epstein-Barr, ma non c'è alcuna spiegazione del motivo per cui popolazioni geneticamente simili con simili carichi di agenti patogeni hanno tassi drasticamente differenti della malattia. La ricerca della SM nel contesto dell'autoimmunità non ha portato ad alcuna conclusione definitiva circa l'eziologia della malattia."

Tuttavia, la comprensione della SM come malattia metabolica piuttosto che autoimmune inizia a focalizzare la malattia e le sue cause.

### L'IPOTESI LIPIDICA

La Corthals ritiene che la causa principale della sclerosi multipla possa essere ricondotta a fattori di trascrizione nei nuclei delle cellule che controllano l'assorbimento, la ripartizione ed il rilascio dei lipidi (grassi e composti simili) in tutto il corpo. L'alterazione di queste proteine, conosciuta come "peroxisome proliferator-activated receptors (PPARs), provocherebbe un sottoprodotto tossico di colesterolo "cattivo" LDL ossidante chiamato a formare le placche sul tessuto colpito. L'accumulo di placca a sua volta innescerebbe una risposta immunitaria, che lo condurrebbe alla formazione di cicatrici. Questo essenzialmente è lo stesso meccanismo coinvolto nell'aterosclerosi, in cui la distruzione dei PPARs provoca l'accumulo delle placche, la risposta immunitaria e le cicatrici nelle arterie coronarie.

"Quando il metabolismo dei lipidi nelle arterie non funziona, si arriva all'aterosclerosi", spiega la



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## Американский эксперт усомнился в иммунной природе рассеянного склероза



Изображение с сайта [aquatictherapist.com](http://aquatictherapist.com)

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Рассеянный склероз, долгое время считавшийся аутоиммунным заболеванием, по мнению антрополога из Колледжа уголовного права Джона Джея (John Jay College of Criminal Justice) профессора Анжелик Корталс (Angelique Corthals) имеет много общего с атеросклерозом коронарных артерий и с большей вероятностью является нарушением жирового обмена, чем болезнью иммунной системы, сообщает EurekAlert!

"Если рассматривать рассеянный склероз в качестве обменного заболевания, то можно объяснить многие его загадочные аспекты, в частности, почему оно больше поражает женщин, чем мужчин, и почему во всем мире возрастает количество случаев рассеянного склероза", - отмечает Корталс.

Причина возникновения рассеянного склероза точно не выяснена. На сегодняшний день общепринятой является аутоиммунная теория, согласно которой иммунная система больного по какой-то причине начинает вырабатывать антитела, поражающие собственные клетки организма (клетки миелинового слоя).

Рассеянный склероз — хроническое заболевание, при котором поражается миелиновая оболочка нервных волокон головного и спинного мозга. При этом на белом веществе мозга образуются характерные очаги разрушения (демиелинизация), или, бляшки рассеянного склероза, которые препятствуют прохождению нервного импульса и, как следствие, нормальной жизнедеятельности организма.

По мнению профессора Корталс, первопричина рассеянного склероза может скрываться в клеточном ядре, в белковых факторах транскрипции, которые контролируют поглощение, расщепление, а также вывод из организма липидов (жиров и жироподобных соединений). Сбой в работе этих белков (они называются рецепторы, активируемые фактором пролиферации пероксисом, Peroxisome proliferator-activated receptors, PPARs) приводит к образованию склеротических бляшек из токсичных производных "плохого" холестерина — окисленных липопротеидов низкой плотности.

Скопление таких бляшек, в свою очередь, запускает иммунную реакцию, которая неизбежно приводит к образованию рубцов на миелиновом слое. "То же самое происходит при развитии атеросклероза", - отмечает Корталс.

По мнению профессора Корталс, гипотезой нарушения липидного обмена можно объяснить и тот факт, что лекарства для понижения уровня холестерина, статины, показали свою эффективность в испытаниях на пациентах с рассеянным склерозом.

Рассеянным склерозом в мире больны 1 миллион 300 тысяч человек.

Гипотеза профессора Корталс опубликована в декабрьском номере ежеквартального издания The Quarterly Review of Biology.

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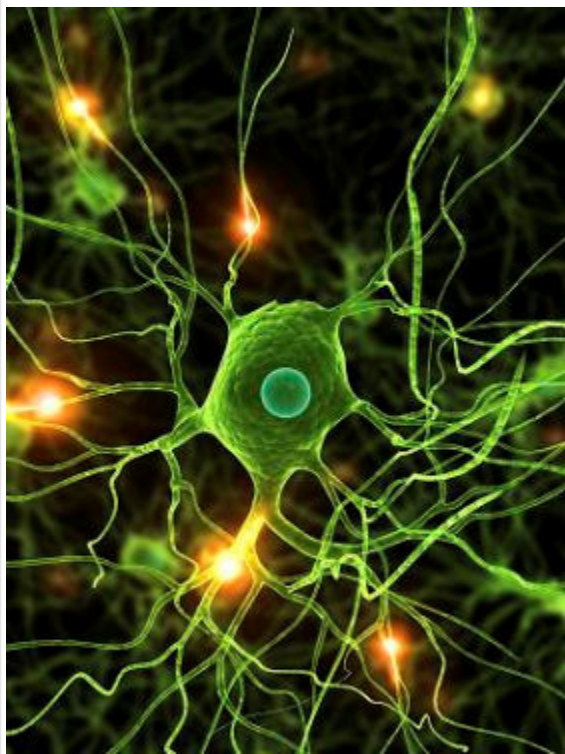
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## MS is a metabolic disorder, claims new study

by **Will Parker** on December 28, 2011 in **Medicine, News**



A controversial new study that frames multiple sclerosis (MS) as a metabolic disorder rather than an autoimmune disease neatly addresses many puzzling aspects of the illness, including why it strikes women more than men and why cases are on the rise worldwide. Appearing in the *The Quarterly Review of Biology*, the study suggests that MS is caused by faulty lipid metabolism and is similar in many ways to coronary

atherosclerosis (hardening of the arteries).

Medical researchers have always theorized that a runaway immune system caused MS, but a full explanation of what triggered the onset of the disease remained elusive. Genes, diet, pathogens, and vitamin D deficiency have all been linked to MS, but evidence for these risk factors is inconsistent and even contradictory.

Author of the new study, Dr. Angelique Corthals, from John Jay College in New York, notes that each time a genetic risk factor has shown a significant increase in MS risk in one population, it has been found to be unimportant in another. “Pathogens like Epstein-Barr virus have been implicated, but there’s no explanation for why genetically similar populations with similar pathogen loads have drastically different rates of disease. The search for MS triggers in the context of autoimmunity simply hasn’t led to any unifying conclusions about the etiology of the disease,” she argues. “Understanding MS as metabolic rather than an autoimmune [disease] begins to bring the disease and its causes into focus.”

Corthals believes that the primary cause of MS can be traced to transcription factors in cell nuclei that control the uptake, breakdown, and release of lipids (fats and similar compounds) throughout the body. Disruption of these proteins, known as peroxisome proliferator-activated receptors (PPARs), causes a toxic byproduct of cholesterol called oxidized LDL to form plaques on the affected tissue.

The accumulation of plaque in turn triggers an immune response, which ultimately leads to scarring. This is essentially the same mechanism involved in atherosclerosis, in which PPAR failure causes plaque accumulation, immune response, and scarring in coronary arteries. “When lipid metabolism fails in the arteries, you get atherosclerosis,” Corthals explains. “When it happens in the central nervous system, you get MS. But the underlying etiology is the same.”

A major risk factor for disruption of lipid homeostasis is having high LDL cholesterol (often referred to as “bad” cholesterol). So if PPARs are at the root of MS, it would explain why cases of the disease have been on the rise in recent decades. “In general people around the world are increasing their intake of sugars and animal fats, which often leads to high LDL cholesterol,” Corthals said. “So we would expect to see higher rates of disease related to lipid metabolism – like heart disease and, in this case, MS.” This also explains why statin drugs, which are used to treat high cholesterol, have shown promise as an MS treatment.

Corthals' lipid hypothesis also sheds light on the link between MS and vitamin D deficiency. Vitamin D helps to lower LDL cholesterol, so it makes sense that a lack of vitamin D increases the likelihood of the disease – especially in the context of a diet high in fats and carbohydrates.

The lipid theory also explains why MS is more prevalent in women. “Men and women metabolize fats differently,” Corthals said. “In men, PPAR problems are more likely to occur in vascular tissue, which is why atherosclerosis is more prevalent in men. But women metabolize fat differently in relation to their reproductive role. Disruption of lipid metabolism in women is more likely to affect the production of myelin and the central nervous system. In this way, MS is to women what atherosclerosis is to men.”

Corthals contends that in the context of autoimmunity, the various risk factors for MS are “frustratingly incoherent,” but in the context of lipid metabolism, they make perfect sense. She hopes that this new understanding of the disease could lead to more research into the role of PPARs, and eventually, new treatments and prevention measures.

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Source: *The Quarterly Review of Biology*

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### MS may not be autoimmune disease

NEW YORK, 1 Jan—Multiple sclerosis, long viewed as primarily an autoimmune disease, is not actually a disease of the immune system, a US researcher says.

Dr Angelique of the John Jay College of Criminal Justice in New York suggests instead that MS is caused by faulty lipid metabolism—in many ways more similar to coronary atherosclerosis—hardening of the arteries—than to other autoimmune diseases.

Considering MS as a

metabolic disorder helps to explain many puzzling aspects of the disease, particularly why it strikes women more than men and why cases are on the rise worldwide, Corthals said.

Multiple sclerosis is mainly characterized by inflammation followed by scarring of tissue called myelin, which insulates nerve tissue in the brain and spinal cord. Over time, this scarring can lead to profound neurological damage, but medical researchers have theorized that a runaway immune system is at fault, but

no one has been able to fully explain what triggers the onset of the disease.

Corthals said the primary cause of MS can be traced to transcription factors in cell nuclei that control the uptake, breakdown, and release of lipids — fats and similar compounds — throughout the body. Disruption of these proteins, known as peroxisome proliferator-activated receptors, causes a toxic byproduct of “bad” low-density lipoprotein cholesterol to form plaque on the affected tissue. The accumulation of plaque in turn

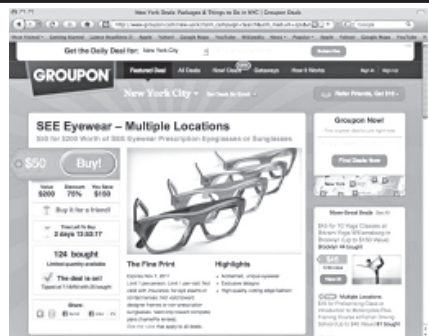


triggers an immune response, which ultimately leads to scarring. Corthals’ framework explains why MS is more prevalent in women.

“Men and women metabolize fats differently,” Corthals said. “In men, problems are more likely to occur in vascular tissue, which is why atherosclerosis is more prevalent in men. But women metabolize fat differently in relation to their reproductive role.”

The findings are published in The Quarterly Review of Biology.

Internet



This screen shot shows eyewear coupons for the New York City area offered by Groupon.com. Daily deal sites such as Groupon and LivingSocial, best known for discounts at local restaurants and spas, are helping some people fill holes in health insurance coverage.

INTERNET

### Diet may help prevent brain shrinkage

CORVALLIS, 1 Jan—Elderly people with higher levels of vitamins B, C, D and E, and omega-3 fatty acids in their blood are mentally sharper, US researchers say.

The study, published in the journal Neurology, also found the higher levels of vitamins and fish body oils resulted in less brain shrinkage typical of Alzheimer’s disease, while “junk food” diets—trans-fats found in baked and fried foods, margarine, fast-food and other less-healthy dietary choices—

produced just the opposite result.

Study co-author Maret Traber, a principal investigator with the Linus Pauling Institute at Oregon State University, and scientists from the Oregon Health and Science University in Portland, Ore, said the study involved 104 people, at an average age of 87, with no special risk factors for poor memory or mental acuity.

The researchers tested for 30 different nutrient biomarkers in their blood, and 42 participants also had

magnetic resonance imaging scans to measure their brain volume.

“The vitamins and nutrients you get from eating a wide range of fruits, vegetables and fish can be measured in blood biomarkers,” Traber said in a statement. “These findings are based on average people eating average American diets. If anyone right now is considering a New Year’s resolution to improve their diet, this would certainly give them another reason to eat more fruits and vegetables.”

Internet

### Vitamin B12 may still help reduce stroke

LONDON, (Ontario,) 1 Jan—Vitamin B therapy still has a role to play in reducing the risk of stroke, US and Canadian researchers suggest. Dr David Spence of The University of Western Ontario and Dr Meir Stampfer of the Harvard School of Public Health said vitamin B therapy was once widely used to lower homocysteine levels.

Too much of this amino acid in the bloodstream was linked to increased risk of stroke and heart attack, but several randomized trials found lowering homocysteine levels with B vitamins did not result in a cardiovascular benefit.

In fact, Spence, a scientist with the Robarts Research Institute at Western’s Schulich School of Medicine & Dentistry, found vitamin B therapy actually increased cardiovascular risk in patients with diabetic nephropathy.

In an commentary published in the Journal of the American Medical Association, Spence and Stampfer said two key issues have been overlooked in the interpretation of the clinical trials — the key role of vitamin B12, and the newly recognized role of renal failure.

“It is now clear that the large trials showing no benefit of vitamin therapy obscured the benefit of vitamin therapy because they lumped together patients with renal failure and those with good renal function,” Spence said in the commentary. “The vitamins are harmful in renal failure, and beneficial in patients with good renal function, and they cancel each other out,” said Spence, the author of “How to Prevent Your Stroke.” The commentary authors also contend most of the trials did not use a high enough dose of vitamin B12.—Internet

### IMF: Greece will miss financial targets

ATHENS, (Greece), 1 Jan—The International Monetary Fund in an official report said Greece’s financial situation is worse than previously thought.

With a new estimate on the country’s economic growth, the IMF said even a 50 percent write-off on Greek debt would be insufficient for Greece to avoid default, Ekathimerini reported Saturday.

To dig Greece out of its financial trough “requires either a deeper

haircut or additional loans from Europe,” an IMF official said. While the Greek economy stumbles, tax revenues have dropped. The previous goal was for Athens to collect \$9 billion in taxes in December, January and February.

Without hitting its target on tax collection, the budget deficit is projected to reach 10 percent of the nation’s gross domestic product, missing another target, that of keeping the deficit below 9 percent of GDP.

Internet



Vehicles on display at an international rental and leasing industry exposition in Nanjing, Jiangsu province. Business analysts and company officials said the car rental industry must focus more on individual customers.—INTERNET

### GM recalls Sonics to inspect brake pads

DETROIT, 1 Jan—GM has announced the recall of 4,296 Chevrolet Sonics sold in the United States because of a potential problem with brake pads.

Company officials said they expect only a few of the vehicles to have defective brake pads, the Detroit Free Press reported. GM decided on the recall after a Sonic was found to have a missing pad during routine service.

There have been no reports of crashes, deaths or injuries, the company said.

The recall involves 2012 Sonics produced at the Orion, Mich., assembly plant between 2 June and 21 Nov, the National Highway Transportation Safety Administration said on its Web site.

Internet

### Companies can foster or destroy innovation

NASHVILLE, 1 Jan—A US researcher says innovation may mean less “thinking out of the box” and more setting up a company structure that overcomes constraints.

David Owens of Vanderbilt University’s Owen Graduate School of Management said business and other leaders need to understand exactly which constraints work against them in order to help create conditions that foster innovation rather than kill creativity.

“Constraints are the parameters within which you must work,” Owens said in a statement. “And for a creative person that’s actually a blessing.”

Owens identified the six most common hurdles to innovation that companies encounter:

— Failures of innovation are failures of ideas, and to meet this challenge companies need to train people to use the tools and processes that help them “think differently” and

enable them to become better at generating and recognizing good ideas.

— A company’s social climate will determine whether an innovation succeeds.

— The company or organization needs a strategy for innovation.

— Innovation fails when a firm competing among a group of rivals in an industry fails to produce something

customers want.

— For an innovation to succeed, it has to be technologically feasible.

“By learning to analyze these constraints in advance, turning from retrospective analysis to proactive strategy development, you can dramatically improve your chances of innovation success,” Owens said.

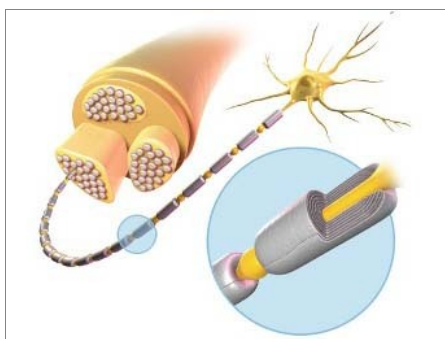
Internet



A cement equipment manufacturing plant in Jiangsu province. Flagging manufacturing conditions signal that weakening external demand is starting to bite, says Qu Hongbin, chief China economist and co-head of Asian Economic Research at HSBC.—INTERNET

Business

## Опровергнута нейродегенеративная гипотеза развития рассеянного склероза



Миелиновая оболочка нейрона. Изображение с сайта [myelinsheath.org](http://myelinsheath.org)

27 февраля 2012 года, 20:11

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Ученые из Германии и Швейцарии опровергли гипотезу о том, что причиной развития рассеянного склероза является повреждение оболочки нервных клеток, сообщает [HealthCanal](#). Исследование провела группа специалистов, возглавляемая Буркхардом Бехером (Burkhard Becher) из Цюрихского университета.

У больных рассеянным склерозом в головном и спинном мозге наблюдаются очаги демиелинизации (бляшки), которые препятствуют проведению нервных импульсов. К настоящему времени причины развития болезни остаются невыясненными. Согласно нейродегенеративной гипотезе, в основе заболевания лежит разрушение миелиновой оболочки нервных клеток. В таком случае аутоиммунное поражение поврежденной оболочки нейронов, является результатом, а не причиной образования бляшек.


В ходе исследования группа Бехера использовала выращенных в лаборатории мышей, у которых имелись врожденные дефекты миелиновой оболочки нейронов. Ученые пытались стимулировать иммунитет грызунов, чтобы зафиксировать развитие патологического процесса в нервной системе. Однако эти эксперименты завершились безрезультатно - симптомы заболевания у животных не появлялись.


В связи с этим исследователи назвали несостоятельной нейродегенеративную гипотезу развития рассеянного склероза. Авторы работы считают, что непосредственно повреждение миелиновой оболочки нейронов не может спровоцировать начало заболевания при нормальной работе иммунной системы.

Исследовательская группа намерена продолжить работу по выяснению причин рассеянного склероза. По словам коллеги Бехера из Мюнхена Торстена Буша (Thorsten Buch), в ходе дальнейших исследований внимание специалистов необходимо сосредоточить не столько на нервной, сколько на иммунной системе.

В декабре 2011 года американский антрополог Анжелик Корталс (Angelique Corthals) поставила под сомнение аутоиммунную природу рассеянного склероза. Она считает, что болезнь обусловлена сбоем в работе белков, которые контролируют жировой обмен. Образующиеся в результате липидные бляшки и запускают иммунные реакции, результатом которых становится повреждение миелиновой оболочки нейронов.

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## SCIENCE

# Disease Diagnosed in a 500-Year-Old Mummy

Observatory

By SINDYA N. BHANOO    JULY 30, 2012

An Inca girl who lived 500 years ago suffered from a bacterial lung infection just before she died, report scientists who have examined her mummy.

The girl, thought to be 15, was sacrificed by the Andean Inca at the summit of Llullaillaco, a 22,000-foot volcano in the province of Salta, Argentina, said Angelique Corthals, a forensic anthropologist at the City University of New York. The girl had a large sore on one leg, leading Dr. Corthals to believe she may have been unwell when she was buried, alive but unconscious, on the mountain.

Dr. Corthals and her colleagues used a technique called shotgun proteomics to compare proteins found in the mummy against large databases of the human genome. The mummy's protein profile fit that of someone with a chronic respiratory infection, said Liliana M. Dávalos, an evolutionary biologist at Stony Brook University and another author of the study.

“This is the first time it has been done on an ancient mummy,” Dr. Dávalos said. “It’s now done routinely on cancer patients and has many human disease

applications, but it hadn't been applied in archaeological work.”

Dr. Dávalos and Dr. Corthals and their colleagues report their findings in the journal PLoS One.

The researchers discovered the mummy, along with those of two other sacrificed children, in 1999.

“They were buried in a tomb, and the tomb was packed solid with volcanic ashes and covered in snow, so they did not desiccate,” Dr. Corthals said. “Their entire bodies were sealed and perfectly preserved.”

The sacrificed youths probably made a journey of as many as 1,500 miles from Cuzco, the capital of the Inca empire, to the summit, Dr. Corthals said. “The girl actually had gray hair, so I think they knew their fate,” she said. “And the little girl and boy also had their teeth ground down.”

The mummies are on view at the Museum of High Mountain Archaeology in Salta.

***Correction: August 7, 2012***

A report in the Observatory column last Tuesday about a diagnosis of bacterial lung infection in the mummy of an Inca girl sacrificed 500 years ago misstated the distance that she and two other youths probably traveled before their deaths. Their journey, from Cuzco, Peru, the capital of the Inca empire, to the summit of the Lullailaco volcano in Argentina, was as long as 1,500 miles, not 3,000.

A version of this article appears in print on July 31, 2012, on page D3 of the New York edition with the headline: Disease Diagnosed in a 500-Year-Old Mummy.

## Maiden shows signs of TB-like infection

Analysis of Incan mummy captures information about immune system activity

By Tina Hesman Saey

Web edition: July 26, 2012

Print edition: [September 8, 2012](#); Vol.182 #5 (p. 9)

As if being a human sacrifice weren't bad enough, a teenager may have been fighting off tuberculosis before being killed on top of a South American volcano 500 years ago.

As she climbed to her death, the immune system of a 15-year-old Incan girl known as the Maiden was combating a bacterial infection caused by a type of *Mycobacterium*, an analysis indicates. Angelique Corthals, a forensic anthropologist at the City University of New York, and colleagues report the findings online July 25 in *PLoS One*.

La Doncella, as the Maiden is called in Spanish, was one of three children whose mummified remains were found near the summit of Lulllaillaco volcano in Argentina in 1999. She, a younger girl and young boy were probably sacrificed in a ritual called Capacocha. But the exact cause of the children's deaths has remained a mystery; their perfectly preserved mummies show no signs of violent trauma.

Corthals wanted to know whether the children were given a fermented corn drink called chicha, which was used to numb sacrifice victims as part of the Capacocha ritual. The alcohol in the drink would have evaporated almost immediately, but the children might still have traces of corn clinging to their lips, she reasoned. Researchers swabbed blood and saliva from the lips of the Maiden and the boy, and snipped off a small piece of the boy's blood-soaked cloak for testing using a technique that identifies proteins contained in the samples. The younger girl's face was damaged by a lightning strike after burial, so the researchers couldn't include her in the study.



### ILL-FATED

This Incan girl, known as the Maiden, was sacrificed on top of a South American volcano 500 years ago. New data suggest the girl had an active infection with a bacterium similar to the one that causes tuberculosis.

Credit: Johan Reinhard

Coauthor Antonius Koller of the State University of New York Stony Brook Medical Center and his colleagues determined which proteins were present in the samples. There was no sign of corn liquor, Corthals says, but the protein profile indicated clearly what the two mummies' immune systems had been up to at the time of death.

The Maiden's immune system was more active than the boy's was, and her swabs contained immune system proteins indicating a chronic lung infection. Modern people fighting off *Mycobacterium* diseases such as tuberculosis make similar proteins. DNA evidence showed that the girl was carrying some type of *Mycobacterium*, although the researchers can't yet nail down which species of the bacterium was infecting her.

The new findings are consistent with radiological exams showing signs of lung and sinus inflammation in the Maiden. The boy showed no signs of active infection.

Other researchers are sure to latch onto the new research approach described in the study, says Robert DeSalle, of the American Museum of Natural History in New York City. "It is going to be the first paper among probably a lot to come looking at infectious diseases among dead people," he says. He predicts that examining the immune systems of long-dead creatures may also help solve some archaeological debates, such as whether woolly mammoths were victims of overhunting or disease.

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## Citations

A. Corthals et al. Detecting the immune system response of a 500 year-old Inca mummy. PLoS One, Vol. 7, July 25, 2012, p. e41244. doi:10.1371/journal.pone.0041244. [\[Go to\]](#)

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## Suggested Reading

B. Bower. Inca mummies emerge from deep freeze. Science News, Vol. 155, April 17, 1999, p. 244. Available online: [\[Go to\]](#)

T. Hesman Saey. Frozen mummy's genetic blueprints unveiled. Science News, Vol. 181, March 24, 2012, p. 5. Available online: [\[Go to\]](#)

## SCIENCE

# Inca Mummy: 'Maiden' Had Lung Infection When Sacrificed, Study Suggests

© 07/26/2012 08:14 am ET | Updated Jul 27, 2012

2.5k



By: Joseph Castro, LiveScience Contributor

Published: 07/25/2012 05:05 PM EDT on LiveScience

The so-called Maiden mummy of a 15-year-old Incan girl who was sacrificed 500 years ago is giving up some secrets, revealing the teenager suffered from a bacterial lung infection at the time of her death, scientists report Wednesday (July 25).

The researchers analyzed tissue proteins, rather than DNA, from the Maiden and another young [Inca mummy](#) who died at the same time.

Over the last decade, DNA techniques have proven useful in helping solve ancient mysteries, such as [how King Tut died](#). But these techniques aren't without faults. For example, finding evidence of a malaria-causing parasite in King Tut's system doesn't necessarily mean the Egyptian king suffered any malaria symptoms. Additionally, the environment can easily contaminate DNA samples, if researchers aren't careful.

On the other hand, analyzing a sample's proteins, which are less susceptible to environmental contamination, yields a whole different set of information. "Being the expression of DNA, proteins really show you what the body is producing at the time when the individual is being sampled — or, in our case, at the time of death," study researcher Angelique Corthals, a forensic anthropologist at the City University of New York, told LiveScience. In particular, proteins can tell you if the body's immune system has activated to fight a disease, she added. [\[The Mummy Quiz: Test Your Smarts\]](#)


## Llullaillaco mummies

In their study, Corthals and her colleagues took lip swabs from two [Andean Inca mummies](#), a 7-year-old boy and "the Maiden," as well as samples from the boy's bloodied cloak. The two [child mummies](#), discovered in 1999, were

originally buried on the summit of the Argentinian volcano Lullailaco, 22,100 feet (6,739 meters) above sea level, after being sacrificed in a ceremonial ritual.

Past research found the boy and girl had been fattened up before sacrifice, being fed a typical peasant diet of potatoes and other common vegetables up until a year before their sacrifice, when evidence suggests they were given “elite” foods like maize and dried llama meat.

Once sacrificed, the freezing temperatures, among other factors, naturally preserved their fattened bodies. [\[Photos of the Inca Child Mummies\]](#)

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“What I really wanted to do originally was see where the blood I found on the mummies’ clothing and lips came from,” Corthals said. “But we found a whole lot more than we were expecting.”

Archaeologists also found a third mummy, a 6-year-old girl, along with the other two. This mummy appears to have been struck by lightning, which could potentially interfere with test results, so Corthals and her team didn’t take any samples from it.



*The three Lullailaco mummies, including that of the 7-year-old boy (shown here), are preserved at Museum of High Mountain Archaeology (MAAM) in Salta, Argentina.*

### Lung infection found

The researchers used a technique called shotgun proteomics. They placed their samples into a device called a mass spectrometer, which broke all of the sample’s proteins into their constituent parts, amino-acid chains.

Sophisticated software compared these parts with existing proteins of the [human genome](#) to determine the actual proteins in the samples, Corthals explained. “You couldn’t use this technique for an organism that we don’t have the complete genome for,” she said.

They found that the Maiden’s profile of proteins match that of a chronic respiratory infection patient. X-rays taken of the Maiden’s lungs after she was discovered also showed signs of a lung infection. To see if the Maiden was

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harboring anything that could cause such an infection, they turned to DNA analysis and discovered evidence of bacteria in the genus *Mycobacterium*, which is known to cause upper respiratory-tract infections and tuberculosis (TB). Statistical models suggested the bacterium falls into the cluster group that causes TB, but the exact species isn't known, likely because its DNA hasn't been sequenced yet.

The Llullaillaco boy didn't have signs of disease or pathogenic bacteria.

The research shows that shotgun proteomics can play a critical role in determining the disease or death in archeological, medical and criminal cases, Corthals said, adding that the method may even be able to determine which pathogen is the killer in a case of multiple infections. For now, Corthals is interested in seeing whether the technique can be used with less pristine samples, such as skeletal material or [Egyptian mummies](#).

Down the line, the protein technique's utility will likely go beyond just archaeology, researchers said. "I expect [the method's] biggest impact will be in criminal forensic science," Corthals said.

The new study is detailed online today (July 25) in the journal PLoS One.

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## 500-year-old Incan mummy had lung infection, probably TB

July 27, 2012 | By Thomas H. Maugh II

Studies of a 15-year-old Incan girl who was sacrificed on an Argentine mountaintop 500 years ago show that she had a lung infection when she died, most likely tuberculosis, researchers reported this week. Two younger children who died with her did not have an infection, they said.

The mummy, known as the Maiden, was discovered in 1999 about 25 yards from the summit of Llullaiaco, a high-elevation volcano in the province of Salta, Argentina, by archaeologists led by Johan Reinhard and Constanza Ceruti of the Mountain Institute in Franklin, W.Va. The Maiden and a 7-year-old boy and a 6-year-old girl had been sacrificed to Pachamama, the earth goddess, in the ritual of Capacocha. The area's freezing temperatures, low humidity, anaerobic environment and presence of natural disinfectants led to remarkable preservation of the bodies, which are now on display at the Museum of High Mountain Archaeology in Salta, Argentina. The mummies are in airtight, self-contained capsules maintained at minus-20 degrees Celsius.

Testing ancient specimens for infections is a tricky business. Because DNA must be amplified, there is a danger of also amplifying extraneous contaminants. And even if a pathogen is present, it doesn't necessarily mean the individual had an active infection.

Angelique Corthals, a forensic anthropologist at the John Jay College of Criminal Justice at City University of New York and her colleagues at SUNY Stony Brook took a different approach. They took tissue swabs from the mouths of the Maiden and the 7-year-old boy and analyzed the proteins that were present. The team reported in the journal PLoS One that the proteins present in the Maiden were characteristic of an active immune response to an infection. DNA analysis suggested that the Maiden was infected by a bacterium from the *Mycobacterium* family, which includes the TB bacterium, and CT scans suggested she suffered from a lung infection. Similar problems were not observed in the boy.

"Our study is the first of its kind since, rather than looking for the pathogen, which is notoriously difficult to do in historical samples, we are looking at the protein profile of the 'patient,' which more accurately tells us that there was indeed an infection at the time of death," Corthals said. "Our study opens the door to solving many historical and current biomedical and forensic mysteries, from understanding why the plague of 1918 was so lethal to finding out which pathogen is responsible for death in cases of multiple infections."

LATimesScience@gmail.com

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# Pneu-mummy-a

**Comparing the protein profile of a 500-year-old Inca mummy to modern humans reveals an active lung infection prior to sacrifice.**

By Hayley Dunning | November 1, 2012

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**MINI MAIDEN:** This little girl (La Nina del Rayo) died at age 6 and was preserved remarkably well by the Andean conditions.

COURTESY OF ANGELIQUE CORTHALS

**I**n 1999, high in the bone-dry plains of the Atacama Desert in Argentina, Johan Reinhard, currently the Explorer-in-Residence at the National Geographic Society, and colleagues uncovered three exceptionally well-preserved corpses. Two children, a girl and a boy aged 6 and 7 respectively, and a 15-year old adolescent they named “the Maiden” had all been sacrificed some 500 years ago and buried near the summit of one of the world’s highest volcanoes, Lullullaco.

The conditions of preservation in the high Andes were so unique that to prepare the mummies for display in Salta, Argentina, curators there consulted forensic anthropologist Angelique Corthals, then at the American Museum of Natural History, to recreate the extreme cold and dryness required to keep the bodies looking fresh and to preserve their tissues and organs for further study. Five years later, in 2009, after the mummies had eventually gone on display, Corthals revisited the museum to check on their condition.

She sampled sputum (mucus coughed up from the lower airways) from the mummies to test whether they had been sedated before their sacrifice, likely with a kind of corn liquor. Corthals also sampled a bloodstained portion of cloth found near the 7-year-old boy's mouth. She used proteomics to map the proteins in the blood sample to determine where in the body the blood had come from, since different sets of proteins are found in the gut compared to the lungs, for example. When Corthals saw the blood profile, she began to realize just how rich in information it was.

"We never expected we would have such a slew of proteins coming out of the sample. We couldn't believe the result," says Corthals. It was so amazing, they ran it again, and got the same bounty of proteins. "We realized the proteins were better preserved than we thought they would be, and we ran very accurate mass spectrometry, which gave us this amazing profile."

The success of the method, called shotgun proteomics, allowed Corthals and the team to answer deeper questions about the mummies. In previous CT scans they had noticed that the eldest mummy, the Maiden, had lesions on her lungs that could indicate infection. They could even see streaks of mucus under both nostrils.

Researchers had previously detected pathogens in ancient samples using DNA analysis, but linking the presence of microbes to a disease state is tricky because some bacteria, for example *Mycobacterium tuberculosis*, can persist in an individual for a prolonged time period without causing active infections. Detecting the immune response of a host, which indicates an active infection, is also possible, but requires the use of antibody-binding immunoassays, which are prone to false positives and negatives when used on archaeological samples.

Corthals compared the Maiden's extensive protein profile to a database containing 87,061 human protein sequences, and found elevated levels of proteins associated with immune response to inflammation of the lungs, similar to those seen in chronic obstructive pulmonary disease and mycobacterial infection.

The team used the boy's protein profile as a control, since he showed no signs of infection in CT scans and radiology analysis (the blood on the cloth was deemed the result of trauma) and had likely undergone a similar amount of protein degradation. The Maiden's inflammatory and immune-response proteins were elevated compared to the boy's, while all other protein levels were comparable.

Mehdi Moini of the Museum Conservation Institute at the Smithsonian Institution, who has recently demonstrated the use of proteomics in dating archaeological samples, says Corthals's work is "yet another fine example of the application of modern mass spectrometry and proteomics technologies to anthropology and museum specimens." He says that this new approach "not only shows the presence of the pathogen, it also demonstrated that the pathogen actually produced an active infection."

As well as corroborating the evidence from CT scans and radiology analysis, Corthals's team constructed the DNA profile of the samples to probe what pathogen was responsible. Phylogenetic analysis revealed

**This work proves that modern instrumentations and techniques are capable of minimizing the guesswork in forensic and historical sampling.**

—Mehdi Moini, Museum Conservation Institute at the Smithsonian Institution

the most likely culprit as part of the pathogenic *Mycobacterium avium-bovis-tuberculosis* complex.

"This work proves that modern instrumentations and techniques are capable of minimizing the guesswork in forensic and historical sampling," says Moini. While 500-year-old mummies were used in this case, Corthals, now at the City University of New York's John Jay College of Criminal Justice, is enthused about myriad potential applications and has already been swamped by e-mail requests for new collaborations. "I'm not going to stop at ancient remains," she says. "One of the interesting things would be to work on the frozen bodies that were preserved with the flu virus from the Spanish flu and see whether we can say anything about the immune system of these people that died from the flu."

Currently, Corthals is working with a team from Brussels University in the "Valley of the Nobles" outside Luxor, Egypt, where she is uncovering 3 millennia of human activity, from high-ranking nobles who lived around 1400 BC to Napoleonic soldiers who were ambushed in the region and had their bodies dumped in one of the Valley's tombs at the beginning of the 19th century. Corthals set up the first ancient-DNA lab in Egypt to try to use genetic analysis to identify the missing mummy of Queen Hatshepsut, one of Egypt's most powerful rulers.

Proteomics could now help solve some of ancient Egypt's most captivating mysteries, such as what really killed the boy king Tutankhamen. "It would be nice, but it would be more challenging, because King Tut's mummy is more damaged, so I don't know what kind of profile we would get," Corthals says. "But it would be very interesting to see even a partial profile."

## Tags

[tuberculosis](#), [TB](#), [proteomics](#), [infectious disease](#) and [archaeology](#)

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November 10, 2012

***Wow really intersting! Maybe the M Tuberculosis have been with us since Inca's period, and is still, one of the most relevant disease in South America.***

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## Related Articles

# Tech News

## Rewriting history through proteins

Today, researchers interested in exploring ancient samples and remains at the molecular level mainly rely on DNA. But proteins might tell us even more about history. Andrew Wiecek examines how protein analysis techniques are shedding new light on Inca history.

At age 15, she was determined to be a rare example of physical and spiritual perfection, and therefore chosen for sacrifice. Preparations began a year beforehand during which time she was confined to a closed house within the Inca capital of Cusco and fed a rich diet of maize and llama meat. She then traveled more than 1200 miles to the snowy summit of the volcanic Mount Lulllaillaco. Consuming an intoxicating meal of cacao leaves washed down with maize beer, she quickly fell asleep only to be covered with volcanic ash and left to die.

Well, at least, that's the story according to Spanish explorers. However, forensic anthropologist Angelique Corthals, an assistant professor at the Stony Brook University School of Medicine and director of Stony Brook's BioBank, isn't quite so sure. But to piece together what was really happening during those final days, Corthals and her team would have to travel back in time, using the latest in proteomics technology to analyze proteins from the young girl's mummified remains. Corthals' efforts would provide a surprising molecular snapshot into the world of this doomed child.

### 500 years later

In 1996, a group of archaeologists uncovered the remains of what appeared to be the 15-year old Inca girl along with two younger children, a boy and a girl, on Mount Lulllaillaco. The cold temperatures and volcanic ash had actually protected their bodies from decomposition. Nicknamed "the maiden," the archaeolo-

gists performed radiocarbon dating and genomic analysis to learn more about who this teenage girl was and whether or not she might have been sacrifice victim from the explorer's stories (1).

The research team's carbon dating data indicated that "the maiden" died around 500 years ago, in agreement with the stories, while dietary isotopic data detected a sudden shift in diet during her final year of life, moving toward rich animal protein. Analysis of mitochondrial DNA samples also defined her haplogroup, further confirming the carbon dating data, and strongly indicating that this mummy was, in fact, the sacrifice victim.

But Corthals, who is also part archeologist and part biomedical researcher, knew this genomic analysis was only scratching the surface of the potential molecular information these samples held. While sequencing ancient DNA can be used to get a list of genes and specific mutations for a given individual, it says nothing at all about how or when those genes are expressed in cells. In contrast, if one were to analyze the proteome, a cell's protein composition, this could actually provide a clearer window into what was physiologically happening when "the maiden" died.

"That's the beauty of proteins, they basically indicate what the individual is expressing at the time of sampling," says Corthals. This means that if you sample a person's proteome today and then resample in a month, the profiles would be different, the result of changes in gene expression in response to external conditions such as disease or diet or something else.

A clearer example of this can be seen when researchers discover pathogen DNA in an ancient sample. They can compare the ancient and the modern versions of the pathogen at the nucleotide level to determine the "age" of the pathogen, or the specific subtype of pathogen in the sample. But the presence of that pathogen DNA, even if it is determined by sequence analysis to not be contamination, doesn't necessarily mean the individual was infected by the pathogen or that their death was a result of the pathogen.

In order to figure those things out, researchers would need to analyze the immune response of the host at the time of death; experiments that require specialized tools and methods capable of analyzing the abundance of proteins involved with, and regulated by, the immune response – from limited samples that are hundreds to thousands of years old.

### Further back in time

At the Natural History Museum of Denmark, postdoctoral fellow Enrico Cappellini studies both ancient DNA and ancient proteins. Like Corthals, he believes ancient proteomics is a strong complement to ancient DNA studies.

From a technical standpoint, there is an advantage to working with ancient proteins: some proteins don't degrade as quickly as DNA. While it is currently difficult to recover DNA from samples that are more than 500,000 years old, collagen—an abundant protein that makes



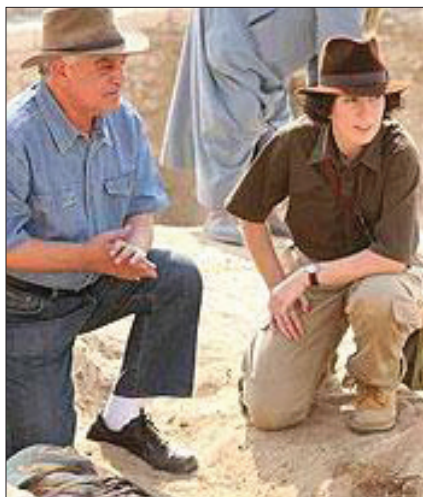
In 1999, archaeologists found the preserved remains of three children who were sacrificed on Mount Lulllaillaco. Source: PLoS One

up connective tissue in vertebrates—has been recovered from samples that are up to 1 million years old.

Of course, not all proteins are as stable and abundant as collagen, and not all samples are preserved in conditions that reduce potential environmental damage. As such, even though researchers have been studying ancient proteins for more than 20 years, successes have been limited to analyzing only a small number of abundant proteins. But this could be changing with the rise of new instruments and protein preparation methods.

In a paper published last year in the *Journal of Proteome Research* (2), Capellini and colleagues analyzed 126 unique proteins from a 43,000-year-old woolly mammoth. “We showed it was possible to go from a very few common proteins, something boring like collagen, to something more interesting like albumin,” explains Capellini. Albumin is a protein that helps transport other biomolecules through the bloodstream of a mammal.

A typical proteomics workflow consists of three separate steps: sample preparation, mass spectrometry, and data analysis. At first, protein samples are purified and separated into smaller fractions using chromatography methods that include liquid and gas-based separation. This step can in many ways be thought of as a “pre-screen,” enabling researchers to separate the components of the complex mixture to enhance mass analysis and also provide some initial information on protein composition prior to more directed analysis. Next, the



Angelique Corthals (right) is part archeologist, part biomedical researcher. Source: Millsaps College

protein fractions are analyzed by mass spectrometry. Here, the proteins and peptides are first ionized and then the resulting fragments introduced into a machine that collects data on ion masses. Finally, the mass spectra obtained from the mass spectrometer are compared with a database of known peptide masses to identify the protein components within the sample.

One key to Capellini’s success in analyzing such a wide range of ancient proteins from the mammoth was to limit loss during sample preparation. In contrast to modern protein studies where more cells can be grown or experiments repeated, ancient samples are

always limited and therefore Capellini’s team had to modify several steps in the traditional proteomics workflow, such as eliminating precipitation steps during sample preparation to reduce the loss of cross-linked proteins.

“This is a very exciting time to get into ancient protein [analysis] because the technological developments that are coming out on a yearly basis are opening up a lot of possibilities,” says Capellini.

## Techniques age quickly

Altering traditional workflows is not the only concern for researchers working with ancient samples — contamination will always be an issue with these samples. And when it comes to ancient protein analysis, keratin, a structural protein that makes up human skin, hair, and nails, is a common contamination culprit.

To combat keratin contamination, most proteomics labs follow strict protocols. For example, Corthals’ lab fractionates peptides using liquid chromatography rather than gel electrophoresis. In gel-electrophoresis, proteins must be removed from a lysis solution, resolved on an electrophoresis gel, and then returned to a solution prior to MS analysis. On the other hand, liquid chromatography-based fractionation keeps proteins in a single solution, reducing the possibility of contamination.

Downstream, the data analysis software used to identify peptides and proteins from MS data has greatly improved over the years. With the expansion of MS spectra databases as more proteomics studies are completed, as well as the creation of new algorithms developed by mathematical biologists to extend mass analysis, peptide identification programs are more accurate and make less false-positive identifications. “That’s not trivial,” says Corthals. “Those people are the unsung heroes because no one wants to hear about the programming.”

But the expansion of databases with new spectra and growth of MS analysis tools does bring up a quandary for those working with ancient proteins: what spectral databases do you search when examining ancient samples? For the woolly mammoth study, Cappellini and colleagues searched against a protein analysis of its modern ancestor, the elephant. And while a search against a high-quality mammoth genome could have potentially also identified new isoforms or similar enzymes with different functions, that genome was published



Mount Lulllaillaco was the site of Inca ritual sacrifices.

in 2008—one of the first examples of sequencing ancient DNA—and only done to 0.7-fold coverage (3).

“We weren’t able to do anything with that,” says Capellini. “But no one is going to embark on the mammoth genome sequencing because it’s already been published. It’s not rewarding from a publication exploitation point of view. So, we had to rely on modern stuff.”

But all the latest techniques to study ancient proteins might already be, well... ancient. Since his woolly mammoth study, Capellini’s team has replaced the mass spectrometer that they used with a new MS system possessing both increased sensitivity and mass accuracy.

“We changed almost everything,” says Capellini. He reservedly notes (this work is not yet published) that for sample preparation, they continue to improve ways to minimize losses and improve recovery especially in the demineralization and digestive steps. “The main point here is we’re not throwing anything away.”

## Not so perfect after all

Armed with these advanced protein analysis tools and methods, Corthals realized it was time to learn more about what happened during those final days for the 15-year-old Inca maiden.

The remains of the maiden and her two younger companions are stored at -20°C in the Museum of High Mountain Archaeology in the city of Salta, Argentina, close to Mount Llullaillaco. Corthals convinced the archeologists to let her take a sample; in the end she was allowed to take three samples: a piece of blood-soaked cloth from the boy and cotton swabs from the lips of the maiden and the boy. Returning to her New York lab, Corthals and her team carefully handled their precious samples, using strict protocols to process the materials for analysis using a liquid chromatography tandem MS LTQ-Orbitrap system.

The results, reported in an article published earlier this year in the online journal *PLoS One* (4), describe the first use of “shotgun proteomics” to detect proteins involved in the anti-bacterial immune response in an ancient sample. As it turns out, the two Inca children — selected because they represented an idealized state of humanity, according to Spanish explorers — were, in fact, battling chronic lung infections.

“It calls into question, first of all, the idea of perfection, in terms of that

these children need to be perfect,” says Corthals. “It also calls into question these secondary sources, which are the only sources we have of the Inca empire because they didn’t have writing. And it opens a whole new field of questions of what was happening [at that moment], making things a little more exciting than we thought they were.”

In the end, Corthals believes that there might be plausible explanations for their findings. For instance, the children might have acquired infections sometime during the months of preparation for the ritual sacrifice, possibly the result of being confined to a closed house with an open fire. Such a smoky environment could have irritated the lungs, allowing for an opportunistic infection. Another possibility is that the infection could have been obtained during the 1200-mile journey from Cusco to Mount Llullaillaco. “It’s the equivalent of walking from Mexico to the Canadian border. For a 15-year-old, that’s pretty tough,” says Corthals.

Moving beyond the Incas, the next step for shotgun proteomics of ancient samples will likely be the use of even older or more damaged samples. In fact, Corthals already has a target in mind here: the frozen corpse of a 1918 Spanish flu victim. “Everybody’s been studying the Spanish flu virus to death, but nobody’s been actually looking at the immune response,” says Corthals. But that trip back in time will have to wait its turn.

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Written by Andrew S. Wiecek. 

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# What was this mummy sick from? Now we know. [updated]



Tim Barribeau

7/27/12 10:30am · Filed to: BIOLOGY



27.7K



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A newly discovered technique could tell us what diseases killed off our ancestors — providing us with more information than we've ever had before. So what exactly infected this 500-year-old Peruvian mummy?

Previous research into ancient diseases has heavily relied on amplifying microbe DNA, a method prone to contamination, and one which could only

confirm the presence of the pathogen, and not whether the person was infected or not. Or else, by using immunoassays — which are likewise easily contaminated, and require searching for specific pathogens.

Angelique Corthals and her team instead turned to protein analysis, looking for the immune systems response in samples taken from the lips of Andean Inca mummies. They separated out the proteins from the DNA, and then ran them through a high-resolution mass spectrometer — a technique called shotgun proteomics. The results from the mass spectrometer were then compared against a human protein database.

The analysis showed evidence of *Mycobacterium sp.* — in other words, a lung infection, a diagnosis that seems supported by the inflammation they found on a CT scan. That's right: They forensically solved what infected a 500 year old mummy.

This technique has the advantage of longevity, as proteins can survive in remains for a substantial amount of time, as well as being less likely to be contaminated.

So, what's the next dead person we can solve mysteries about? Anyone know where Alexander the Great's corpse is?

Correction: An earlier version of this article stated that the research discovered what killed the mummy, that was in error. The mummies were in fact sacrifices to to Pachamama, the earth goddess. What this technique detected was that she had a lung infection at the time. I deeply regret this error - sorry about that folks. Bad science blogger, no cookie.





THE SCIENCES 60-SECOND SCIENCE

# Mummy Had Lung Infection, Technique Reveals

Shotgun proteomics on a corpse can determine whether someone was actually suffering from a disease rather than just carrying it. Evelyn Lamb reports

August 14, 2012

Five-hundred years ago, a 15-year-old Incan girl was sacrificed, along with two other children. Her mummy has now revealed that she had an active lung infection at her death. Because a technique called shotgun proteomics has been used to determine whether someone was actually suffering from a disease rather than just carrying it. The report appears in the journal *PLoS ONE*. [Angelique Corthals et al., [Detecting the Immune System Response of a 500-Year-Old Inca Mummy](#)]

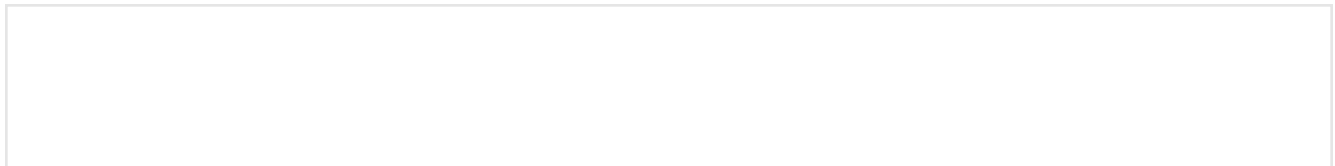
Previous research into ancient diseases has used DNA analysis to determine the presence of pathogens. But with DNA, there's no way to tell latent infections from the full-blown, misery-inducing ones.

Researchers analyzed protein samples from the mummies of two of the slain children. The girl's proteins indicated an immune response to bacteria, perhaps a pathogen related to tuberculosis. Other evidence, such as mucus under her nose and lung abnormalities, strengthened the diagnosis. The seven-year-old boy, on the other hand, showed no signs of infection.

This is the first time the technique has been used. It's a small sample, but further development of shotgun proteomics has the potential to improve our understanding of ancient disease, as well as assisting in tomorrow's forensic investigations.

—Evelyn Lamb

*[The above text is a transcript of this podcast.]*



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# Diagnosis of Ancient Illness

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By **SAMIR S. PATEL**

Friday, October 05, 2012

The Black Death, brucellosis, leprosy: The pathogens that cause these diseases have been identified in ancient remains by their DNA. But the presence of such DNA doesn't necessarily mean that the person who carried it was sick. For example, one can carry the bacterium that causes tuberculosis for years without suffering from a serious cough, fever, and weight loss.

In the case of three well-preserved 500-year-old mummies found in 1999 on high-and-dry Lulluillaco peak in Argentina, forensic examination and DNA tests suggested that one of them—a 15-year-old girl known as the “Lulluillaco Maiden”—suffered from a lung infection. But the DNA was degraded and the finding wasn't definitive. Recently, forensic pathologist Angelique Corthals of Stonybrook University noticed what looked like traces of blood and mucus around the maiden's mouth. She and her colleagues used swabs to take samples, hoping to determine where in the body the blood had come from. The team employed a technique called shotgun proteomics, used in modern medicine to look for biomarkers of diseases such as cancer, which involves separating and identifying specific proteins. “Lo and behold, we actually found a lot,” she says. “We didn't expect so many proteins would survive 500 years. We saw a whole profile of the body's immune system.”

Samples from the maiden showed the presence of several proteins strongly associated with severe, chronic lung inflammation. Alongside the DNA and other tests, the protein profile clearly showed the maiden suffered from a lung infection at the time of death, caused by the genus of bacterium that causes tuberculosis.

Proteomics has several advantages over DNA testing in identifying ancient diseases. Proteins degrade more slowly than DNA. The technique is also cheaper and less susceptible to contamination by modern sources. And because proteomics shows immune response to active disease, it can in some cases be used to infer cause of death. But not for the maiden—she was a sacrifice.

## Протеомика помогла поставить диагноз мумии с Льюльяйльяко



Мумия девушки со склона вулкана Льюльяйльяко. Фото авторов исследования

26 июля 2012 года, 16:55

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Благодаря применению методов протеомики американским ученым впервые удалось выделить белковый профиль прижизненного иммунного ответа на бактериальную инфекцию у пятисотлетней мумии, установив тем самым, что в момент смерти болезнь находилась в активной стадии. Работа [опубликована](#) 25 июля в журнале PLoS ONE.

Объектом исследования стали мумии пятнадцатилетней инкской девушки и двух детей помладше, обнаруженные археологической экспедицией в 1999 году у вершины вулкана Льюльяйльяко (Lullailasco) в аргентинской провинции Сальта. Мумифицированные тела людей, похороненных заживо около пятисот лет тому назад, чрезвычайно хорошо сохранились благодаря уникальному микроклимату, сложившемуся на склоне вулкана - низким температурам, сухому воздуху, анаэробной среде и присутствию природных дезинфицирующих веществ.

Как правило, выявление патогенных инфекций у мумий происходит на основании обнаружения в останках фрагментов ДНК бактерий. Однако этот метод позволяет лишь констатировать присутствие патогенной флоры в организме, но судить о том, был ли человек болен накануне смерти, на основании этой информации нельзя.

Для преодоления этой проблемы авторы исследования применили методы протеомики - науки по изучению белков и их взаимодействий в организме. Они взяли мазки с тканей губ мумии девушки и мумии одного из детей, а затем сравнили обнаруженные белки с базой данных человеческих геномов. Оказалось, что белковый профиль, полученный с губ девушки, полностью совпадает с белковым профилем больных респираторной инфекцией, свидетельствующем об остром иммунном ответе организма. В частности, был обнаружен белок катепсин G, присутствие которого бывает связано с хронической обструктивной болезнью легких.

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Проведенный параллельно анализ ДНК показал присутствие в организме патогенной бактерии *Mycobacterium*, вызывающей заболевания верхних дыхательных путей и туберкулез. Кроме того, рентгеновское исследование легких мумии девушки показало наличие в них следов воспаления на момент смерти.

При этом протеомическое исследование, анализ ДНК и рентгеновское обследование другой мумии не обнаружило свидетельств наличия респираторной инфекции.

"Само по себе выявление патогенов в древних останках не является новостью, но до сих пор было невозможно определить, был ли инфекционный агент активным или латентным, - цитирует EurekAlert! руководителя группы, Анжелику Корфалс (Angelique Corthals) из колледжа криминальной юстиции имени Джона Джея при Городском университете Нью-Йорка. - Установление иммунного белкового профиля "пациента" дает возможность точно установить, был ли он болен в момент смерти". Новая методика, по мнению Корфалс, может помочь в решении многих исторических и современных биомедицинских и криминальных загадок. Например, приблизиться к пониманию причин пандемии гриппа-испанки в 1918 году, или выявить, какие именно патогенные бактерии ответственны за гибель людей при эпидемиях, полагает Корфалс.

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# Diagnostic d'infection pulmonaire sur une momie de 500 ans

Mise à jour le jeudi 26 juillet 2012 à 11 h 46 HAE



The Maiden Photo : Angelique Corthals

Une infection pulmonaire bactérienne a été diagnostiquée chez l'une des trois momies incas datant de 500 ans découvertes en 1999 dans les Andes argentines.

Les enfants de Llullallaico, comme on les appelle, avaient été retrouvés congelés en parfait état de conservation à 6700 m d'altitude.

Les corps de deux jeunes filles et d'un garçon contenaient encore tous leurs organes. Du sang était encore présent dans leur cœur et dans leurs poumons, comme s'ils étaient morts récemment.

Dans les présents travaux, la chercheuse Angelique Corthals du John Jay College of Criminal Justice et ses collègues ont analysé les protéines qui se trouvaient dans l'organisme de deux de ces momies afin d'évaluer l'état de leur système immunitaire au moment de leur décès.

L'une d'elles, surnommée *The Maiden* (la jeune fille), était porteuse d'une bactérie s'apparentant à la mycobactérie, agent pathogène à l'origine des infections des voies respiratoires supérieures et de la tuberculose de nos jours.

De plus, une radiographie des poumons de la jeune fille d'une quinzaine d'années a montré qu'elle souffrait d'une infection aux poumons au moment de sa mort.

Aucun signe d'infection n'a été décelé chez l'autre momie. La détection d'agents pathogènes dans de vieux tissus n'est pas nouvelle, mais jusqu'à présent, il était impossible d'établir si l'agent infectieux était latent ou actif au moment de la mort.

Selon les chercheurs financés par la société *National Geographic*, l'utilisation de leur technique permettra certainement d'élucider de nombreux mystères historiques, par exemple la raison de la virulence de la grippe de 1918 qui avait fait jusqu'à 100 millions de morts selon de récentes réévaluations.

Le détail de ces travaux est publié dans la revue *PLoS ONE*.

## En complément

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[Detecting the Immune System Response of a 500 Year-Old Inca Mummy \(en anglais\)](#)

## Incan mummy frozen after human sacrifice still has infection in lungs after 500 years - giving new insight into diseases of the past

- First time infection has been diagnosed in ancient body
- New technique could be used to study diseases such as Spanish flu
- Could be used to prevent re-emergence of deadly diseases of past
- Study on 500-year-old mummy frozen on Argentinean volcano

By **ROB WAUGH**

**PUBLISHED:** 05:33 EST, 26 July 2012 | **UPDATED:** 07:27 EST, 18 March 2015

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A 500-year-old frozen Incan mummy known as 'The Maiden' was suffering from a bacterial infection when she died - and being able to 'diagnose' the disease could lead to new insights into diseases of the past.

The discovery could help defend against new illnesses - or the re-emergence of diseases of the past.

The mummy was suffering from an illness similar to tuberculosis when she was sacrificed on the Argentinian volcano Lullullaico, 22,100 feet above sea level.

The find - using a new technique of swabbing the lips and comparing the swabs with those of current patients - is the first time a disease has been 'diagnosed' in such an ancient body.

'Pathogen detection in ancient tissues isn't new, but until now it's been impossible to say whether the infectious agent was latent or active,' says Cortals.

'Our technique opens a new door to solving some of history's biggest mysteries, such as the reasons why the flu of 1918 was so devastating. It will also enhance our understanding of our future's greatest threats, such as the emergence of new infectious agents or re-emergence of known infectious diseases.'

The analysis was possible because of the incredible preservation of the mummy, which is so well-preserved there were still lice in her hair.

The team swabbed the lips of two Andean Inca mummies, buried at 22,000-foot elevation and originally discovered in 1999, and compared the proteins they found to large databases of the human genome.



The older girl's face - which showed red ochre markings - was creased from the place it rested on her shawl

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The view from the summit of Lulluillaco volcano where the children were found. The children were plucked from these slopes in 1999 by a team who battled for three days through driving blizzards and 70mph winds to reach the summit



Child sacrifice was called capacocho. The process of capacocho could begin years before the selected person was killed. A mummified body of a child who was killed during one such sacrifice is pictured here

They found that the protein profile from the mummy of a 15-year old girl, called 'The Maiden,' was similar to that of chronic respiratory infection patients, and the analysis of the DNA showed the presence of probably pathogenic bacteria in the genus Mycobacterium, responsible for upper respiratory tract infections and tuberculosis.

In addition, X-rays of the lungs of the Maiden showed signs of lung infection at the time of death.

The mummies were found in 1999.

'The doctors have been shaking their heads and saying they sure don't look 500 years old but as if they'd died a few weeks ago,' said U.S. archaeologist and expedition member Johan Reinhard at the time.

'And a chill went down my spine the first time I saw her hands because they look like those of a person who is alive.'

It's thought that the children were chosen by the Incas for their beauty and sacrificed in a ceremony called a capacocho.

**THE ICE MAIDEN: MYSTERY OF THE THREE UNIQUE MUMMIES FOUND FROZEN HIGH IN THE ANDES**

Along with the remains of two younger children, the teenager was plucked from the slopes of a cloudswept volcano in 1999 by a team who battled for three days through driving blizzards and 70mph winds to reach the summit 22,000ft above sea level.

There, the archaeologists spotted a rectangular walled area, dug down through five feet of rocks and soil and finally uncovered an Incan burial platform.

One of the team was lowered headfirst into the icy pit, his colleagues hanging onto his ankles, so that he could scrape away the soil and pull the dead children out with his hands.

The three Children of Lulluillaco, as the mummies came to be known after the mountain on which they met their death, were found with an extraordinary collection of elaborate gold, silver and shell statues,

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'The Incas didn't do this very often,' according to Reinhard.

'The sacrifices were children because they were considered to be the most pure.'

They were not sacrificed to feed or appease the gods but, rather, 'to enter the realm of the gods and live in paradise with them. It was considered a great honour, a transition to a better life from which they would be expected to remain in contact with the community through shamans (holy men).'

textiles, pots containing food and even an extravagant headdress made from the white feathers of an unidentified bird.

But it was the state of the bodies, preserved not by embalming, like Egyptian mummies, but simply by the natural deep-freeze in which they were abandoned, that scientists found most remarkable.



The place of sacrifice: The burial site of the three children on top of Lulluillaco Volcano



Ritual killings were common within the Incan culture. In 1999 three Children of Lulluillaco, who found deep frozen were found with an extraordinary collection of elaborate gold, silver and shell statues, textiles and pots containing food The children included a 13-year-old known as the 'Lulluillaco Maiden'

were in Calabasas

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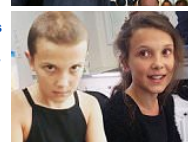
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### Amazingly well preserved 500-year-old mummified Incan child



0:00 / 0:30

The Incas believed that by scaling the snow-topped heights of the mountains they could get closer to the heavens and communicate better with the gods.

Detecting diseases in ancient remains is often fraught with difficulty, especially because of contamination.

Techniques based on microbe DNA can easily be confused by environmental contamination, and they can only confirm that the pathogen was present, not that the person was infected, but the researchers behind the study, led by Angelique Corthals of the John Jay College of Criminal Justice, City University of New York, found a way around this problem.

They used proteomics, focusing on protein rather than DNA remains, to profile immune system response from degraded samples taken from 500 year-old mummies.









Proteomics, DNA, and x-rays from another mummy found together with the Maiden did not show signs of respiratory infection.

'Our study is the first of its kind since rather than looking for the pathogen, which is notoriously difficult to do in historical samples, we are looking at the immune system protein profile of the 'patient', which more accurately tells us that there was indeed an infection at the time of death.'

'Our study opens the door to solving many historical and current biomedical and forensic mysteries, from understanding why the plague of 1918 was so lethal, to finding out which pathogen is responsible for death in cases of multiple infections.'

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(<https://i1.wp.com/www.scientias.nl/wp-content/uploads/2012/07/juanita.jpg?fit=600%2C300&ssl=1>)

## Aan Incagoden geofferd meisje had longinfectie

© 26 juli 2012 ✎ Caroline Kraaijvanger 🗨️ 6



**Het zat dit meisje niet mee. Ze werd op 15-jarige leeftijd aan de goden van de Inca's geofferd. En nu blijkt uit onderzoek dat ze ook al leed aan een ernstige longinfectie.**

Dat schrijven wetenschappers in het blad *PLoS ONE* (<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0041244>). Ze baseren hun conclusie op een onderdeel van de 500 jaar oude resten van het meisje. De mummie – bijgenaamd Juanita – is uitzonderlijk goed bewaard gebleven en kan ons dus heel veel vertellen over het leven uit die tijd.

## Longinfectie

Uit het onderzoek blijkt dus dat het meisje aan een longinfectie leed. Het vaststellen van zo'n infectie bij een 500 jaar oud lijk is niet zo heel gemakkelijk. In het verleden slaagden onderzoekers er niet in om een ziekteverwekker in oude lichamen op te sporen. Maar het bleek lastig om vast te stellen of die ziekteverwekker daar enkel aanwezig was of dat deze ook al echt een infectie had veroorzaakt. Maar nu zijn de onderzoekers er dan toch in geslaagd om de aanwezigheid en activiteiten van de ziekteverwekker te achterhalen.

## Aanpak

De onderzoekers verzamelden proteïnes die zich op de lippen van het meisje bevonden. Ze vergeleken deze met proteïnes die reeds in kaart zijn gebracht. Zo ontdekten ze dat de proteïnes en de verhoudingen waarin deze voorkwamen sterk leken op de verhouding proteïnes die bij patiënten met een longinfectie aan de luchtwegen werd aangetroffen. Een analyse van het DNA wees vervolgens uit dat het meisje waarschijnlijk een bacterie uit het geslacht *Mycobacterium* onder de leden had. Dergelijke bacteriën veroorzaken onder meer infecties aan de luchtwegen en TBC. Röntgenfoto's van de longen van Mummie Juanita toonden bovendien aan dat ze ook echt aan een longinfectie leed. Voor de zekerheid voerden de onderzoekers hetzelfde onderzoek ook uit met een andere mummie die nabij Juanita werd teruggevonden. Deze mummie vertoonde geen sporen van een infectie aan de luchtwegen.

## WIST U DAT...

...onlangs ook al [een Koreaanse mummie met hepatitis B](http://www.scientias.nl/koreaanse-mummie-met-hepatitis-b) (<http://www.scientias.nl/koreaanse-mummie-met-hepatitis-b-gevonde/65114>) werd ontdekt?

## Belangrijk

Het onderzoek is van groot belang, zo benadrukt wetenschapper Angelique Corthals. "Het

opmerken van ziekteverwekkers in oude weefsels is niet nieuw, maar tot op heden was het onmogelijk om vast te stellen of een ziekteverwekker latent of actief was." De onderzoekers met hun aanpak in de toekomst nog veel meer prangende vragen te kunnen beantwoorden. Bijvoorbeeld hoe het kan dat de griep die in 1918 aan miljoenen mensen het leven kostte, zo vernietigend toesloeg. "Het vergroot ook ons begrip omtrent de grootste bedreigingen van de toekomst, zoals de opkomst van nieuwe of de terugkeer van oude infectieziektes."

Mummie Juanita werd in 1995 ontdekt. De mummie lag op grote hoogte begraven en was heel bevroren. Doordat Juanita bevroren was, is zowel haar lichaam als haar kleding uitstekend behouden gebleven. Wetenschappers hebben Juanita de afgelopen jaren uitgebreid bestudeerd. Zo blijkt de 15-jarige meisje aan een flinke klap op het hoofd te zijn overleden.


#### Bronmateriaal:

"Ancient Incan Mummy Had Lung Infection, According to Proteomics Analysis (<http://www.sciencedaily.com/releases/2012/07/120725200302.htm>)" - PLoS ONE (via [Sciencedaily.com](http://www.sciencedaily.com)).

De foto bovenaan dit artikel is afkomstig uit PLoS ONE doi:10.1371/journal.pone.0041244.

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AUGUST 15, 2012

# 500-YEAR-OLD INCAN MUMMY SUFFERED FROM A LUNG INFECTION BEFORE BEING SACRIFICED

DANIEL MCCALL

Researchers have already been able to work out that the 15-year-old Incan mummy known as “The Maiden” that was discovered alongside two other mummies died as part of a sacrifice roughly 500 years ago, but new research has revealed that the girl was also suffering from a lung infection at the time of her death.

The mummy was first discovered in over a decade ago along with the other children on top of Mount Ampato near Arequipa, Peru. Due to the extremely frigid temperatures in the area, the remains of the Maiden and the other two children were remarkably well preserved.

Using a technique called “shotgun proteomics,” Angelique Corthals, a forensic anthropologist at the City University of New York, and a team of researchers analyzed tissue proteins to determine what was going on in the young girl’s body at or around the time of her death. Surprisingly, researchers discovered that the mummy had a lung infection — possibly even tuberculosis.

Here’s how the discovery was made, as per Live Science’s [report](#):

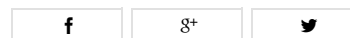
“[Researchers] placed [the mummies’] samples into a device called a mass spectrometer, which broke all of the sample’s proteins into their constituent parts, amino-acid chains. Sophisticated software compared these parts with existing proteins of the human genome to determine the actual

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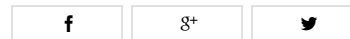


**HELLO, NEW FEBREZE WITH DOWNY. GOODBYE, ODORS.**

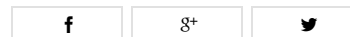
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**ALAYNA JEANNE ERTL FOUND DEAD: POLICE FIND BODY OF MISSING 5-YEAR-OLD MINNESOTA GIRL HOURS AFTER HER ABDUCTION**



**NINA DOBREV'S RETURN TO THE...**

# Científicos diagnostican enfermedad a una momia incaica de 500 años

Expertos analizaron con innovadoras técnicas los restos de una adolescente de unos 15 años, que habría sido sacrificada en la cima del volcán Lullullaco.

AP

domingo, 05 de agosto de 2012 6:36

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Una imagen de la momia de la joven conocida como "La doncella" en un museo de Salta.

Foto: AP

SANTIAGO.- Una joven inca que vivió hace 500 años sufrió de una infección a los pulmones causada por bacterias justo antes de morir, según informaron científicos que se dedicaron a examinar la momia.

La muchacha, cuya edad fue estimada en 15 años, fue sacrificada en la cumbre del volcán Lullullaco, de 6.739 metros de altura, ubicado en la actual frontera entre Chile y Argentina, según dijo Angelique Corthals, una antropóloga forense de la City University de Nueva York.

La joven tenía una irritación en una pierna, lo que llevó a Corthals a creer que pudo haber estado

enferma cuando fue enterrada, viva pero inconsciente, en la cima del volcán.

Corthals y sus colegas usaron una técnica llamada proteómica de segunda generación ("shotgun proteomics") para comparar las proteínas encontradas en la momia con grandes bases de datos del genoma humano. El perfil proteico de la momia calzó con alguien con una infección respiratoria crónica, afirmó Liliana M. Davalos, bióloga evolutiva en la Universidad de Stony Brook y coautora del estudio.

"Esta es la primera vez que se ha hecho en una momia antigua", dijo Davalos. "Se hace normalmente en pacientes de cáncer y tiene muchas aplicaciones para enfermedades humanas, pero no se había aplicado a trabajo arqueológico", añadió.

Davalos, Corthals y sus colegas plasmaron sus descubrimientos en la publicación "PLoS One".

Investigadores argentinos descubrieron la momia, junto a otras dos de niños que fueron sacrificados, en 1999.

"Fueron enterrados en una tumba, que estaba llena de cenizas volcánicas sólidas y cubiertas por nieve, por lo que no se desecaron", dijo Corthals. "Sus cuerpos enteros fueron sellados y preservados perfectamente", añadió.

Los jóvenes sacrificados hicieron un viaje de 4.800 kilómetros desde Cusco, la capital del Imperio Inca, hasta la cima, según dijo Corthals, y probablemente aquel viaje fue estresante.

"La muchacha incluso tenía cabellos grises, así que creo que sabían cuál sería su destino", afirmó. "La niña y el niño también tenían sus dientes hundidos", agregó.

Las momias se encuentran en exposición en el Museo de Arqueología de Alta Montaña en Salta, Argentina.

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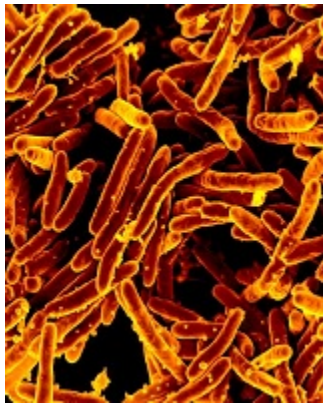




## Inka-Mumie hatte eine Lungenentzündung

### Immunproteine verraten akute Infektion bei einem vor 500 Jahren gestorbenen Mädchen

**Zum ersten Mal haben Forscher bei einer 500 Jahre alten Mumie eine akute Infektion nachgewiesen. Demnach litt das 15-jährige Inka-Mädchen, dessen Relikte auf einem Andengipfel entdeckt worden waren, an einer Lungenentzündung, möglicherweise sogar an Tuberkulose. Indizien für die Infektion lieferte dabei nicht allein der Erreger der Krankheit, sondern die Immunreaktion der Mumie, wie die Wissenschaftler im Fachmagazin "PloS ONE" berichten. Sie hatten Genaktivität und Proteine der Mumie analysiert und dabei gezielt nach Anzeichen für eine aktive Abwehrreaktion gesucht. Ein Erreger könne im Körper anwesend sein, auch ohne dass dies gesundheitliche Folgen habe. Erst wenn man nachweise, dass das Immunsystem auf diesen Erreger aktiv reagiere, habe man einen echten Beleg dafür, dass dieser Mensch vor seinem Tode tatsächlich krank war, sagen die Forscher.**



Bakterien der Art  
*Mycobacterium tuberculosis*

© **NIAID**

"Bisher war es unmöglich zu sagen, ob ein in einem alten Gewebe entdeckter Krankheitserreger aktiv war oder inaktiv", erklärt Erstautorin Angelique Corthals von der City University of New York. Diese Studie sei die erste, die sich mit Hilfe modernster genanalytischer Methoden auch die Immunreaktion des vor langer Zeit verstorbenen Patienten angeschaut habe. "Diese Methode öffnet ganz neue Möglichkeiten, einige der größten Rätsel der Geschichte zu lösen", sagt Corthals. So könne man nun beispielsweise genauer untersuchen, warum die Grippe von 1918 so verheerende Folgen hatte. Aber auch in Kriminalfällen lasse sich zukünftig besser feststellen, ob beispielsweise ein im Körper gefundener Erreger tatsächlich die Todesursache gewesen sei.

### Inka opferten die Kinder einst der Erdgöttin

Die Forscher hatten zwei von drei Mumien untersucht, die 1999 auf dem Andengipfel Lullaiillaco in Argentinien gefunden worden waren. Der sieben Jahre alte Junge und das 15-jährige Mädchen waren vor rund 500 Jahren von den Inka zu Ehren der Erdgöttin Pachamama geopfert worden. Kälte und Trockenheit haben ihre Körper bis heute nahezu unverseht konserviert. Für ihre Analysen entnahmen die Wissenschaftler den heute in einem Museum im argentinischen Salta aufbewahrten Mumien Speichel- und Blutproben.



Inka-Mumien, die 1999 auf dem Andengipfel Lullaiillaco in Argentinien wurden

© **Corthals et al / PloS ONE**

Zunächst suchten die Forscher in den Proben nach DNA-Spuren von Krankheitserregern. In denen des Mädchens fanden sie das Erbgut von Erregern der Gattung *Myobacterium*. Zu dieser Bakteriengruppe gehören neben dem Erreger der Tuberkulose auch einige, die Lungenentzündungen hervorrufen. Anschließend analysierten die Forscher die Proteine in den Mumienproben und suchten dabei besonders nach Eiweißen, die das Immunsystem im Falle einer akuten Infektion ausschüttet.

"Wir haben bei dem Mädchen zwei Gruppen von Proteinen entdeckt, die auf eine schwere Entzündung der Lunge hindeuten", schreiben Corthals und ihre Kollegen. Weitere Proteine seien Anzeiger für eine Infektion der Atemwege gewesen. Als die Forscher die Lunge des Mädchens durchleuchteten, fanden sie dort Veränderungen, die ebenfalls auf eine Lungenentzündung hindeuteten. Alles deute darauf hin, dass das



15-jährige Mädchen zum Zeitpunkt seiner Opferung bereits krank war und an einer Lungenentzündung, vielleicht verbunden mit einer Infektion der oberen Atemwege litt, sagen die Forscher. Der Junge hingegen sei offenbar gesund gewesen, bei ihm habe man keinerlei Anzeichen für eine akute Infektion festgestellt.  
(doi:10.1371/journal.pone.0041244)

(NPO, PLoS ONE, 27.07.2012)

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## Detectan infección pulmonar en una momia inca de 500 años

Redacción

BBC Mundo

Jueves, 26 de julio de 2012



Los niños de Lullallaico. a) La Doncella; b) El Niño y c) La Niña. Foto: gentileza Angelique Corthals, Antonius Koller, Dwight W. Martin, Robert Rieger, Emily I. Chen, Mario Bernaski, Gabriella Recagno, Liliana M. Dávalos.

**El uso novedoso de una técnica de análisis permitió a científicos en Estados Unidos determinar que una de las más célebres momias incas padecía de una infección pulmonar en el momento de su muerte.**

La joven de 15 años conocida como La Doncella falleció hace 500 años y fue hallada en 1999 enterrada en el hielo a unos 6.700 metros de altura junto a otros dos niños cerca de la cima del volcán Lullallaico en la provincia de Salta, en Argentina. Los niños habrían sido ofrecidos por los incas a sus deidades.

La joven está sentada, con las piernas flexionadas y los brazos apoyados sobre el vientre. Su cabello tiene pequeñas trenzas, lleva un vestido marrón ceñido a la cintura por una faja y sus hombros están cubiertos por un manto sostenido por un prendedor de plata.

En lugar de realizar un análisis de ADN en muestras de la momia, los científicos de la City University en Nueva York recurrieron a la proteómica, el estudio de proteínas. Es la primera vez que esta técnica se utiliza para analizar los restos de momias incas.

"Nuestro estudio es el primero de su tipo, ya que en lugar de buscar el patógeno, miramos al perfil proteico del sistema inmunológico del paciente", dijo Angelique Corthals, de la Facultad John Jay de Justicia Criminal de City University.

### Respuesta inmunológica

Detectar enfermedades en momias de cientos de años es extremadamente difícil debido a la contaminación de las muestras.

Las técnicas basadas en el análisis de ADN microbiano sólo pueden confirmar que el patógeno estaba presente, pero no que la persona estaba infectada.

Corthals y sus colegas encontraron una solución para este problema. Recurrieron a la proteómica y obtuvieron un perfil proteico de la respuesta

**Nuestro estudio es el primero de su tipo, ya que en lugar de buscar el patógeno, miramos al perfil proteico del sistema inmunológico del paciente"**

Angelique Corthals, City University de Nueva York

### Contenido relacionado

[Una momia peruana, por dentro](#)

## En fotos



**La impresionante naturaleza de Estados Unidos**

## Destacamos



**¿Por qué la conexión de internet en Venezuela es tan lenta?**

Recientes estudios han revelado que la velocidad de internet en Venezuela es de las más lentas de América Latina. BBC Mundo le explica por qué ver un vídeo de corrido es un lujo de pocos en el país.



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En cualquier momento de su carrera, es probable que le toque estrenarse en el manejo de un equipo de trabajo. Aprenda cómo evitar los errores que muchos principiantes inevitablemente cometen.



**Se filtran fotos íntimas de Kim Kardashian y Vanessa Hudgens**

Se trata de un nuevo caso de filtración de imágenes comprometedoras de estrellas de Hollywood. Esta vez también se vieron involucradas la actriz Kaley Cuoco y la cantante Avril Lavigne.

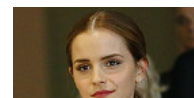


**Las fallas de seguridad que harán más difícil tomarse una foto en la Casa Blanca**

Muchos turistas se sorprenden de lo fácil que es asomarse a las rejas de la Casa Blanca para tomarse una foto. Eso puede cambiar tras una falla de seguridad que llevó al Servicio Secreto a aumentar sus medidas de precaución.

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"Feminismo no es sinónimo de

inmunológica a partir de las muestras obtenidas con isopos de los labios de las momias.

Cuando un patógeno ataca, el sistema inmunológico se defiende y esta respuesta genera un perfil proteico característico.

Los investigadores compararon ese perfil obtenido de las muestras con los encontrados en bases de datos del genoma humano y encontraron que era similar al de pacientes con infecciones respiratorias crónicas.

Un análisis separado de ADN mostró la presencia de una bacteria probablemente del género Mycobacterium. Rayos X de los pulmones de La Doncella revelaron además señales de infección en el momento de la muerte.

Análisis de proteómica, ADN y rayos X de otra momia hallada junto a La Doncella no revelaron sin embargo la presencia de infección pulmonar.

### Misterios

"La detección de patógenos en restos de este tipo no es nueva, pero hasta ahora había sido imposible determinar si el agente infeccioso estaba latente o activo", señaló Corthals.

"Nuestra técnica abre una nueva vía para resolver algunos de los mayores misterios de la historia, como por qué la pandemia de 1918 fue tan devastadora o cuál fue el patógeno letal en el caso de infecciones múltiples".

"También nos permitirá comprender mejor las amenazas del futuro, como la emergencia de nuevos agentes infecciosos o la reaparición de enfermedades".

El estudio fue publicado en la revista científica online PLoS ONE.

### PROTEÓMICA

La palabra "proteoma" es la unión de los términos "proteína" y "genoma".

La proteómica es el estudio de las proteínas, su estructura, función y sus modificaciones.

### Nuestra técnica abre una nueva vía para resolver algunos de los mayores misterios de la historia"

Angelique Corthals

odiar a los hombres".

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# Diagnosing Ancient Disease

**Molecules in the remains of ancient humans reveal the pathogens that plagued them**

By *Sarah Everts*



Credit: Manolis Papagrigorakis



Credit: Newscom

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The dental remains of victims of

**In 1994**, construction workers in Athens came across a mass grave containing around 150 people lying haphazardly on top of each other as if they had been buried in haste.

By dating pieces of pottery found alongside the human remains, archaeologists pinpointed the deaths to approximately 430 B.C., suggesting that the people buried in the grave were probably victims of the Plague of Athens, a pandemic of great historical significance for Western culture.

A mysterious pathogen hit Athens while it was under a Spartan siege during the Peloponnesian War that took place between the competing city-states. Nearly a third of Athens' inhabitants and many of the soldiers trying to defend the city died in the pandemic. Many scholars point to the Plague of Athens as a contributor to the beginning of the end of the Golden Age of Greece, said **Manolis J. Papagrigorakis** <<http://www.tedxacademy.com/talks>



**130 B.C. Plague of Athens**  
found in a mass grave revealed  
the pandemic was caused by  
typhoid fever.

**/manolis-papagrigrorakis---faces-  
from-the-distant-pa>** , a Greek  
orthodontist who was part of a research  
team that studied the grave skeletons to  
determine the pathogen responsible for the  
epidemic. He described the project last  
month in Berlin, at a standing-room-only session of the European Congress of Clinical  
Microbiology & Infectious Diseases.

Until the discovery of the mass grave, the best clues about the nature of the deadly pathogen came from the Greek historian Thucydides, Papagrigrorakis said. Thucydides' gruesome account describes patients with inflamed tongues, fetid breath, skin pustules, violent spasms, and eventually, for those who did survive, the loss of fingers, eyes, and memory. The historical account helped researchers narrow down a list of possible infectious agents: Plague, typhoid, typhus, smallpox, and measles were all contenders. But to conclusively identify the Plague of Athens pathogen, researchers needed to analyze the remains of victims. So Papagrigrorakis' team analyzed the dental pulp from several individuals from the mass grave and found, in the preserved dental tissue, the DNA of *Salmonella enterica* serovar Typhi, the causative agent of typhoid fever.

Making infectious disease diagnoses centuries, and sometimes millennia, after the death of a patient is called paleomicrobiology, and it's a field that's been growing over the past two decades, said **Helen Donoghue** <<https://iris.ucl.ac.uk/iris/browse/profile?upi=HDDON27>> , a paleomicrobiologist from University College London, who also spoke at the conference. Before molecular techniques were up to snuff, researchers had to rely primarily on historical accounts and physical signs of infectious disease to make diagnoses. For example, long-term tuberculosis victims can have characteristic lesions on their bones and collapsed vertebrae symptomatic of tuberculosis that are still visible in 1,000-year-old skeletons, she said.

Then in the 1990s, analytical technology advanced to the point where researchers were able to analyze the DNA and other molecular residues left in or on long-dead individuals. That's when paleomicrobiologists took things a step further and began

**cen**g for traces of pathogen DNA, proteins, and lipids in ancient remains such as **skeletons and mummies** <<http://cenblog.org/artful-science/2012/01/10/making-use-of-a-medical-museums-oddities/>> .

**Paleomicrobiology** can answer important historical questions, Donoghue said, such as what pathogen was responsible for devastating infectious disease outbreaks in history or which infectious pathogens existed in the Americas before the arrival of European colonists.

It can also help clarify the evolution and spread of pathogens through time and space, such as whether humans first acquired tuberculosis from infected cows after animal domestication—a theory long believed to be true but recently disproven by researchers in the field.

The field adopted molecular techniques beginning in 1993, Donoghue said, when University College London researchers Mark Spigelman and Eshetu Lemma proposed that the polymerase chain reaction—which was being used at the time to amplify the human DNA found in skeletons—might also be used to detect *Mycobacterium tuberculosis*, the causative agent of tuberculosis, in the same remains (*Int. J. Osteoarchaeol.* 1993, DOI: **10.1002/oa.1390030211** <<http://dx.doi.org/10.1002/oa.1390030211>> ). After doing proof-of-principle tests on a dozen bone samples from Borneo to Britain and across the time span of millennia, the team reported that the technique could have “wide application” in helping to diagnose diseases of antiquity.



#### **TICK TROUBLE**

Paleomicrobiological analysis of the Tyrolean iceman revealed he was suffering from lyme disease when he died of an arrow wound.

Credit: Marco Samadelli/EURAC

A year later, an **American team reported finding** <<http://www.pnas.org/content/91/6/2091.abstract>> *M. tuberculosis* in a lung sample taken from a 1,000-year-old Peruvian mummy. This research provided the first molecular evidence that

**08&en** Tuberculosis existed in the Americas prior to the arrival of European colonists, and it helped to resolve what had been a long-standing debate about the origin of tuberculosis in the New World (*Proc. Natl. Acad. Sci. USA* **1994**, *91*, 2091).

Since then, researchers have identified many more infectious disease agents from a wide variety of samples. For example, scientists have shown that the 5,300-year-old Tyrolean iceman discovered in the Alps in 1991 had Lyme disease—although it was an arrow to the back that finally killed him (*Nat. Commun.* 2012, DOI:[10.1038/ncomms1701](https://doi.org/10.1038/ncomms1701) <<http://dx.doi.org/10.1038/ncomms1701>> ). Other research, such as a study by Didier Raoult and his colleagues at the University of the Mediterranean, in Marseille, France, has shown that the Black Death, a pandemic that killed more than 75 million people in Europe between 1348 and 1350, was likely a coinfection of *Yersinia pestis*, the causative agent of the famous bubonic plague, and *Bartonella quintana*, which causes trench fever.

In 1998, when Raoult and coworkers found *Y. pestis* in the remains of Black Death victims buried in a mass grave in France, some researchers didn't believe their conclusion that this was the cause of the plague, preferring to stick to theories that the infectious agent had been viral or a different bacterial pathogen (*Proc. Natl. Acad. Sci. USA* 1998, DOI: [10.1073/pnas.95.21.12637](https://doi.org/10.1073/pnas.95.21.12637) <<http://dx.doi.org/10.1073/pnas.95.21.12637>> ).



One reason researchers were skeptical was because plague from *Y. pestis* was long thought to be spread by fleas on rats. Black Death had traveled too quickly across Europe for the rat-flea infection model to be valid, especially because it had quickly traversed rural areas that did not have the rat population to account for such rapid infection rates. Furthermore, Black Death had continued to spread in winter, when rodent fleas die off, Raoult said.

Discovering that people in the French mass grave

**C&EN**  
**ANCIENT REMAINS**

These victims of the 14th-century Black Death epidemic from Bondy, France, helped researchers show that the causative agent of the epidemic was a coinfection of plague and trench fever.

Credit: Cyril Le Forestier

were coinfecting with trench fever's *B. quintana* helped Raoult's team resolve the debate. *B. quintana* is spread by human lice, and in the 14th century "people were just covered in lice," Raoult said.

So if the people in the mass grave had one infectious disease spread by human lice, maybe the pandemic's *Y. pestis* was a strain that could also live in human lice instead of rat lice. That suggested Black Death had been spread by travel of humans with body lice, rather than by rats with body lice. This year, when human body lice in the Congo were found to contain a strain of *Y. pestis*, more people in the field accepted the theory that *Y. pestis* was involved in Black Death, Raoult said.

You might think that extracting the causative agents of deadly pandemics from ancient remains would make the scientists who do this research afraid of getting infected. "Of course we take the necessary precautions" to stay safe in the lab, Raoult said, but in reality paleomicrobiology researchers are often more concerned about accidentally contaminating their ancient samples with DNA from modern infectious disease agents.

That's why the field has established a potpourri of measures to prevent contamination. When sampling from a skeleton, researchers typically extract the dental pulp, which can harbor infectious agents but is also protected from contamination over centuries or millennia by the enamel around it. Amplification of bacterial DNA found in the dental pulp is often split between multiple labs so that results can be verified.

Such contamination concerns as well as the growing sensitivity of analytical technologies have inspired researchers to look for other molecular markers for pathogenic infection in ancient remains. For example, **David E. Minnikin** <<http://www.birmingham.ac.uk/schools/biosciences/staff/profile.aspx?ReferenceId=36569&Name=professor-david-e-minnikin>> and his colleagues at the University of Birmingham, in England, have pioneered the detection of tuberculosis pathogen lipids from skeletal remains.

Using mass spectrometry and gas chromatography, they've measured mycocerosates



**lipidolipenates** in the remains of a 9,000-year-old Neolithic woman and child who suffered from tuberculosis—the oldest known cases of the disease. These fatty acids are specific to *Mycobacterium*, properties that are key to their use as ancient biomarkers, Donoghue said. Although proteins are often longer lasting than lipids or DNA, “it’s hard to find proteins that are specific to particular bacteria,” she added.

**Because it is so difficult** to find pathogen-specific proteins in ancient samples, **Angelique Corthals** <<http://newswise.com/articles/stony-brook-scientists-detect-immune-response-of-a-500-year-old-mummy>> at SUNY’s Stony Brook School of Medicine has found a way to discover the presence of pathogens indirectly. In particular, Corthals looks for characteristic human immune system proteins produced as the body tries to defend itself from a particular infectious agent.



#### TRACES OF TUBERCULOSIS

This 500-year-old Incan mummy had well-preserved immune proteins in her bodily fluids that revealed a bacterial lung infection.

Credit: Angelique Corthals

For example, last year she reported her analysis of several 500-year-old Incan mummies that had been found in a frozen grave at nearly 7,000 feet in the Andes Mountains. Two of the mummies were so well preserved that Corthals sampled phlegm, blood, and other bodily fluids found in and near the mummies’ mouths and noses and then conducted a proteomic and genetic analysis of the fluids (*PLoS One* 2012, DOI: [10.1371/journal.pone.0041244](http://dx.doi.org/10.1371/journal.pone.0041244) <<http://dx.doi.org/10.1371/journal.pone.0041244>> ).

In the case of a 14-year-old female mummy called the Maiden, samples of her bodily fluids contained DNA from a *Mycobacterium* species, as well as immune system proteins commonly found in chronic lung disease. In another mummy of a young boy called El Niño, the fluid in his mouth contained proteins typically produced during high-altitude pulmonary edema, a deadly condition when lungs fill with fluid.

As researchers get better at analyzing ancient human remains to find molecular proof of the sicknesses that plagued and sometimes killed them, many outstanding

**Research** questions about past diseases and pandemics may be answered. But this research is helping contemporary humans as well. Corthals said some of the methodologies developed to study the Peruvian mummies could be adopted for forensic bodily fluid analysis. And insights into the origins and evolution of tuberculosis and other infectious pathogens may help researchers control their spread and virulence in the future.

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### 印加儿童木乃伊或为活人祭品



“尤耶亚科火山少女”死前曾服药。  
图片来源:Johan Reinhard-Leslie

**本报讯** 500多年前, 三名儿童爬上阿根廷的尤耶亚科火山后再踏上归途, 据推测, 她们可能成为了活人献祭的牺牲品。她们保存完好的木乃伊于1999年被发现, 科学家希望通过研究木乃伊重建她们生命的最后几个月。新的证据表明, 这三名儿童曾定期摄入古柯和酒精, 相较于仪式因素, 这些药物对她们的死亡产生了更大的影响。

考古学家将这三具木乃伊称作“尤耶亚科火山少女”。据推测, 她们遇难时已经13岁, 死于印加文化的祭祀仪式——capacocha。她们被杀害或是被丢弃在高山的山峰上等死。尸体在小的神殿内被发现, 由于近7000米海拔的高山上气候寒冷干燥, 尸体被自然风化为木乃伊。

未参与该研究的美国石溪大学医学院法医人类学家Angelique Corthals说: “在capacocha仪式中, 古柯和酒精的重要性是我们很早就意识到的, 很庆幸这次终于得到了证实。” Corthals一直致力于研究木乃伊。

尽管历史资料显示, 被选为capacocha仪式的祭品是一种荣耀, 领导该研究的英国布拉德福德大学的考古学家Andrew Wilson认为, 在她们死前的数周, 酒精已经被注入其体内以起到镇静效果。但是古柯的存在使事情在某种程度上变得复杂化——因为古柯会引起血管收缩, 从而使体温小幅度上升。

尽管目前尚不清楚这些药物的结合是如何影响山顶上的“尤耶亚科火山少女”的身体和思维, 但Wilson根据发现推测, 其中至少有一个女孩是在药物作用镇静后, 被丢弃在神殿里等待死亡的。其他在高海拔地区发现的印加人木乃伊显示有头部创伤, 而尤耶亚科山的木乃伊似乎是平静地死去。没有外在迹象显示, 她们在死亡前曾有呕吐或排便, 她们身边被原封不动的供品包围, 这意味着在死前她们没有奋力挣扎。

(段歆潏)

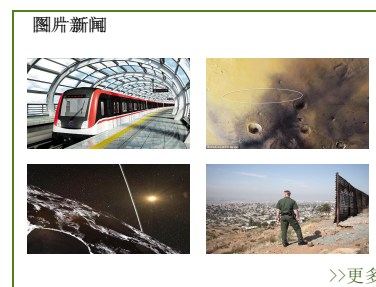
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