Nobel Conference

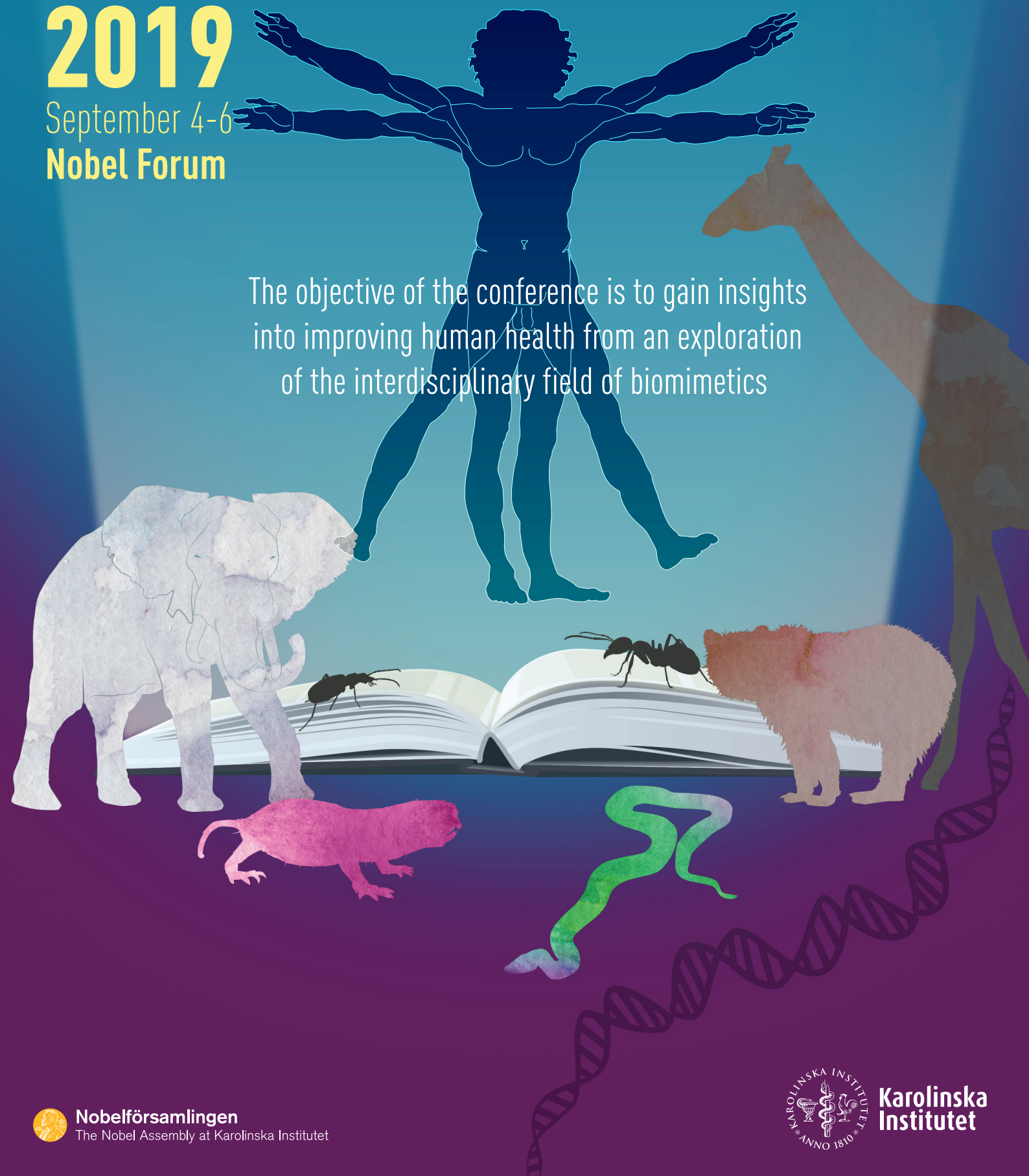
Bio-inspirational medicine

Using nature to unlock access to opportunities in health

2019

September 4-6

Nobel Forum



The objective of the conference is to gain insights into improving human health from an exploration of the interdisciplinary field of biomimetics

Nobelförsamlingen
The Nobel Assembly at Karolinska Institutet

Karolinska Institutet

Welcome to the Nobel Conference "Bioinspirational medicine – Using nature to unlock access to opportunities in health" Sept 4-6 2019

There are over 8 million species in this world that live in widely varying environments, from hot thermal fissures to cold arctic settings. These species have evolved over millions of years and vary markedly in how they have adapted to their environments. In the last several decades it has been recognized that the studies of how species have succeeded in surviving in different environments and with different resources may provide not only insights into disease but also novel means for developing treatments.

During the meeting, we provide an overview of related approaches which are turning to the natural world for insights to better understand, treat, and prevent human "burden of life style" pathologies from heart disease and cancer to degeneration and aging. We suggest that expanding biomedical investigation beyond its decades old conventional practices to new approaches based on a broad awareness of the diversity of animal life and comparative physiology can accelerate innovations in health care under the motto "Nature knows best".

Local organizing committee

Peter Stenvinkel
Professor, Karolinska Institutet

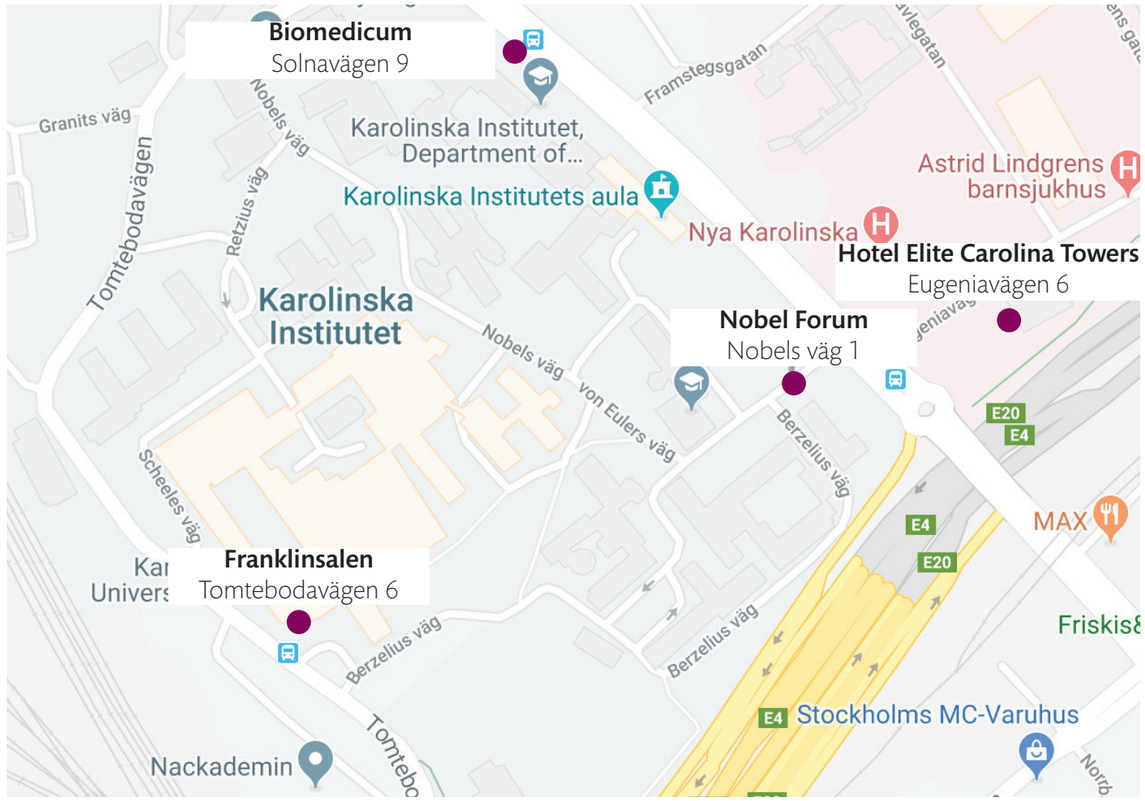
Annika Wernerson
Professor, Karolinska Institutet

Karolina Kublickiene
Docent, Karolinska Institutet

Birgitta Strandvik
Professor, Karolinska Institutet

Martin Schalling
Professor, Karolinska Institutet

MAP OF KAROLINSKA INSTITUTET



About Karolinska Institutet - A Medical University

Karolinska Institutet is one of the world's foremost medical universities. Our vision is to make a significant contribution to the improvement of human health; our mission is to conduct research and education and to interact with the community.

As a university, Karolinska Institutet is Sweden's single largest centre of medical academic research and offers the country's widest range of medical courses and programmes.

Since 1901 the Nobel Assembly at Karolinska Institutet has selected the Nobel laureates in Physiology or Medicine.

The Nobel Assembly at Karolinska Institutet, which appoints the laureates, consists of 50 members selected from the professors at Karolinska Institutet. Through its work with the Nobel Prize, Karolinska Institutet has gained a priceless contact network and a unique insight into medical research findings around the globe.

Karolinska Institutet was founded by King Karl XIII in 1810 as an "academy for the training of skilled army surgeons". Today, Karolinska Institutet is a modern medical university and one of the foremost in the world.

With our close relationship to the clinical milieu, a well established infrastructure and a stable financial situation, Karolinska Institutet has excellent prerequisites for sustaining high quality research and education.

PROGRAM

OBJECTIVE: The objective of this conference is to gather leading biomedical researchers to gain and develop insights from the interdisciplinary field of biomimetics in service of improving human health.

FORMAT: Sessions with 30-min lectures followed by discussions

TARGET AUDIENCE: Scientific leaders representing a range of disciplines, including ecology, technology, biology, chemistry, epidemiology, veterinary medicine, zoology, medicine, basic scientists among others.

INTERNATIONAL ADVISORY BOARD: Rick Johnson USA, Johanna Painer Austria, Ole Fröbert Sweden, Makoto Kuro-o Japan, Paul Shiels UK, Lars-Uno Larsson Sweden

LOCAL ORGANIZING TEAM, KAROLINSKA INSTITUTET: Peter Stenvinkel, Karolina Kublickiene, Martin Schalling, Birgitta Strandvik, Annika Wernersson

Note! The scientific program may be subjected to change.

Photo: Ulf Sirborn

SEPTEMBER 4

07:30-08:30 **REGISTRATION AT NOBEL FORUM** (across the street from Hotel Elite Carolina Tower)

08:30-08:45 **Opening and welcome:**
Prof. Ole Petter Ottersen, President Karolinska Institutet, Stockholm, Sweden
Prof. Peter Stenvinkel, Dept of Renal Medicine, Karolinska Institutet, Stockholm, Sweden

08:45-10:15 **Plenary lectures: Chair Peter Stenvinkel**

Biomimicry – innovations inspired by nature
Prof. Julian Vincent, Honorary Professor, Heriot-Watt University, Edinburgh, UK

Evolution, adaptation and the common challenges of life on earth
Prof. Barbara Natterson-Horowitz, Department of Human Evolutionary Biology, Harvard, Boston, USA

Bio-inspired innovation in medical breakthroughs
Prof Victor Dzau, President, National Academy of Medicine, Washington, USA

10:15-10:45 **COFFEE BREAK**

10:45-12:00 **Biomimetics and the environment: Chair Martin Schalling**

Fructose metabolism as a common evolutionary pathway of survival associated with climate change, food shortage and drought
Prof. Rick Johnson, Division of Renal Diseases and Hypertension, University of Colorado, Aurora, USA

From emperor penguins to newborn mammals: huddling as a way to decrease energy expenditure while maintaining a high body temperature
Prof. Y Le Maho, Emeritus Director of Research at the Centre National de la Recherche Scientifique, Université de Strasbourg & Centre Scientifique de Monaco, France

Discussion

12:00-12:15 **GROUP PHOTO OUTSIDE NOBEL FORUM**

12:15-13:15 **LUNCH**

13:15-15:00 **Evolution and genetics: Chair Rick Johnson**

Building Darwinism from the bottom Up
Prof. Steven A. Benner, Foundation for Applied Molecular Evolution, USA

Evolutionary basis for the human diet: consequences for human health
Prof. Peter Andrews, Natural History Museum, Department of Anthropology, University College London, UK

Functional genomics in non-model organisms
Prof. Leif Andersson, Department of Medical Biochemistry and Microbiology, Uppsala, Sweden

Discussion

15:00-15:30 **COFFEE BREAK**

15:30-17:45 **Ageing – lessons from the animal kingdom: Chair Paul Shiels**

Nutrients and ageing: what can we learn from animal biology?
Prof. Paul Shiels, Wolfson Wohl Translational Research Center, Institute of Cancer Sciences, MVLS, University of Glasgow, UK

Phosphate handling during evolution and in the animal kingdom: Implications for human ageing
Prof. Makoto Kuro-O, Division of Anti-aging Medicine, Center for Molecular Medicine, Jichi Medical University, Yakushiji, Shimotsuke, Tochigi, Japan

Gut microbial community composition - what can we learn from the animal kingdom?
Prof. Paul O´Toole, School of Microbiology and APC Microbiome Institute, Cork, Ireland

The naked truth: Unusual immune features of the naked mole-rat that may contribute to exceptional longevity and prolonged good health
Prof. Rochelle Buffenstein, Calico Life Sciences, South San Francisco, USA

Discussion

18:00-18:15 **BUSES LEAVE FROM NOBEL FORUM**

19:00-21:00 **BUFFET DINNER AND TOUR OF STOCKHOLM CITY HALL** sponsored by Stockholms City & County Council

SEPTEMBER 5

08:30-10:15 **Biomimetic applications - Lessons from hibernating animals (I): Chair Johanna Painer**

Metabolic adaptations in hibernating mammals
Prof. Thomas Ruf, Research Institute of Wildlife Ecology, University of Veterinary Medicine Vienna, Austria

Biomimetics - Nature's roadmap to insights and solutions for burden of life style diseases
Prof. Peter Stenvinkel, Dept. of Renal Medicine Karolinska University Hospital, Stockholm, Sweden

Mechanisms of organ protection during mammalian hibernation
Prof. Rob H. Henning, Department of Clinical Pharmacy and Pharmacology, University Medical Center Groningen, The Netherlands

Discussion

10:15-10:45 **COFFEE BREAK**

10:45-12:30 **Biomimetic applications - Lessons from hibernating animals (II): Chair Ole Fröbert**

Why are hibernating bears of interest to cardiologists?
Prof. Ole Fröbert, Örebro University Hospital, Örebro, Sweden

Environmental lead (Pb) exposure: Are bears "naturally" protected?
Prof. Jon Arnemo, Inland Norway University of Applied Sciences & Swedish University of Agricultural Sciences, Norway

Physical inactivity and preservation of muscle mass: Lessons from hibernation
Prof. Etienne Lefai, Proteostasis Team, UNH 1019, INRA, Université Clermont Auvergne, France

Discussion

12.30-13:30 **LUNCH**

13:30-15:15 **Ingenious solutions in the animal kingdom (I): Chair Birgitta Strandvik**

Neurodevelopment: The escalation of mental ill-health threatens the sustainability of humanity
Prof. Michael Crawford, Reproductive Physiology, Chelsea and Westminster Hospital. Imperial College, London, UK

The ecology of collective behaviour
Prof. Deborah Gordon, Department of Biology, Stanford University, Stanford, USA

Marine bioactive compounds as a source for new drugs
Prof. Jeanette Hammer Andersen, The Arctic University of Norway, Tromsö, Norway

Discussion

15:15-15:45 **COFFEE BREAK**

15:45-17:00 **Ingenious solutions in the animal kingdom (II): Chair Lars-Uno Larsson**

Polar bears: Can their fur help us increase the efficacy of solar panels?
Dr. Mohammed Q. Khattab, Faculty of Civil Engineering and Architecture, Kärnten University, Vienna, Austria

Biomimetically inspired injection of fuel and diesel exhaust fluid
Per Tunestål, Competence Center for Combustion Processes, Lund University, Lund, Sweden

Discussion

17:15 **BUSES LEAVE FROM NOBEL FORUM**

18:00-23:00 **DINNER AND TOURS OF SKANSEN ZOO AND OUTDOOR MUSEUM**

SEPTEMBER 6

08:30-10:15 **Ingenious solutions in the animal kingdom (III): Chair Karolina Kublickiene**

Insights from wildlife medicine: Comparative nephrology between carnivorous felids and humans
Dr. Johanna Painer, Department of Integrative Biology and Evolution, University of Veterinary Medicine Vienna, Austria

Spider silk: Can it help us find novel proteins for the treatment of human disease?
Prof. Janne Johansson, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden

What can giraffes teach us about high blood pressure?
Prof. Christian Aalkjaer, Department of Biomedicine, Aarhus University and Department of Biomedical Science, Copenhagen University, Denmark

Discussion

10:15-10:45 **COFFEE BREAK**

10:45-12:00 **Ingenious solutions in the animal kingdom (IV): Chair Annika Wernerson**

Fatty acids in the burmese python: Implications for cardiac growth
Prof Leslie Leinwand, Biofrontiers Institut, University of Colorado, Boulder, USA

Mechanisms for cancer resistance in elephants: the study of Peto's paradox to treat human patients
Prof. JD Shiffman, Departments of Pediatrics, University Utah School of Medicine, Salt Lake City, USA

Discussion

12.00-13:00 **LUNCH**

END OF NOBEL CONFERENCE

JIM Journal of Internal Medicine

Founded in 1863

The organisers are grateful for the support from the Journal of Internal Medicine and the publication of reviews summarizing parts of the Nobel conference

Biomimetics: Nature's roadmap to insights and solutions for burden of life style diseases.
Stenvinkel P, Painer J, Johnson R, Natterson-Horowitz B.

The brown bear as a translational model for sedentary lifestyle related diseases.
Fröbert O, Fröbert AM, Kindberg J, Arnemo J, Overgaard MT

The role of the microbiota for sedentary life style disorders and ageing. Lessons from the animal kingdom.
O'Toole PW and Shiels P.

Survival in the setting of climate change, food shortage and droughts: Identification of a common evolutionary pathway of survival.
Johnson RJ, Stenvinkel P, Andrews P, Nakagawa T, Andres-Hernando A, Rodriguez-Iturbe B et al

JIM Journal of Internal Medicine is an independent journal, published on behalf of the Association for Publication of the Journal of Internal Medicine.

JIM features original clinical articles within the broad field of general and internal medicine and its subspecialities. Jim also supports and organizes scientific meetings in the form of symposia within the scope of the journal.

Welcome to visit our colourful website at www.jim.se

Separate Workshop by The Medici Group and Karolinska Institutet

13:00-14:00 **Lecture by Frans Johansson - The Medici Effect: Innovation at the intersection**
CEO, founder of The Medici Group, New York, USA
Hörsalen Biomedicum, Solnavägen 9, KI

14:00- 17:00 **The Medici Method Workshop: Diversity Drives Innovation** (by invitation only)
Frans Johansson, The Medici Group, New York, USA
Franklinsalen, KI

17:10-17:30 **Funding opportunities for biomimetic research**
Alexander Schenk, European Investment bank, Stockholm, Sweden
Franklinsalen, KI

17:40-18:00 **Film presenting examples of opportunities in biomimetics.**
Prof. Claes Andren, VD Nature Artbevarande & Foto AB, Ljungskile, Sweden
Franklinsalen, KI

15:00-19:00 **LIGHT FOOD AND DRINKS WILL BE SERVED IN BETWEEN**

WE ARE GRATEFUL FOR THE SUPPORT AND COLLABORATION OF OUR PARTNERS TO MAKE THE EVENTS POSSIBLE:

The local organisers are grateful for the assistance from Ann Hellström (Nobel administration), Erika Tanos (KI DevReg) and Kjell Erlandsson (IT technician).

NOTES

Biomimicry – innovations inspired by nature

JULIAN VINCENT
Honorary Professor, Heriot-Watt University, Edinburgh, UK

In the mid-1990s I spent some time in New Zealand working on the fracture properties of wood. A 'Friday afternoon' investigation into the way a woodwasp drills holes in wood to lay its eggs suggested several ideas for projects. Eight years later I included this story in a seminar at Imperial College, London. Ferdinando y Baena, a newly appointed lecturer in medical robotics, was intrigued by this and, over a few beers, we hatched the concept of a steerable intracranial endoscope. Some 13 years later still, with his professorship, several large grants and an international team, Ferdinando has brought the endoscope to approaching clinical tests.

This story is a chain of chance. If similar successes are to be gained, biomimetics must become easily available to informed and objective search and planning by technologists and designers who do not know any biology. I shall show how this can be achieved by an ontology using the concept of 'trade-off' to define and explore a technical problem and implement a biological solution, if one exists.

The other, no less important, step in the route to harnessing the advantages of biomimetics, is how to make it attractive to industry.

Evolution, adaptation and the common challenges of life on earth

BARBARA NATTERSON-HOROWITZ
Department of Human Evolutionary Biology, Harvard, Boston, USA

The natural world contains countless evolved adaptations to the challenges of life on Earth. These challenges are essentially the same for animal life: avoidance of infection, predation and starvation, protection from oxidative stress, thermal extremes, UV radiation and others. Multitudes of adaptations to these challenges exist among the over 8 million other animal species estimated to exist on our planet. These evolved adaptive physiologies in non-human animals may offer innovative strategies for approaching complex or intractable challenges in human medicine. This talk advances the premise that biomedical innovation can be accelerated through the identification of these animal physiologies, characterization of their underlying physiologic processes, and understanding of the role ecology and evolutionary processes play in them. Supporting examples from cardiovascular medicine and neuropsychiatry will be presented.

Bio-inspired innovation in medical breakthroughs

VICTOR J DZAU
MD, President, National Academy of Medicine, Washington, USA

Significant advances in human health have stemmed from basic research on lower organisms and insights from animal biology. Indeed, we have seen major breakthroughs and lifesaving therapies, in areas such as cardiovascular disease, immunology, cancer, and more. For example, consider the discovery of penicillin, based on Alexander Fleming's observation that bacteria surrounding mold colonies in culture were dying, to the discovery of breakthrough therapies, such as statins and ACE inhibitors, which can be traced to research on fungi and snake venom.

Going forward, we are likely to see even more breakthroughs emerge from basic research on lower organisms and animal biology such as CRISPR gene editing, DNA repair and regenerative medicine. Furthermore, new bio-inspired medical devices and innovations are likely to emerge in clinical use. The approach of one health – or "the collaborative effort of multiple disciplines–working locally, nationally, and globally–to attain optimal health for people, animals and the environment" is likely to help mitigate infectious disease outbreaks and pandemics.

Dr. Dzau will provide a broad overview of the historical insights and breakthrough therapies derived from research on nature. He will discuss current and emerging research areas of bio-inspired innovation in biomedical investigation.

Fructose metabolism as a common evolutionary pathway of survival associated with climate change, food shortage and droughts

RICHARD J JOHNSON[1],
Peter Stenvinkel[2], Peter Andrews[3], Laura G Sánchez-Lozada[4], Takahiko Nakagawa[5], Eric Gaucher[6], Ana Andres-Hernando[1], Bernardo Rodriguez-Iturbe[4], Carlos Roncal Jimenez[1], Gabriela Garcia[1], Duk-Hee Kang[7], Dean R Tolan[8], and Miguel A. Lanaspa[1]

[1]Division of Renal Diseases and Hypertension, University of Colorado Anschutz Medical Campus, Aurora, CO, USA; [2]Division of Renal Diseases, Karolinska Institutet, Stockholm, Sweden; [3]Museum of Natural History, London, United Kingdom; [4]Dept. of Nephrology, INC Ignacio Chávez. Mexico City. Mexico; [5]Department of Nephrology, Rakuwakai Otowa Hospital, Kyoto, Japan; [6]School of Biological Sciences, Georgia Institute of Technology, Atlanta, GA; [7]Division of Renal Diseases, Ewha University, Seoul Korea, [8]Department of Biochemistry, Boston University, Boston, MA, USA

During the last 450 million years, there have been at least five major extinctions related to changes in climate and atmospheric gasses. While studies of those animals that went extinct can be informative, it is the adaptability of the survivors that may provide key insights into basic pathways for survival in settings where conditions are adverse. Here we describe a common survival pathway that is used by many species as a means for providing adequate fuel and water, while also providing some protection from a decrease in oxygen availability. Specifically, the nutrient fructose, whether supplied in the diet (primarily fruits and honey), or endogenously (via activation of the polyol pathway) appears to preferentially shift the organism towards the storing of fuel (fat, glycogen) that can be used to provide energy and water, while also providing some protection from a decrease in oxygen availability.
>>Cont.

Specifically, the nutrient fructose, whether supplied in the diet (primarily fruits and honey), or endogenously (via activation of the polyol pathway) appears to preferentially shift the organism towards the storing of fuel (fat, glycogen) that can be used to provide energy and water. Fructose also causes sodium retention and raises blood pressure and likely helped survival in the setting of dehydration or salt deprivation. Finally, by shifting energy production from the mitochondria to glycolysis, it reduced oxygen demands to aid survival in situations where oxygen availability is low. The actions of fructose are driven in part by the stimulation of vasopressin and the generation of uric acid. Indeed, at least twice in history, mutations occurred during periods of massive extinction that enhanced the activity of fructose to generate fat, with the first being a mutation in vitamin C metabolism during the Cretaceous Paleogene mutation and the second being a mutation in uricase that occurred during the Middle Miocene Disruption. Today, however, the excessive availability of fructose due to the intake of refined sugar and high fructose corn syrup is driving multiple "burden of life style" diseases, including obesity, diabetes, high blood pressure and many cancers.

From emperor penguins to newborn mammals: huddling as a way to decrease energy expenditure while maintaining a high body temperature.

YVON LE MAHO
Emeritus Director of Research at the Centre National de la Recherche Scientifique, Université de Strasbourg & Centre Scientifique de Monaco.

The resting metabolic rate of endothermic animals, i.e. animals that are able to maintain through internal functions a high body temperature, is related to the body surface of heat loss. Accordingly, the larger are the animals the smaller is the ratio between their body surface area and their volume of heat of production. This explains why the resting metabolic rate per unit body mass of larger animals is more than 20-fold lower than the metabolic rate of the tiny shrew or humming-bird. A further stage is therefore when animals are decreasing their surface area by huddling tightly together, as do emperor penguins when breeding during the severe Antarctic winter. Depending on the location of the colonies, the ambient temperature may drop to -50°C or be not as low but with winds that may reach more than 200 km/h.

About 60 years ago, the pioneers in Antarctic biology already demonstrated that this social thermoregulatory behavior is the key for male emperor penguins to assume the entire task of the incubation, which involves a fast of about 120 days. Indeed, they found that huddling allows a drop of 50% in the rate of weight loss during fasting. Using stable isotopes, we confirmed the drop in metabolic rate induced by huddling. About two thirds of the 38% metabolic reduction is attributable to the reduction in cold-exposed body surfaces and one-third to the mild microclimate created within the groups. Yet, a high body temperature is maintained in huddling male emperor penguins with an egg, which is obviously essential for the incubation.

The problem however is that after about 45 minutes a tropical environment is induced into the huddle. Thus, emperor penguins do not spend days and weeks in the warmth of the huddles as indicated in texts books. They regularly break the huddle to avoid overheating. It was therefore of a great interest to investigate the effect of huddling in newborn mammals. We found that huddling is also reducing metabolic rate in rabbit pups, the saved energy being channeled into processes of growth and fat accretion. Their body temperature is maintained at a high value, a condition not only for the physiological processes involved in this growth but also because newborn rabbits with a low body temperature are unable to suckle during the 5 minutes a day their mother is available for nursing. Yet, because of their naked skin, huddling newborn rabbits do not have to face overheating as do emperor penguins with their efficient plumage. In conclusion, whatever is body size, huddling is of a behavior of a critical importance as an energy saving mechanism in situations where a high body temperature has to be maintained.

Building darwinism from the bottom up

STEVEN A. BENNER
Foundation for Applied Molecular Evolution, USA

The possibility of increasing the number of replicable nucleotides in DNA and RNA (collectively xNA) above the four found in standard terran DNA and RNA was noted a quarter-century ago. However, only recently has the broader scientific community come to recognize that "artificially expanded genetic information systems" (AEGIS) also expand the functional potential of nucleic acids, allowing them to perform better roles that are not purely genetic. This includes the laboratory evolution of DNA-like molecules that bind small molecules, act as ligands for receptors, or even catalyze reactions. This talk will present recent work in synthetic biology that has rewritten xNA, including the development of DNA polymerases, RNA polymerases, and reverse transcriptases that synthesize and interconvert information in DNA and RNA molecules built from more than four nucleotides. This is transforming our ability to create functional xNA molecules via laboratory in vitro evolution (LIVE) applied to expanded genetic alphabets. These include molecules that bind specifically to cancer cells, deliver drugs to cancer cells, bind and inhibit anthrax toxins, and catalyze reactions, all better than products of LIVE applied to standard GACT libraries.

Evolutionary basis for the human diet: consequences for human health

PETER ANDREWS
Natural History Museum, London, UK

Interpreting human evolution in the fossil record is based on direct evidence of fossil remains, interpretations of the environment with which they are associated, and circumstantial evidence based on analogies with the present day. Fossil evidence shows apes and early human ancestors were fruit-eaters living in seasonal habitats, aided by the uricase mutation at about 15Ma. Rapid cooling at the end of the middle Miocene (15-12Ma) increased seasonality in Africa and Europe; the climate was stable in the later Miocene and Pliocene (15-6Ma), and both apes and early hominins were living both on the ground and in trees. These conditions persisted for about the first three million years of hominin evolution (6-3Ma). At the end of the Pliocene, early species of Homo started to introduce more meat into their diet.

This change coincided with developing bipedalism, stone tool technology and increase in brain size above that of the apes, all present in Homo habilis. This species still lived in woodland habitats, however, not savanna, and the major habitat shift in human evolution occurred at 1.8Ma with the origin of Homo erectus. This later species had increased body size, greater hunting skills with increased meat in their diet, control of fire and understanding about cooking food, and finally the move from woodland to savanna. Circumstantial evidence suggests that group size increased with this move, facilitating the transmission of knowledge from one generation to the next in Homo erectus. The earliest fossils of Homo sapiens appeared about 300kyr, but they had separated from Neanderthals by 480kyr and probably slightly earlier. Their diet began to shift towards grain-based foods about 100kyr, and settled agriculture developed about 10kyr. This pattern remains for many populations to this day.

Functional genomics in non-model organisms

LEIF ANDERSSON
Department of Medical Biochemistry and Microbiology, Uppsala University

I will present some lessons of relevance for human medicine from our genomic studies of non-model organisms, domestic animals and the Atlantic herring. Domestic animals have gone through dramatic phenotypic changes during the last 10,000 years since domestication. We have exploited this to reveal genetic changes of critical importance for their adaptation to the farm environment. For instance, our characterization of a locus explaining differences in muscularity between wild boars and domestic pigs resulted in the discovery of a previously unknown transcription factor and a mechanism regulating muscle growth and the size of internal organs most likely in all placental mammals, including human. Similarly, we have identified a gene controlling gait in horses by coordinating muscle contractions during locomotion. It is likely that a similar mechanism is present in all vertebrates.

The Atlantic herring is one of the most abundant vertebrates on earth with a global population size of about 1,000 billion fish, about 90 billion of these are found in the Baltic Sea only. In fact, the herring is one of the few marine fish that has been able to colonize the brackish Baltic Sea. We have performed whole genome sequencing of the Atlantic and Baltic herring and revealed hundreds of gene regions showing striking genetic differences between these populations. I will describe some of the genetic changes that has allowed the herring to the ecological conditions in the Baltic Sea and which genetic changes determine the timing of reproduction.

Nutrients and ageing: what we can learn from animal biology

PAUL SHIELS
Wolfson Wohl Translational Research Center, Institute of Cancer Sciences, MVLS,
University of Glasgow, UK

Ageing is a process of decline in physiological function and capability over time. It is an anticipated major burden on societal health-care costs due to an increasingly aged global population. Accelerated biological ageing is a feature of age-related morbidities, which also appear to share common underpinning features and hall marks which are common across taxa. Additionally, in mammals this is accompanied by low-grade persistent inflammation, phosphate toxicity, diminished Nrf2 activity and a low diversity gut microbiome. The trajectory of age-related health is also impacted on by individual exposome differences over the life course, which reflects the interplay between the genome and the environment.

This is manifest as allostatic (over)load reflecting burden of lifestyle/disease at both a physiological and molecular level. A link between nutrition, age-related health and longevity has been consistently described across taxa, although its mechanistic basis is still not fully understood. This is pertinent to how age related health is influenced by the 'foodome' (i.e. the individual diet, its ingredients and their chemical structure), particularly dietary restriction. What is also becoming more apparent is that genetic heterogeneity appears to play a major role in the responsiveness of individuals to a particular dietary intervention. While dysregulated nutrient sensing is postulated as a key component of the hallmarks of ageing, in mammals there may be additional, related features, such as hyper-phosphataemic generation of calciprotein particles, (CPPs) and changes in microbiota. Hyper-phosphataemia appears to be a fundamental component of age-related health in mammal linked to frequent consumption of red meat. >>Cont.

Significantly, red meat consumption provides a mechanistic basis for affecting the microbiota and their contribution to age related health, via the production of the pro-inflammatory agent TMAO, which has been implicated in the diseasome of ageing and mortality. This is also pertinent to recent observations indicating that diets lacking sufficient fruit and vegetable intake lack phenolic acids that can be converted by key gut microbes to alkyl catechols. This both affects the availability of methyl donors required for maintenance of the epigenome and provision of alkyl catechol Nrf2 agonists which are mediators of cellular stress defenses. Significantly, alkyl catechols, such as fisetin and quercetin, have been identified as potent senolytic agents, able to induce apoptosis in senescent cells. Elimination of senescent cells by a range of senolytic agents has already been demonstrated to increase lifespan and health span in preclinical models.

Phosphate handling during evolution and in the animal kingdom: Implications for human ageing

MAKOTO KURO-O
Division of Anti-aging Medicine, Center for Molecular Medicine, Jichi Medical University, 3311-1 Yakushiji, Shimotsuke, Tochigi 329-0498, Japan

During the evolution of skeletons, terrestrial vertebrates acquired the bone made of calcium-phosphate. By keeping the extracellular fluid in a supersaturated condition regarding calcium and phosphate ions, they create the bone when and where they want simply by providing a cue for precipitation. To secure this strategy, they acquired a new endocrine system to strictly control the extracellular phosphate concentration. In response to phosphate intake, fibroblast growth factor-23 (FGF23) is secreted from the bone and acts on the kidney through binding to its receptor Klotho to increase urinary phosphate excretion, thereby maintaining phosphate homeostasis. The FGF23-Klotho endocrine system, when disrupted, results in hyper-phosphatemia and ectopic calcium-phosphate precipitation in mice and humans.

In addition to disturbed phosphate homeostasis, mice lacking Klotho suffer from premature ageing. They exhibit multiple organ atrophy, arteriosclerosis, cardiac hypertrophy, sarcopenia, cognition impairment, frailty, and a shortened lifespan associated with chronic non-infectious inflammation, which are a phenocopy of patients with renal failure. Besides calcium-phosphate deposition in extraosseous tissues, hemodialysis patients bear colloidal nanoparticles containing calcium-phosphate in the blood, which are termed calciprotein particles (CPP). CPP have the ability to induce cell damage and inflammation and thus may be responsible for the accelerated ageing. In fact, removal of CPP from the blood in mini-pigs undergoing hemodialysis using a CPP adsorption column improves their life expectancy and vascular calcification. Terrestrial vertebrates with the bone made of calcium-phosphate may be destined to age due to ectopic calcium-phosphate.

Gut microbiome and ageing - what can we learn from the animal kingdom?

PAUL W. O'TOOLE
School of Microbiology and APC Microbiome Institute, Cork, Ireland

The gut microbiome is the community of microorganisms that resides in the gastrointestinal tract, comprising of hundreds of species of bacteria, fungi, bacteriophages, protozoa and mammalian viruses. The bacterial microbiome is best characterized, and after a decade of recent intense study, it is now appreciated that alterations in gut microbiome composition and function are associated with intestinal and extra-intestinal diseases, by largely unknown mechanisms. >>Cont.

Differences in the microbiome of human subjects also co-vary with ageing-related health loss, and the microbiome of centenarians is distinct from that of healthy older adults. However, because the microbiome is influenced by diet, lifestyle, geography and environment, it is challenging to untangle cause and consequence in microbiome-ageing interaction.

The best understood host benefits associated with the microbiome are release of energy from complex dietary carbohydrates, modulation of metabolism, modulation of inflammation, competitive inhibition of gut pathogens, and production or modulation of neuroactive substances. All these properties probably co-evolved with the host. Comparison of the gut microbiome of humans with that of different animals has identified shared and host-specific taxa and bacterial functions that can be related to different diets and alimentary tract physiology. Study of ageing in model organisms is less directly translatable because the standard model animals are typically smaller, age at faster rates, are genetically in-bred, and consume a restricted diet. Notwithstanding these differences, loss of overall microbiome alpha diversity and increased proportional abundance of pro-inflammatory pathobionts is a feature of ageing in many animals. Using animals as models for experimental intervention, transfer of the gut microbiome of young or old conventional mice to young germ-free mice caused differential effects on inflammation and gut barrier function. The defective germinal centre reaction in Peyer's patches of aged mice could be rescued by faecal transfers from younger adult mice into aged mice or by immunisation with cholera toxin. However, transfer of gut microbiome from healthy or frail older people into germ-free or conventional mice resulted in only minor differences in innate immune state.

Animal models or natural ageing in animals can provide hypothesis-generating data or mechanistic leads, but caution must be exercised in relating this back to ageing humans, in whom microbiome-ageing effects must ultimately be independently confirmed.

The naked truth - Unusual immune features of the naked mole-rat that may contribute to exceptional longevity and prolonged good health

ROCHELLE BUFFENSTEIN
Calico Life Sciences, San Francisco, USA

The mouse-sized naked mole-rat (Heterocephalus glaber) is extremely long-lived (>35 years) for its body size and does not comply with Gomperzian mortality laws. They show no increase in risk of dying as they get older, even at ages far beyond their allometrically predicted maximum lifespan, and at ages 25-fold greater than that of reproductive maturity. When compared to the deterioration of the human body during aging, this subterranean-dwelling rodent shows little age-associated physiological declines, maintaining heart health, bone quality, and reproductive capacity for more than 75% of its known lifetime and is unusually cancer resistant. These remarkable phenotypes suggest that naked mole-rats maintain cellular and systemic homeostasis well beyond sexual maturity and into their third decade of life. Understanding how animals with exceptional longevity, like the naked mole-rat, are able to resist the vagaries of aging may provide pivotal insights into mechanisms that may prolong human health and attenuate age-related diseases.

We therefore hypothesized that the immune system of the naked mole-rat might have evolved unique features that confer enhanced immune surveillance or prevent the age-associated increase in morbidity documented in other mammalian species. We mapped the immune system of the naked mole-rat and compared it to that of the short-lived and cancer-prone mouse. In contrast to the mouse, the naked mole-rat immune system is characterized by a high myeloid-to-lymphoid cell ratio that includes a novel lipopolysaccharide responsive, granulocyte cell subset. Surprisingly, we also find that the naked mole-rat lacks canonical natural killer (NK) cells. These unusual features suggest that this extraordinarily long-lived species relies primarily upon an atypical myeloid-biased mode of innate immune surveillance and challenge our current understanding of the role of mammalian immunity in prolonged good health.

Metabolic adaptations in hibernating mammals

THOMAS RUF
Research Institute of Wildlife Ecology, University of Veterinary Medicine Vienna, Austria

Hibernating mammals enter a state of hypometabolism in torpor by actively suppressing energy-consuming pathways such as gene expression, protein synthesis, mitosis, or ATP-dependent transport. By employing coordinated metabolic rate depression in all tissues hibernators reach a reduction of oxygen consumption typically by >90%, compared with basal metabolic rate. However, individuals that can afford to do so, i.e., those with large body energy reserves, avoid long torpid states at low body temperature (Tb). This points to risks and potential drawbacks of hibernation. One such risk is failure of cardiac function that hibernators counteract by massively increasing the capacity to remove Ca++ from the cytosol of cardiac myocytes, which is augmented by high levels of Linoleic acid in membrane phospholipids.

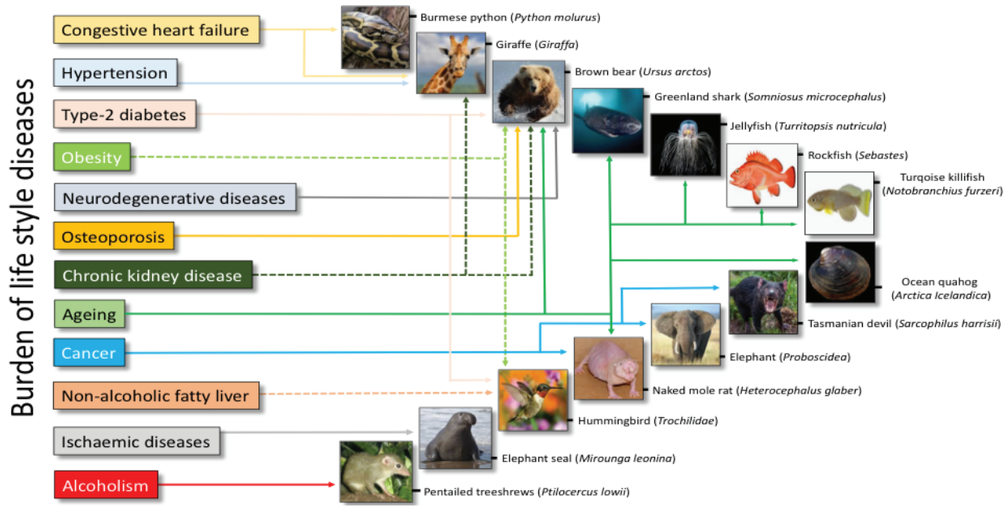
A second potential cost of torpor is cellular damage by production of reactive oxygen species (ROS), for instance in terms of telomere shortening. Oxidative stress particularly occurs during periodical rewarming from torpor if the initial Tb is low. There are, however, hibernators that benefit from hypometabolism without paying the costs of hypothermia: Large mammals, specifically bears, as well as lemurs (primates) in Madagascar, can reach the same levels of metabolic suppression as other hibernating mammals, while maintaining core Tb above 30 °C. It has been suggested that any attempts to induce biostasis for medical reasons in humans or donor organs should focus on mimicking metabolic depression as it occurs during this type of "warm torpor".

Biomimetics - Nature's roadmap to insights and solutions for burden of lifestyle diseases

PETER STENVINKEL
Dept. of Renal Medicine Karolinska University Hospital, Stockholm, Sweden

There are over 8 million species in this world that live in widely varying environments, from hot thermal fissures to cold arctic settings. These species have evolved over millions of years and vary markedly in how they have adapted to their environments. In the last several decades it has been recognized that the studies of how species have succeeded in surviving in different environments and with different resources have been recognized to provide not only insights into disease but also novel means for developing treatments.

A new approach is to turn to the natural world for insights to better understand, treat, and prevent human "burden of life style" pathologies from heart disease and cancer to degeneration and premature aging. Examples from the animal kingdom suggest that superior anti-oxidant defence mechanisms with enhanced NRF2-expression have been developed during evolution to protect animals during extreme environmental conditions, such as deep-sea diving, hibernation and habitual hypoxia. Lessons from evolution, the animal kingdom and conditions of accelerated ageing clarify a major role of a controlled NRF2-KEAP1 system in healthy ageing and well-being. >>Cont.



Examples of species that already have been identified as being of interest for finding novel targets for "burden of life style" diseases that accumulate as we get older. Among a number diseases that often tend to cluster (diseasome), studies of some species in nature have already provided some clues for better treatment of congestive heart failure, hypertension, type-2 diabetes, obesity, neurodegenerative diseases, osteoporosis, chronic kidney disease, ageing, cancer, non-alcoholic fatty liver, ischaemic diseases and alcoholism.

Mechanisms of organ protection during mammalian hibernation

ROBERT H. HENNING
Department of Clinical Pharmacy and Pharmacology, University Medical Center Groningen, The Netherlands

Metabolism is key to life, with normal metabolism being accelerated or derailed in almost any disease. Consequently, applying hibernation, i.e. controlled lowering of metabolism and/or mobilizing protective mechanisms, has a large therapeutic potential to protect organ integrity in acute and chronic conditions.
Hibernation is a state of controlled metabolic depression and comprises a highly effective survival strategy, as it halts ageing and even prolongs lifespan. Hibernation consists of two alternating phases: torpor and arousal. In torpor bouts, metabolism is reduced down to as low as 2-5% of normal, resulting in dramatic physiological changes, including a profound drop in body temperature (Tb), heart and ventilation rates and activity. Torpor phases are alternated with shorter interbout arousal episodes, in which metabolic rate, Tb and other physiologic parameters rapidly normalize. Remarkably, once aroused, animals do not show signs of organ damage or organ disuse (atrophy). Despite hibernation being known for decades, its fundamental mechanisms are hitherto largely undisclosed.

Because of the large and fast changes in metabolic rate, hibernators face injurious effects of repetitive oxidative stress due to hypothermia, hypoperfusion and/or reperfusion upon arousal. There is compelling evidence that hibernators are superior in resisting such oxidative stress, e.g. by upregulation of various anti-oxidant systems mainly driven by the Nrf-2 route. Protection from organ damage may also involve metabolic adaptations, suppression of the blood clotting and immune response, and increased production of hydrogen sulfide (H2S). Consequently, hibernating animals show resistance to injury in experimentally induced ischemia-reperfusion of various organs.
Nevertheless, on close examination, organs of torpid animals show clear signs of specific adaptations or even damage. E.g. torpid brain neurons display both a notable loss of synaptic connections and profound hyperphosphorylation of the tau protein, a hallmark of Alzheimer's disease. Likewise, lungs of torpid hamster show expression of smooth muscle actin and TGFβ, and deposition of extracellular matrix, as found in asthma and COPD. Remarkably, such damage emerging in torpor is fully resolved during a subsequent arousal phase. >>Cont.

Collectively, these data imply that hibernators deploy a dual strategy to prevent organ damage: increased resistance and superior repair. Recent research indicates that both may represent cell-autonomous features, as the traits are preserved in cultured cells from hibernators. I will focus on the role of the H2S pathway in organ protection, and discuss how disclosure of its mechanism led to development of a novel class of drugs, capable of protection from oxidative injury through their mitochondrial action. Further, I will discuss if and how hibernators deal with oxidative DNA damage, i.e. the only molecule that relies exclusively on repair, rather than simple discarding and resynthesis.

Why are hibernating bears of interest to cardiologists?

OLE FRÖBERT
Örebro University Hospital, Sweden

Sedentary lifestyle accelerates biological aging, is a major risk factor for developing metabolic syndrome and is associated with cardiovascular disease, diabetes mellitus, kidney failure, sarcopenia and osteoporosis. In contrast to the linear path to worsening health in humans with metabolic syndrome, brown bears have developed a circular metabolic plasticity enabling these animals to tolerate obesity and a "sedentary lifestyle" during hibernation and exit the den metabolically healthy in spring. Bears are close to human physiology-wise, much closer than rodents, the preferred experimental animals in medical research, and may better serve as translational model to develop treatments for lifestyle-related diseases. In my talk, I will describe aspects of brown bear hibernation survival strategies and touch on conceivable experimental strategies to learn from bears.

Environmental lead (Pb) exposure: Are bears "naturally" protected?

JON M. ARNEMO
Inland Norway University of Applied Sciences & Swedish University of Agricultural Sciences

Lead (Pb) is a highly toxic element and there is no safe level of exposure. Lead-based ammunition is widely used to hunt wild animals and lead exposure from spent ammunition is a global One Health issue. Humans are exposed from consuming game meat and scavenging birds and mammals are poisoned from eating gut piles and slaughter remains left in nature.The brown bear is a scavenger that can be used as a sentinel species for ecosystem lead contamination. Sampling of free-ranging Scandinavian brown bears in spring and early summer, shortly after hibernation, showed high blood lead levels, indicating a significant environmental lead exposure. The mean (range) blood lead level in 155 samples was 94 (32-221) µg/L, which is almost 90% higher than the CDC reference level for humans (formerly known as the «level of concern») (50 µg/L) and 8 times higher than the EFSA threshold for developmental neurotoxicity (12 µg/L). More than 95% of the bears had blood lead levels that would be considered unhealthy in humans.
Two main questions arise from these results: 1) Where is the lead coming from? Although we predict that lead from spent ammunition is a major cause of lead exposure, we cannot yet exclude other sources, such as berries and ants. Bears eat large quantities of berries and are also consuming considerable amounts of ants. The current lead levels in these food items in the bears' home ranges are unknown. 2) Are there any health effects? At the moment, we have no indication that the high blood lead levels are causing negative health effects in the bears. One interesting finding is that bears have 2.5-3.5 times higher blood taurine levels than humans. Taurine is an amino acid known to be protective against neurotoxicity and other effects of oxidative stress from lead in laboratory animals. We hypothesize that bears may be protected against lead toxicity by their high blood levels of taurine.

Physical inactivity and preservation of muscle mass: Lessons from hibernation

ETIENNE LEFAI
Proteostasis Team, UNH 1019, INRA, Université Clermont Auvergne, France

Muscle atrophy is one of the main deleterious consequences of ageing, diseases (e.g. cancers and AIDS), and physical inactivity. It is especially detrimental to locomotion, heat production, and metabolism thus leading to frailty, increased dependency and metabolic disorders. Apart from being a major clinical problem for older people, muscle loss is also observed during physical inactivity, which has become a major leading cause of death worldwide. Although basic knowledge regarding the underlying mechanisms of muscle atrophy is continuously growing, essentially from rodent models and clinical trials in humans, there are still no efficient therapeutic strategies for its prevention and treatment.

Hibernating bears exhibit a strong and unique ability to preserve muscle mass in conditions of muscle disuse and food deprivation, conditions during which muscle atrophy is observed in human. Bears remain inactive in winter during up to seven months without arousal episodes (without eating, drinking, urinating or defecating), with only very limited loss in muscle protein content and strength, whereas muscle and fibre cross-sectional area are preserved.

Underlying mechanisms have not been understood yet, but our approaches combine molecular and cellular studies of bear muscle as well as human muscle cells exposed to bear serum. Our recent demonstration of trans-species effects of bear serum controlling protein degradation in cultured human muscle cell holds promising potential. Hence, exploration of winter bear serum therefore holds potential for developing new tools to fight human muscle atrophy and related metabolic disorders.

Neurodevelopment: The escalation of mental ill-health threatens the sustainability of humanity

MICHAEL A CRAWFORD
Reproductive Physiology, Chelsea and Westminster Hospital. Imperial College, London, UK

This presentation is based on the priority in human biology being the brain. Our genome differs from that of the chimpanzee by only 1.5%. To ensure future health and intelligence will require mimicking conditions in evolution which powered the advancement of the brain from the 350cc of the chimpanzee to the 1.450cc of the Herto fossil, 160,000 years ago. This tells us, human biology is adapted to wild foods which evolved the brain. We wish to make the case for this principle based on the following considerations in evolution:

- The role of essential lipids to intra-cellular specialization, cell specialization and speciation in the Cambrian is largely unappreciated but had to be pivotal.
- The compositional data show the dominance of docosahexaeoic acid (DHA) in the lipid rich, signalling membranes of photoreceptors, synaptic and neuronal structures.
- The evolution of this system occurred some 600 – 500mya in the sea and has remained the same since.

>>Cont.

- A theoretical reason for this extreme conservation based on the quantum mechanical properties of its unique π-electron arrangement, offers an explanation for the precision of the signal, consciousness, neural memory and recall.
- Encephalization to H. sapiens depended on promotion of neurodevelopment. This could not have happened without the above resource and specifically without DHA.
- The bulk of in H. sapiens takes place before birth. Hence the supreme importance of maternal nutrition and health especially before conception.
- The failure of food and agricultural policy to serve the brain is in our view, responsible for the escalation of mental ill-health and decline in measures of intelligence since 1950.
- The escalation of mental ill health and decline in IQ, if allowed to continue, obviously threatens the sustainability of humanity.
- Reversal requires the restoration in the food system, of the principles which propelled encephalization towards H. sapiens.

Reference:
Crawford MA, et al (2013) A quantum theory for the irreplaceable role of docosahexaenoic acid in neural cell signalling throughout evolution Prostaglandins Leukot Essent Fatty Acids (PLEFA); 88(1):5-13.

The ecology of collective behaviour

DEBORAH M GORDON
Department of Biology, Stanford University, USA

Collective behaviour operates without central control, through interactions among individuals. The process that regulates collective behaviour evolves in relation with a dynamic environment. Similar ecological constraints, in many natural systems from cells to ants, may lead to similar processes that regulate collective behaviour. Some important aspects of the dynamics of the environment include stability, the threat of rupture or disturbance, the ratio of inflow and outflow of resources or energy, and the distribution of resources. These correspond to the dynamics of collective behaviour, including the rate of amplification, how feedback instigates and inhibits activity, and whether information is spatially centralized. The collective behaviour of ant colonies is based on simple olfactory interactions. Ant species differ enormously in the algorithms that regulate collective behaviour, reflecting diversity in ecology. An example is the contrast between the regulation of foraging by harvester ants in the desert, where life is tough but stable, and by arboreal turtle ants in the tropical forest, where life is easy but unpredictable. These correspondences in dynamics may provide insight into the diversity of collective behaviour in other systems. For example, the collective behaviour

Marine bioactive compounds as a source for new drugs

JEANETTE HAMMER ANDERSEN
The Arctic University of Norway, Tromsö, Norway

The success of natural products in drug discovery is unparalleled, more than 60 % of the new chemical entities introduced into the clinic originated from, or were inspired by, natural products. >>Cont.

In particular, for anticancer therapeutics, where nearly half of the currently marketed drugs are derived from natural products. Plant-derived cytotoxic compounds such as paclitaxel, vincristine, epothilones, doxorubicin, etoposide, and camptothecin are all widely used in cancer therapy today. More recently, the oceans have received growing interest as a source for new useful bioactive compounds. The marine environment comprises the majority of the global biodiversity. The wide-ranging genetic variation has engendered unique biosynthetic pathways that produce structurally diverse small organic molecules that extend the chemical space. In 1969, the first marine-derived anti-cancer drug, cytarabine (Cytosar-U®), was approved. This has since been followed by three additional marketed marine derived anticancer drugs, including trabectedin (ET-743, Yondelis®). Currently, several other marine natural products are under clinical evaluation. As the marine environment and its organisms have become more accessible over the last decades, it is expected that the ocean will be the next great source of novel chemistry.

Our research group, Marbio, UiT explore Arctic and sub-Arctic marine organisms, searching for compounds with activities against cancer, bacteria and diabetes as well as compounds with immunomodulatory and anti-oxidative effects. Our screening campaign has been based on a classic bioassay-guided fractionation approach. We are screening a unique collection of cold-water invertebrates and marine microorganisms, and we have identified several novel bioactive molecules.

Polar bears: Can their fur help us increase the efficacy of solar panels?

KHATTAB MOHAMMED
Qasim, Faculty of Civil Engineering and Architecture, Kärnten University, Austria

Researchers around the world have been working on developing bioinspired energy systems, motivated by the fact that nature, through evolution, has been developing thermal harnessing and insulation strategies that meant to work and last efficiently. Notably, animals living in the polar regions; e.g., arctic hares and polar bears, have gone through inspiring adaptations to survive the extreme environment of the Arctic. This lecture introduces the polar bear´s thermal and optical adaptations, and discusses innovative available prototypes based on those adaptations.

In the case of the polar bear, the fur´s transparent hair contains no pigments but provides scattering centers via its hollow structured cores. This gives the fur the advantage to appear white as a result of the back-scattering of the incident visible light of all frequencies without suffering the problem of photo-degradation. However, a percentage of the incident light is scattered forward, traveling down the hairs, until it is dissipated into heat and trapped within the fur. At the same time, the fur is efficiently retaining the thermal radiation emitted from the animal´s body, therefore, it is not possible for IR-thermography to detect the polar bear easily.
The efficiency of solar energy conversion into heat of a system is mainly determined by its optical properties. The theory of solar energy conversion based on polar bear fur, though being controversially discussed, offers unique opportunities and solutions. Such solutions promise more efficient solar energy conversion, by optimizing the transformation of the incident light into heat while suppressing the thermal radiation heat losses.

Biomimetically inspired injection of fuel and diesel exhaust fluid

PER TUNESTÅL
Competence Center for Combustion Processes, Lund University, Lund, Sweden

The Bombardier beetle and its defensive spray against enemies has inspired the development of automotive injectors for both fuel and diesel exhaust fluid for exhaust after treatment. The beetle utilizes flash boiling caused by chemical heating of a liquid in a cavity connected to the atmosphere through a passive valve that opens when the pressure differential becomes high enough. In the biomimetic injectors, the chemical heating is replaced by electrical heating and the passive valve is replaced by a set of electromagnetic valves that add flexibility and robustness to the device.

It turns out that the sprays generated by these injectors feature high momentum and small droplet sizes which improves mixing and reduces wall wetting. Injection of fuel directly into a combustion chamber with high back pressure has also been unsuccessfully attempted due to the excessive temperatures required to overcome the vapor pressure and achieve flash boiling.

Insights from wildlife medicine: Comparative nephrology between carnivorous felids and humans

JOHANNA PAINER
Dept of Integrative Biology and Evolution, University of Veterinary Medicine, Vienna, Austria

We investigated correlations between dietary habits and ecological distribution in different wildlife mammals compared to their blood renal parameters and kidney morphology. Different embryonic developments created different renal systems, ranging from smooth faced and uni-pyramidal to multilobed and multipyramidal reniculated kidney architectures, showing different abilities to concentrate urine. While some mammalian kidneys are highly resistant towards hypoxic or toxic damages, felidae kidneys are highly susceptible towards damages and often suffer from chronic kidney disease.

Evolutionary adapted to being obligatory carnivorous, their serum levels of creatinine, blood urea nitrogen and phosphorous are significantly increased compared to all other mammals. Understanding the impact of animal protein based diets in other mammals, may contribute to the prevention of chronic kidney disease development and progress in human patients.

Spider silk: Can it help us find novel proteins for the treatment of human disease?

JAN JOHANSSON,
Anna Rising, Gefei Chen, Médoune Sarr and Nina Kronqvist, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden

Several types of biomedically relevant proteins, including many self-assembling peptides and membrane proteins, are difficult to produce due to uncontrolled aggregation during synthesis, storage and purification. Spiders can produce and store silk proteins (spidroins) at huge concentrations (exceeding the total protein concentration in the cytosol) by sequestering the very aggregation-prone regions of spidroins in micellar structures, where the very soluble N-terminal domain (NT) forms the shell. We have developed a method that mimics the way spiders produce proteins and have harnessed NT to produce also non-spidroin aggregation-prone proteins. We designed a charge-reversed mutant (NT*) that is stabilized and hypersoluble compared to wildtype NT. Fusions to NT* yield up to ten times more of soluble protein in Escherichia coli compared to fusions with conventional solubility tags. NT* allows unprecedented efficient production and high-resolution structural studies of biologic drugs, in particular a lung surfactant protein that is used for treatment of neonatal respiratory distress syndrome and a molecular chaperone with activity against Alzheimer disease.

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What can giraffes teach us about high blood pressure?

CHRISTIAN AALKJÆR
Department of Biomedicine, Aarhus University and Department of Biomedical Science, Copenhagen University, Denmark

Because of the size of the giraffe the cardiovascular system of giraffes is challenged by gravity. The cardiovascular system of humans is also challenged by gravity but because giraffes can be up to 5-6 m tall the challenge is much more severe in giraffes. Giraffes may therefore be a good model to study the influence of gravity on the cardiovascular system. The pressure of the blood in arteries will increase with about 75 mmHg per meter towards the ground. Giraffes like other mammals have an arterial pressure of about 100 mmHg at the head. They have a pressure of above 200 mmHg at heart level, i.e. the blood pressure of giraffes is about 200 mmHg, and they could be expected to have pressures well in excess of 400 mmHg near the hoofs. The giraffe heart manages to pump out blood at the high pressure (200 mmHg) without having extra thick walls because the heart pumps out relatively small volumes of blood every minute. When giraffes take their heads down to drink from a water pond the arterial pressure at the head increases from about 100 mmHg to about 250-300 mmHg within a second. The giraffe protects the head against pressure-induced catastrophes during drinking by reducing pressure at the heart and consequently at the head and by constricting the small arteries immediately upstream for the capillaries and thereby reducing the pressure in the fragile capillaries.

Fatty acids in the Burmese python: Implications for human health

LESLIE LEINWAND
Biofrontiers Institute, University of Colorado, USA

Given the proven potential for uncovering novel biology and for drug discovery by studying animals that have evolved extreme biology to survive, we have employed the postprandial Burmese python as an animal model to discover novel pathways of beneficial cardiac adaptation and we have data suggesting that the python is resistant to lipotoxicity and metabolic syndrome. An infrequent feeder, the Burmese python exhibits a ~40-fold increase in overall metabolic rate and a 160-fold increase in plasma triglycerides within a day of eating a meal that can equal its body mass. This extreme metabolic demand activates potent, rapid and reversible organ growth, including beneficial cardiac enlargement. Despite very high circulating triglycerides there is no cardiac lipid accumulation. Instead, the heart increases expression and activity of genes involved in lipid handling, mitochondrial oxidative capacity, and free radical scavenging.

We identified a novel combination of three fatty acids (FAs) (myristic, palmitic, and palmitoleic) in postprandial python plasma that when administered to either pythons or mice promotes cardiac adaptation with no signs of pathologic lipid signalling. We carried out an experiment in which the snakes were given free access to food for three months, and they ate almost continuously. Despite enormous weight gain including obesity, the snakes suffered no negative health consequences. Instead, they inactivated stress signalling in the heart. We believe that exploration of the biology of the Burmese python will reveal novel signalling pathways that may lead to therapeutics for disease.

Mechanisms for cancer resistance in elephants: the study of Peto's paradox to treat human patients

JOSHUA D SCHIFFMAN
Department of Pediatrics, University Utah School of Medicine, Salt Lake City, USA

Elephants have been evolving for over 60 million years, including growing to a size greater than 100 times that of humans. In addition, elephants can live up to 70 years of age. With such increased cellular mass and extended longevity, nearly every elephant should succumb to cancer due to so many cells dividing for so often during their extended lifespan. Remarkably, elephants only develop cancer at the very low rate of less than 5%. This surprising natural protection from cancer in large and long-lived species like the elephant has been termed "Peto's paradox." Through genomic and functional studies, Dr. Schiffman and his colleagues discovered that elephants have evolved 40 copies (20 versions) of TP53 instead of the 2 copies (1 version) found in humans.

TP53 has been called the Guardian of the Genome due to its ability to protect cells from turning into cancer through either DNA repair or cell death from apoptosis. Recent research by Dr. Schiffman's team has shown that the extra copies of elephant p53 (EP53) work together in a unique fashion to trigger more robust apoptosis than human p53. This talk will explore the mechanism of cancer resistance in elephants through EP53 function, as well as through other accelerated evolutionary regions in the elephant genome. We also will discuss a new translational medicine now being tested based on EP53 and cancer resistance in elephants. Finally, we will briefly cover other exploratory work related to Peto's paradox and evolution's solution to avoiding cancer across large and long-lived species.

The Medici Effect: Innovation at the Intersection

FRANS JOHANSSON
CEO, founder of The Medici Group, New York, USA

Inspired by Frans Johansson's best-selling book The Medici Effect (Harvard Business Press, 2004 & 2017), The Medici Effect Experience will enable participants to step into The Intersection: a place where ideas from different disciplines, industries, and cultures collide to create innovative breakthroughs.

This four-hour session includes a groundbreaking keynote by world-renowned speaker and best-selling author, Frans Johansson; and a 3-hour interactive workshop that will immerse participants in an innovation process that leverages the diverse perspectives and disciplines in the room, fueling creativity and rapid ideation. Participants will leave the session having made transformative connections and armed with tools to both drive innovation and unearth ground-breaking solutions.

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