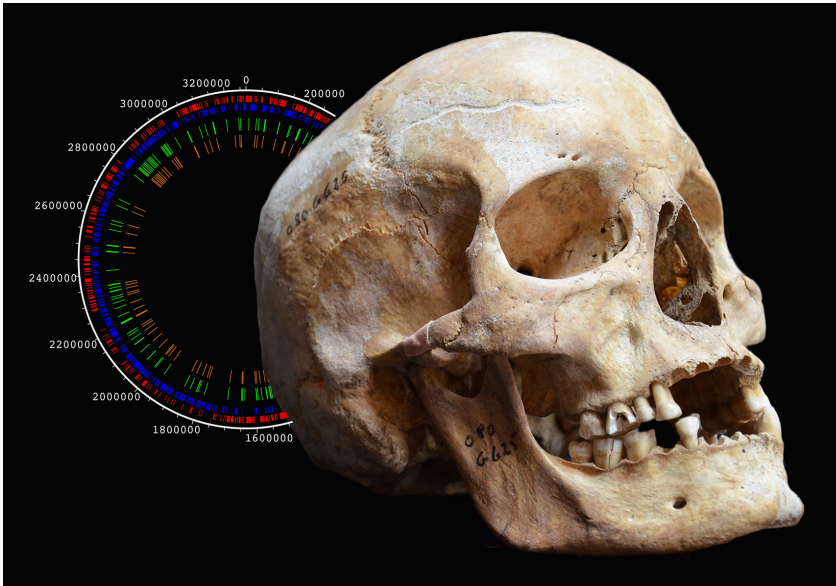# IEMNews

Skull of a Leprosy victim from the St. Jørgen cemetery in Denmark with the *Mycobacterium leprae* genome reconstructed from this individual.
Image ©: B. Krause-Kyora

What can we learn from ancient pathogens?

There is no doubt that pathogens have contributed to shape our history as humans either directly as human infectious diseases or indirect as diseases of our crops or animal livestock. Many major human pathogens were probably transmitted as zoonoses from domestic animals to humans causing severe diseases such as measles, pertussis or tuberculosis. Opportunities for potential zoonotic events can be found during major changes in the human lifestyle starting from Neolithic transition to the industrialization cumulating in our globalized world of today. Our history is full of examples for pandemics that had major impacts on our past, however, the causative agents remain unknown till today.

At this point, research on ancient pathogens comes to the rescue as it allows to identify unknown causative agents of past pandemics using a combination of ancient DNA and next generation sequencing and to reconstruct their genomes. Pathogens can be traced through time and their evolution can be analyzed from broader perspective via understanding of their past. Moreover, the ancient strains can be used to estimate how fast a pathogen changes over time allowing more accurate predictions for the pathogen's future like adaptions to antibiotics.

Working on ancient pathogens has been a key part of my research in the last seven years and will also be the main focus of the Paleogenetics team at the IEM that I lead since December 2017. In one of our long-term projects we try to trace the origins of leprosy and its causative agent *Mycobacterium leprae* through time within a large international collaboration. In our present study, we analyzed 10 newly reconstructed medieval *M. leprae* genomes including the so far oldest *M. leprae* genome from one of the earliest known cases of leprosy in the United Kingdom—a skeleton from the Great Chesterford cemetery with a calibrated date of 415–545 AD. Interestingly, the Great Chesterford strain is very similar to those found in modern-day red squirrels and supports the hypothesis that squirrels and the squirrel fur trade were a factor in the spread of leprosy amon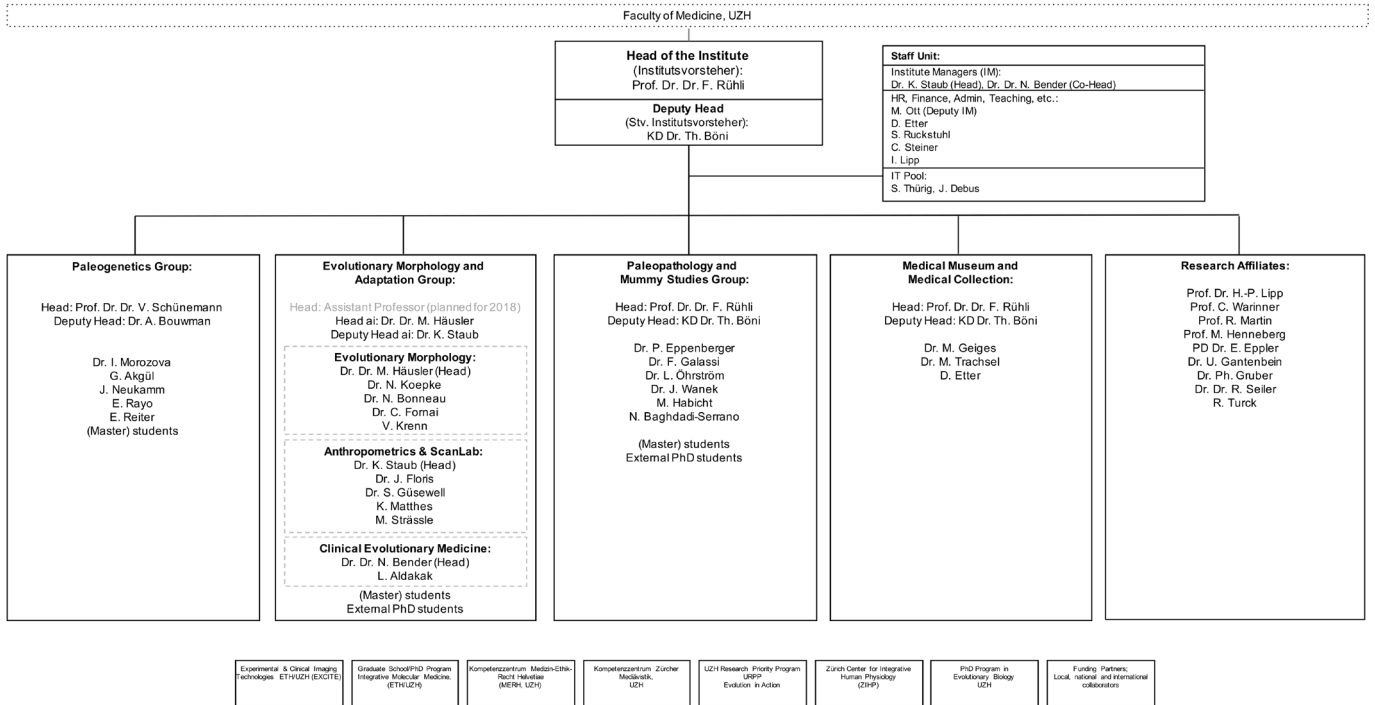g humans in Europe during the Medieval Period. With this genetic time transect of *M. leprae* diversity in Europe over the last 1500 years we find four major *M. leprae* lineages present in the Early Medieval Period, and three lineages within a single cemetery from the High Medieval Period. Altogether we detect a higher genetic diversity of *M. leprae* strains in medieval Europe at various time points than previously known. Based on this diversity it is plausible that leprosy may already have been widespread throughout Asia and Europe in Antiquity or that it might have originated in Western Eurasia.

However, as the dynamics of *M. leprae* transmission throughout human history are still not fully resolved we will continue to investigate on the origins of leprosy. Furthermore, we are organizing an international symposium to bring together researchers from various fields working on the origins of leprosy to create an interdisciplinary view on this key question in leprosy research.

Prof. Dr. Dr. Verena Schünemann
IEM Assistant Professor for Paleogenetics

IEM organigram

Institute of Evolutionary Medicine (IEM) (as March 2018)

Faculty of Medicine, UZH

Head of the Institute
(Institutsvorsteher):
Prof. Dr. Dr. F. Rühli

Deputy Head
(Stv. Institutsvorsteher):
KD Dr. Th. Böni

Staff Unit:
Institute Managers (IM):
Dr. K. Staub (Head), Dr. Dr. N. Bender (Co-Head)
HR, Finance, Admin, Teaching, etc.:
M. Ott (Deputy IM)
D. Etter
S. Ruckstuhl
C. Steiner
I. Lipp
IT Pool:
S. Thürig, J. Debus

Paleogenetics Group:

Head: Prof. Dr. Dr. V. Schünemann
Deputy Head: Dr. A. Bouwman

Dr. I. Morozova
G. Akgül
J. Neukamm
E. Rayo
E. Reiter
(Master) students

Evolutionary Morphology and Adaptation Group:

Head: Assistant Professor (planned for 2018)
Head ai: Dr. Dr. M. Häusler
Deputy Head ai: Dr. K. Staub

Evolutionary Morphology:
Dr. Dr. M. Häusler (Head)
Dr. N. Koepke
Dr. N. Bonneau
Dr. C. Fornai
V. Krenn

Anthropometrics & ScanLab:
Dr. K. Staub (Head)
Dr. J. Floris
Dr. S. Güsewell
K. Matthes
M. Strässle

Clinical Evolutionary Medicine:
Dr. Dr. N. Bender (Head)
L. Aldakak

(Master) students
External PhD students

Paleopathology and Mummy Studies Group:

Head: Prof. Dr. Dr. F. Rühli
Deputy Head: KD Dr. Th. Böni

Dr. P. Eppenberger
Dr. F. Galassi
Dr. L. Öhrström
Dr. J. Wanek
M. Habicht
N. Baghdadi-Serrano

(Master) students
External PhD students

Medical Museum and Medical Collection:

Head: Prof. Dr. Dr. F. Rühli
Deputy Head: KD Dr. Th. Böni

Dr. M. Geiges
Dr. M. Trachsel
D. Etter

Research Affiliates:

Prof. Dr. H.-P. Lipp
Prof. C. Warinner
Prof. R. Martin
Prof. M. Henneberg
PD Dr. E. Eppler
Dr. U. Gantenbein
Dr. Ph. Gruber
Dr. Dr. R. Seiler
R. Turck

Experimental & Clinical Imaging Technologies ETH/UZH (EXCITE) | Graduate School/PhD Program Integrative Molecular Medicine, (ETH/UZH) | Kompetenzzentrum Medizin-Ethik-Recht Helvetiae (MERH, UZH) | Kompetenzzentrum Zürcher Mediävistik, UZH | UZH Research Priority Program URPP Evolution in Action | Zürich Center for Integrative Human Physiology (ZIHP) | PhD Program in Evolutionary Biology UZH | Funding Partners; Local, national and international collaborators

Vision and mission statement

We are a leading international and globally connected research, teaching and service institute which is part of the medical faculty at the University of Zurich. We analyse ancient biological material and associated data to better understand modern human health issues and diseases. Due to specialist scientific expertise, excellent infrastructure and state-of-the-art methodologies, we are able to work on various interdisciplinary research questions in the context of the field of Evolutionary Medicine. Our core competencies include:

• In the area of morphology: Clinical Anatomy; Variability and adaptation of body morphology as a function of sex, robustness, time (Microevolution), socio-economic factors (etc.); Macroevolution of joint pathologies.

• In the area of imaging: application of modern imaging techniques (MRI, terahertz) on historical tissues; Radiological diagnosis of pathologies.

• In the area of ancient DNA: Co-evolution of diseases and the human genome (evolution of human pathogens, microbiome analyses etc.); Service for Archaeology/Historical Anthropology (paternity testing, sex determination).

• Maintaining the historic Medical Collection for both scientific research and inter-museal exchange.

• Ethical considerations for research on historical human tissues.

We will increase the recognition of the research field of Evolutionary Medicine and expand academic teaching of the subject within and outside the Faculty of Medicine. This will be of a sustainable value for our stakeholders at the University of Zurich, in the research community of evolutionary medicine and adjacent areas, to the economy and ultimately for society in general.

Words from our international collaboration partners

Prof. Dr. Almut Nebel
University of Kiel, Germany

Prof. Dr. Ben Krause-Kyora
University of Kiel, Germany

The origins of leprosy, one of mankind's oldest and most stigmatized diseases, are still surrounded by many mysteries as the spread and diversity of its causative agent, *Mycobacterium leprae*, over the last millennia remain widely unknown. Back in 2011 we started the first experiments to uncover leprosy's past using next generation sequencing techniques to reconstruct medieval *M. leprae* genomes within the framework of a large international collaboration.

That was also time when we first met Verena Schünemann, who currently joined the IEM as an assistant professor for Paleogenetics and had already been one of the driving forces of the leprosy project back then. Together we explored the diversity of *M. leprae* strains in North-Western Europe and found a relationship of late medieval strains from Europe to modern strains circulating in wild armadillos and human patients in South-Western USA. Moreover, we discovered the conserved nature of *M. leprae* genomes that acquired only 20-30 mutations per 1000 years and performed the first de novo assembly of an ancient bacterial pathogen. We detected that the genome architecture was very similar in ancient and modern *M. leprae* strains.

This was only the beginning of a very fruitful long-term collaboration on ancient leprosy that recently resulted in a follow up publication on medieval *M. leprae* strains in Europe revealing an unexpected high diversity in these strains. Beside this we investigated the host-pathogen coevolution in the first case-control study based on ancient DNA (aDNA). We used skeletal material from 85 individuals with signs of severe leprosy from the twelfth and thirteenth centuries in Odense, Denmark and compared it with 223 medieval Danish and Northern German skeletons that did not demonstrate any signs of leprosy. The analyses show that the immune variant HLA-DRB1 15:01 rendered people more susceptible to leprosy. Because lepers were isolated and could not reproduce owing to their disease, they did not pass on this risk factor. The HLA variant is today linked to the appearance of inflammatory diseases, such as sarcoidosis, ulcerative colitis, multiple sclerosis or type 1 diabetes. The HLA antigen causes bacteria to be recognised, among other things, and triggers a targeted immune reaction in the body.

We just visited the IEM last month and are planning to expand our collaboration with Verena and her team on leprosy and other diseases. Currently, we are very much looking forward to Verena's symposium on "Towards the origins of leprosy: molecular approaches to understand one of mankind's oldest diseases" in the coming weeks and are very pleased to also present our research on the host genomic side of leprosy there.

Words from a new member of the IEM

Katarina Matthes, MSc
IEM Research Assistant Evolutionary
Morphology and Adaptation Group

After graduating from the hearing acoustics engineering program at the University of Applied Sciences in Lübeck, Germany, in 2009 I worked for several years as a research audiologist at Phonak AG in Stäfa. Due to my research work, my interest in statistics and research in human health grew and I became more passionate about large data sets and applied statistics. During that time I decided to enroll in the biostatistics graduate program at the University of Zurich. In June 2014, I earned my Master's degree in Biostatistics at the University of Zurich. Since then, I work at the Cancer Registry Zurich and Zug as Biostatistician and have started my Ph.D. at the Epidemiology, Biostatistics and Prevention Institute, which is expected to be completed in May 2018.

Finally, in March 2018, I joined the IEM, where I am involved in two teaching fund projects. In the first project "Online-Tool Living Statistics", led by Kaspar Staub, I develop an online-tool to make statistics and complex data more tangible, approachable and understandable for students. For this project, data of students such as body height are used for analysis. As part of basic statistics lectures the students voluntarily collect data of body size and some additional control variables on themselves and enter them anonymously in an online tool. With the help of the tool simple analyzes such as mean, median, differences or standard deviations can be made and are visualized in an easy and well understandable way.

In the second project "Visual Analytics" I work with Patrick Eppenberger. In collaboration with the ZHdK "Visual Analytics" will be taught in an interdisciplinary teaching module by using problem-based peer learning and e-learning. The main goal is interdisciplinary and actively interaction between UZH and ZHdK students to broaden their perspectives of their way of thinking and visualization. To explain the basics of "Visual Analytics" I will develop similar tools as in the "Living Statistics" online tool to make statistics and visualization exciting and interactive, for example the influence of used colors, line thickness or background colors of a graphic can be adjusted and thus effects easily be studied.

IEM-publications (selected publications since last IEM News Aug/2017)

Bender N, Vinci L, Fäh D et al. Übergewicht und Lebensstil - Auswertung der menuCH-Daten. BAG-Schlussbericht 2017, accepted.

Bouwman A, Shved N, Akgül G et al. (2017). Ancient DNA investigation of a medieval german cemetery confirms long-term stability of CCR5-Δ32 allele frequencies in Central Europe. Human Biology; An International Record of Research, 89(2):119-124.

Cramer L, Brix A, Matin E et al. (2017). Computed Tomography-Detected Paleopathologies in Ancient Egyptian Mummies. Current Problems in Diagnostic Radiology, 47(4):225-232.

Floris J, Kuster M, Woitek U (2017). Armutsgrenzen in der Stadt Zürich während des Ersten Weltkriegs. Traverse: Zeitschrift für Geschichte, Zürich, 2017(3):97-112.

Floris J, Staub K, Stohr C, Woitek U (2018). Changes in Mortality in Switzerland, 1880-1910. Schweizerisches Jahrbuch für Wirtschaftsgeschichte, accepted and in press

Galassi F, Bender N, Habicht M et al. (2018). St. Catherine of Siena (1347–1380 AD): one of the earliest historic cases of altered gustatory perception in anorexia mirabilis. Neurological Sciences, 39(5):939-940.

Galassi F, Habicht M, Rühli F et al. (2017). A unique case of stroke and upper limb paralysis in a mid-18th century natural mummy. Circulation Research, 121(4):338-340.

Galassi F, Varotto E, Zanatta A (2018). Did Antonio Vallisneri (1661-1730) really describe frontal sinus osteoma? Unexpected insights for paleo-neuroparasitology. Neurological Sciences, epub March 22.

Genoud M, Isler K, Martin R (2018). Comparative analyses of basal rate of metabolism in mammals: data selection does matter. Biological Reviews of the Cambridge Philosophical Society, 93(1):404-438.

Hershkovitz I, Weber G, Fornai C et al. (2018). The earliest modern humans outside Africa. Science, 359(6374):456-459.

Ioannou S, Henneberg R, Henneberg M (2018). Presence of dental signs of congenital syphilis in pre-modern speciemen. Archives of Oral Biology, 85:192-200.

Koepke N, Floris J, Pfister C et al. (2018). Ladies First: female and male adult height in Switzerland, 1770-1930. Economics and Human Biology, 29:76-87.

Lipp HP (2017). Evolutionary shaping of adult hippocampal neurogenesis in mammals–cognitive gain or developmental priming of personality traits?. Frontiers in Neuroscience, 11:420.

Myburgh J, Staub K, Rühli F et al. (2017). Secular trends in stature of late 20 th century white South Africans and two European populations. HOMO Journal of Comparative Human Biology, 68(6):433-439.

NCD Risk Factor Collaboration (2017). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128,9 million children, adolescents, and adults. Lancet, 390(10113):2627-2642.

Saniotis A, Henneberg M, Sawalma AR (2018). Integration of Nanobots Into Neural Circuits As a Future Therapy for Treating Neurodegenerative Disorders. Frontiers in Neuroscience, 12:153.

Schuenemann VJ, Avanzi C, Krause-Kyora B et al. (2018). Ancient genomes reveal a high diversity of Mycobacterium leprae in medieval Europe, PLoS Pathogens, 14(5):e1006997.

Spiessberger A, Baumann F, Häusler M et al. (2018). A Posterior Oblique Approach to the Lumbar Disk Spaces, Vertebral Bodies, and Lumbar Plexus: A Cadaveric Feasibility Study. Clinical Spine Surgery, 31(1):E8-E12.

Staub K, Henneberg M, Galassi F et al. (2018). Increasing variability of body mass and health correlates in Swiss conscripts, a possible role of relaxed natural selection? Evolution, Medicine, and Public Health, epub May 5.

Staub K, Floris J, Koepke N et al. (2018). Comparison between BMI, waist circumference and waist-to-height ratio in Swiss young adult males: A cross-sectional study. BMJ Open, accepted.

Vågene A, Herbig A, Campana M et al. (2018). Salmonella enterica genomes from victims of a major sixteenth-century epidemic in Mexico. Nature Ecology and Evolution, 2(3):520-528.

Voikar V, Krackow S, Lipp HP et al. (2017). Automated dissection of permanent effects of hippocampal or prefrontal lesions on performance at spatial, working memory and circadian timing tasks of C57BL/6 mice in IntelliCage. Behavioural Brain Research, epub Sept 18.

Yao L, Li H, Martin R (2017). Tracing the phylogeographic history of Southeast Asian long-tailed macaques through mitogenomes of museum specimens. Molecular Phylogenetics and Evolution, 116:227-238.

You W, Henneberg M (2017). Cancer incidence increasing globally: The role of relaxed natural selection. Evolutionary Applications, 11(2):140-152.

You W, Symonds I, Rühli F et al. (2018). Decreasing birth rate determining worldwide incidence and regional variation of female breast cancer. Advances in Breast Cancer Research, 7(1):1-14.

Upcoming events

- Symposium: Towards the origins of leprosy. IEM, Zurich, May 23, 2018
- World Congress on Mummy Studies, Tenerife, May 21-25, 2018
- International Conference Evolutionary Medicine: Health and Diseases in Changing Environment, Vilnius, June 5-8, 2018
- Paläopathologisches Kolloquium: Malformations, IEM, Zurich, June 22, 2018
- Society for Molecular Biology and Evolution Conference, Yokohama, July 8-12, 2018
- World Economic History Congress, Boston, July 29-August 3, 2018
- Annual Meeting of the International Society for Evolution, Medicine, and Public Health, Park City, August 1-4, 2018
- International Symposium on Biomolecular Archaeology, Jena, September 18-21, 2018

New IEM-members

The IEM is happy to welcome the following members to the institute:

- Prof. Dr. Dr. Verena Schünemann, Head Paleogenetics Group
- Judith Neukamm, PhD Student Paleogenetics Group
- Ella Reiter, Technician Paleogenetics Group
- Katarina Matthes, Research Assistant Anthropometrics Group
- Dr. Sabine Güsewell, Biostatistician Anthropometrics Group

Selected media reports

- SRF Television Puls, May 9, 2018
- Tagesanzeiger, May 7, 2018
- Youreporter, Nov 14, 2018
- Le Temps, Oct 20, 2017
- ScienceNews, Oct 13, 2017
- UZH News, Oct 10, 2017