http://www.bbc.com/news/uk-england-wiltshire-34156673

Stonehenge researchers 'may have found largest Neolithic site'

Stone monoliths found buried near Stonehenge could have been part of the largest Neolithic monument built in Britain, archaeologists believe.

The 4,500-year-old stones, some measuring 15ft (4.5m) in length, were discovered under 3ft of earth at Durrington Walls "superhenge". The monument was on "an extraordinary scale" and unique, researchers said.

The Stonehenge Hidden Landscapes team has been creating an underground map of the area in a five-year project. Remote sensing and geophysical imaging technology has been used to reveal evidence of nearly 100 stones without the need for excavation.

The monument is just under two miles (3km) from Stonehenge, Wiltshire, and is thought to have been a Neolithic ritual site. Experts think it may have surrounded traces of springs and a dry valley leading into the River Avon. Although no stones have been excavated they are believed to be fashioned from sarsen blocks found locally. Sarsen stones are sandstone blocks found mainly on Salisbury Plain and the Marlborough Downs in Wiltshire. A unique sarsen standing stone, The Cuckoo Stone, remains in the field next to Durrington Walls.

The stones are believed to have been deliberately toppled over the south-eastern edge of the bank of the circular enclosure before being incorporated into it.

Lead researcher Vince Gaffney, of the University of Bradford, said: "We don't think there's anything quite like this anywhere else in the world. "This is completely new and the scale is extraordinary."

Archaeologist Nick Snashall said: "The presence of what appear to be stones, surrounding the site of one of the largest Neolithic settlements in Europe adds a whole new chapter to the Stonehenge story."

The earthwork enclosure at Durrington Walls was built about a century after the Stonehenge sarsen circle, but archaeologists believe the newly discovered stone row could have been put in place at the same time or even earlier.

Andy Rhind-Tutt, Heritage Trust founder, described the findings as "an incredible discovery". He and University of Buckingham researchers have been involved in another nearby site, Blick Mead, thought to be at least 9,500 years old.

Mr Rhind-Tutt fears this and other sites could be damaged or lost to a planned A303 road tunnel past Stonehenge. "It's a big concern to all of us, especially as we are at the tip of the iceberg with this particular discovery, and it would be horrible to destroy one of the most significant sites in the world," he said. "The hidden treasure trove of the Stonehenge landscape just begs the question about why are all these incredible structures here?"

David Jacques, from the University of Buckingham, who is Blick Mead project manager, described the find as "absolutely brilliant "and a "game changer". "All the monuments have a relationship with each other," he said.

"So rather than just 'atomising' them and looking at them as individual entities there are deliberate lines of sight or knowledge that things are just over the hill.

"When you put that together in the late Neolithic - there's something vibrant, exciting and dynamic [about the find]."

The findings were being announced on the first day of the British Science Festival being held at the University of Bradford.

http://www.eurekalert.org/pub_releases/2015-09/uou-dgm090215.php

Did grandmas make people pair up?

Human longevity from grandmothering tied to human coupling

SALT LAKE CITY - If you are in a special relationship with another person, thank grandma - not just yours, but all grandmothers since humans evolved.

University of Utah anthropologist Kristen Hawkes is known for the "grandmother hypothesis," which credits prehistoric grandmothering for our long human lifespan. Now, Hawkes has used computer simulations to link grandmothering and longevity to a surplus of older fertile men and, in turn, to the male tendency to guard a female mate from the competition and form a "pair bond" with her instead of mating with numerous partners.

"It looks like grandmothering was crucial to the development of pair bonds in humans," says Hawkes, senior author of the new study published online in the Sept. 7 edition of the journal Proceedings of the National Academy of Sciences.

"Pair bonds are universal in human societies and distinguish us from our closest living relatives," Hawkes and colleagues write in the study. "Our hypothesis is that human pair bonds evolved with increasing payoffs for mate guarding, which resulted from the evolution of our grandmothering life history."

That conclusion contradicts the traditional view that pair bonding "resulted from male hunters feeding females and their offspring in exchange for paternity of those kids so the males have descendants and pass on genes," Hawkes says. The grandma hypothesis holds that "the key to why moms can have next babies sooner is not because of dad bringing home the bacon but because of grandma helping feed the weaned children. That favored increased longevity as longer-lived grandmothers helped more."

The new study focuses on the resulting excess of older males competing for mates, a likely source of men's preference for young women. "This is different than what you see in chimpanzees, where males prefer older females," says Hawkes, a distinguished professor of anthropology and National Academy of Sciences member.

As human longevity increased, there were "lots more old guys, so you have an increasing number of males in the paternity competition, and the only way you can become a father is with a fertile female, which means younger females. So males who had preference for younger females were more likely to leave descendants."

Hawkes performed the study with first author James Coxworth, a postdoctoral fellow at the University of Utah; mathematical biologist Peter Kim, a former University of Utah postdoctoral researcher now at the University of Sydney; and computer specialist John McQueen, also at University of Sydney.

The grandmother hypothesis and pair bonding

Hawkes, University of Utah anthropologist James O'Connell and UCLA anthropologist Nicholas Blurton Jones first published the grandmother hypothesis in 1997-1998 studies, based on observations that began in 1984 of Tanzania's Hazda people, who live by hunting and gathering food like our ancestors. The researchers noted the importance of older Hazda women digging tubers to feed youngsters who weren't strong enough to dig tubers themselves.

Female chimps rarely live past childbearing years, usually into their 30s and sometimes their 40s. Human females often live decades past their child-bearing years - and that may have begun with our early Homo relatives 2 million years ago.

The grandmother hypothesis says that before then, few females lived past their fertile years. But changing environments led to the use of food like buried tubers that weaned children couldn't dig themselves. So older females helped feed the kids, allowing their daughters to have the next baby sooner.

By allowing their daughters to have more kids, grandmothers' longevity genes became increasingly common in the population and human lifespan increased. A 2012 computer simulation study by Hawkes and colleagues supported the hypothesis, finding that without grandmothering, simulated lifespans reach equilibrium when they match those of great apes, but with grandmothering, the computed lifespans get longer like those of humans, often into the 70s or 80s.

Previous research by others also has shown a link between "mate guarding" - in which various male animals guard their female mate against competing suitors when the male-female ratio is high - to the development of pair bonding in humans.

Pair bonding includes but doesn't require an exclusive relationship - polygamists can have multiple pair bonds - but it does mean "a special and persistent relationship between a male and female. Even something like two people going together for a couple of months - that's a pair bond," Hawkes says. "Copulation alone doesn't count. In humans, there's emotional weight to social relationships, certainly to pair bonds."

Chimps, by contrast, have no persistent, special pairing relationships between a particular male and female. A female chimp in heat mates with multiple males. Species from dung flies to primates guard their mates to ensure others don't mate with them.

Simulating the evolution of grandmothering

As human lifespans grew longer, women's fertility continued to end by about age 45, while older men remained fertile. The new study indicates the ratio of fertile men to fertile women increased over time. "That's what made it advantageous for males to guard a female and to develop a pair bond with her," Hawkes says.

For the study, the researchers ran computer simulations of human evolution - 30 simulations with grandmothering and 30 without.

The simulations showed how male-female sex ratios changed over time to become increasingly male-dominated - unlike real nonhuman great ape populations, which have more fertile females than fertile males. For example, the ratio of males to females in fertile ages rose from 77 males per 100 females without grandmothering to 156 males per 100 females with grandmothering in 30,000 to 300,000 simulated years.

Unlike humans, most mammal species have more fertile females than fertile males. "This male bias in sex ratio in the mating ages makes mate-guarding a better strategy for males than trying to seek an additional mate, because there are too many other guys in the competition," Hawkes says. "The more males there are, the more their average reproductive success goes down."

The researchers also showed the male-female sex ratios in the simulations matched closely with those of living populations, namely, chimps, which lack grandmothering and are the only other great apes with good demographic data, and four human hunter-gatherer societies in Africa and South American.

The study then cites previous studies of both living animals - from dung flies to mammals - and computer simulations to show that when the ratio of fertile males to females is high, mate-guarding is likely.

"Mate-guarding and pair bonds are not necessarily the same, but they have in common the tradeoff between paying attention to the current partner and seeking another," Hawkes says. There also is previous research showing that, like mate-guarding, "human pair bonds have the characteristic of male proprietary claims on females."

The lengthening of adult lifespan via grandmothering involves evolution in prehistoric time; increasing average lifespans in recent centuries are attributed

largely to huge reductions in infant and child mortality due to clean water, sewer systems and other public health measures.

Many anthropologists argue that increasing brain size in our ape-like ancestors was the major factor in humans developing lifespans different from apes. But Hawkes' 2012 study ignored brain size, hunting and pair bonding, and showed that even a weak grandmother effect led to human longevity. Indeed, she believes the shift to grandmothering was the foundation for several important steps in human evolution, including longer adult life spans, increased brain size, empathy, cooperation and pair bonding.

http://bit.ly/1LleTRS

Stone-age people were making porridge 32,000 years ago

Going on the palaeo diet? Don't put down your porridge just yet. Hunter-gatherers ate oats as far back as 32,000 years ago – way before farming took root.

This is the earliest known human consumption of oats, say Marta Mariotti Lippi at the University of Florence in Italy and her colleagues, who made the discovery after analysing starch grains on an ancient stone grinding tool from southern Italy.

The Palaeolithic people ground up the wild oats to form flour, which they may have boiled or baked into a simple flatbread, says Mariotti Lippi.

They also seem to have heated the grains before grinding them, perhaps to dry them out in the colder climate of the time. Mariotti Lippi notes that this would also have made the grain easier to grind and longer-lasting.

This multi-stage process would have been time consuming, but beneficial. The grain is nutritionally valuable, and turning it into flour would have been a good way to transport it, which was important for Palaeolithic nomads, she says.

Cereal fuel

To see the benefits of a plant-based diet, you only need to know that society has been largely fuelled by processed grains for the last 10,000 years, says archaeologist Matt Pope of University College London. "There is a relationship there to be explored between diet, experimentation with processing plant food and cultural sophistication."

This is another example of the advances made by Europe's Gravettian culture, which produced technology, artwork and elaborate burial systems during the Upper Palaeolithic era, says Erik Trinkaus at Washington University in St Louis, Missouri. "These people were described 15 years ago as 'Hunters of the Golden Age', and the details of that are still being filled out."

Mariotti Lippi's team hopes to continue studying ancient grinding stones to find out more about the Palaeolithic plant diet. Grinding stones go back a long way, says Trinkaus, and people may well have been pounding and eating various wild grains even earlier than 32,000 years ago.

"We've had evidence of the processing of roots and cattails," but here we've got a grain, and a grain that we're very familiar with," says Pope. "If we were to look more systematically for ground stone technology we would find this is a more widespread phenomenon."

Journal reference: PNAS, DOI: 10.1073/pnas.1505213112

http://exm.nr/1EPmPOB

Whisky aged on NASA's International Space Station tastes different

Vials of a Scotland-based whisky spent more than two years at the International Space Station. The samples are now back on Earth.

Back in October 2011 Ardbeg Distillery on Islay, the southernmost island of the Inner Hebrides of Scotland, sent a vial of whisky to the International Space Station courtesy of Houston based Nanoracks. The idea was the see if microgravity affects the way that whisky ages, particularly the way terpenes that are the building blocks of food and liquors behave. A similar vial was kept on Earth as a comparison. The BBC reported Monday that the contents of the two vials were sampled and compared. As it turns out, pronounced differences were noted.

The Earth sample aged pretty much as expected. "The sample had a woody aroma, reminiscent of an aged Ardbeg style, with hints of cedar, sweet smoke and aged balsamic vinegar, as well as raisins, treacle toffee, vanilla and burnt oranges.

"On the palate, its woody, balsamic flavours shone through, along with a distant fruitiness, some charcoal and antiseptic notes, leading to a long, lingering aftertaste, with flavours of gentle smoke, tar and creamy fudge."

The space sample had some remarkable differences, however. "Its intense aroma had hints of antiseptic smoke, rubber and smoked fish, along with a curious, perfumed note, like violet or cassis, and powerful woody tones, leading to a meaty aroma.

"The taste was very focused, with smoked fruits such as prunes, raisins, sugared plums and cherries, earthy peat smoke, peppermint, aniseed, cinnamon and smoked bacon or hickory-smoked ham. The aftertaste is intense and long, with hints of wood, antiseptic lozenges and rubbery smoke."

Whether the experiment will ever have practical applications remains to be seen. At the current costs of space travel, "space aged whisky" would be the most expensive "bit of the dram" that has ever been distilled. Such a product might find a niche in the luxury market. Anyone lucky to taste space whisky would be able to boast about it until his or her last day.

On the other hand, future space explorers might like to have some home distilled adult beverages to toast the latest adventure on the high frontier. Thinking ahead for just such a need, Ballantine has created a glass that will contain a shot of whisky and allow one to drink from it without having to suck it up through s straw, according to Gizmag. One would think that Lt. Commander Montgomery Scott, a future space explorer who appreciated a good whisky, would approve.

http://www.eurekalert.org/pub_releases/2015-09/uoca-nsc090215.php

Nature: Study creates cell immunity to parasite that infects 50 million

Looking beyond antibiotics and sanitation to explore the third strategy for infectious disease control

There are two common approaches to protecting humans from infectious disease: Targeting pathogens and parasites with medicines like antibiotics, or dealing with the conditions that allow transmission. A paper published today in the journal Nature Scientific Reports demonstrates the effectiveness of a third strategy: Adjusting the landscape of the human body to remove the mechanism that allows pathogens to cause disease. The discovery is the result of serendipity and collaboration between high-level scientists in different fields.

"It was pure luck that I ended up on this paper," says Dan Theodorescu, MD, PhD, director of the University of Colorado Cancer Center. "Bill Petri and I had been social friends for years - Christmas parties, that kind of thing. When I was at Virginia it happened that we were on a recruitment committee together and the candidate was late, so we started talking."

His conversation with William A. Petri, Jr., MD, PhD, chief of the Division of Infectious Diseases & International Health at the University of Virginia led to the idea of applying an innovative cancer science technique to the study of infectious disease. With first author Chelsea Marie, PhD, postdoctoral researcher in the Petri Laboratory at Virginia, the group decided to silence genes in human cells to discover if the loss of any single gene would confer immunity to the parasite E. histolytica, which infects 50 million people and causes 40,000-110,000 deaths via severe diarrhea worldwide.

"Chelsea is a fearless experimenter. She took a library of cells that Dan had developed in his work with bladder cancer and then sequentially killed them with E. histolytica parasites," Petri says.

Specifically, the group used the technique called RNAi to create a library of bladder cancer cells with thousands of independent, silenced genes. Then they challenged these cultures with the parasite E. histolytica.

"We do this all the time in cancer research," Theodorescu says. "Commonly, we're looking for genes that, when silenced, will make cells more susceptible to chemotherapy."

In this case the analogue of chemotherapy was the infectious, dangerous pathogen. "This amoeba is a cluster bomb - a voracious killer. In the back of my mind I was thinking the parasite was going to decimate the host cells no matter what we did with their genetics," Marie says.

For the vast majority of cells in this genome-wide screen, Chelsea Marie was correct; E. histolytica decimated many thousands of these independent cell cultures. However, a small number of cells seemed to resist the parasite. Was this the random chance of lucky survival or had silenced genes somehow offered immunity to these cells? To find out, Marie discarded the killed cells and retested the cells that had survived; again she infected these survivor cells with E. histolytica.

"It wasn't a fluke," says Marie. "We did this over nine generations of cells, each time selecting the cells that survived and then re-applying the parasite. Over these generations of selection, we saw the cultures becoming more and more enriched for cells lacking specific genes."

Using next generation sequencing, Marie identified the genes that conferred resistance and found that many were involved in managing the flow of potassium into and out of human cells. Specifically, the identified genes KCNA3, KCNB2, KCNIP4, KCNJ3, and SLC24A3 are involved in what is called potassium transport. A follow-up experiment showed that new intestinal cells treated with E. histolytica showed potassium efflux - the flow of potassium from inside a cell out through the cell wall - directly before cell death.

"We started to see a pretty clear line of reasoning," says Theodorescu. "The parasite was causing potassium efflux right before cell death and cells that happened to be unable to transport potassium didn't die."

To ensure that lack of potassium transport was, in fact, causing resistance to the parasite, the group reversed the direction of their experiments. Marie started with new cells and used drugs to block their ability to transport potassium. Blocking potassium efflux created cells that were resistant to E. histolytica.

"There is a clear need for new drugs targeting E. histolytica," Petri says. "Right now there is a single antibiotic that works against this parasite. We know that eventually the parasite will develop resistance to the antibiotic and at that point there's no plan B. This could be the plan B - targeting the human genes that enable the parasite to cause disease."

Marie is pushing forward. She recently learned from a mentor at John's Hopkins how to isolate stem cells from human tissue to grow what she calls "mini guts" to

test therapeutics that may be useful in human patients. And technological advances make this study's general technique more efficient, allowing the use of what are called CRISPR libraries instead of RNAi screens.

"This is a major finding with translational implications for this infection that causes so many deaths worldwide, but also proof that this cancer-science approach can be used to explore genetic mechanisms of resistance in the field of infectious disease," Theodorescu says.

The field of infectious disease has been focused on the infection, targeting pathogens and their transmission. This study shows that in addition to characteristics of the parasite, mortality due to disease can be prevented by manipulating characteristics of the host.

http://www.eurekalert.org/pub_releases/2015-09/ind-lso090815.php

Light shed on the underside of the 'cocktail effect' of endocrine disruptors

Chemical substances that are safe for humans when taken in isolation can become harmful when they are combined.

Three research teams bringing together researchers from Inserm and CNRS in Montpellier have elucidated in vitro a molecular mechanism that could contribute to the phenomenon known as the "cocktail effect." This study is published in the journal Nature Communications.

Every day we are exposed to many exogenous compounds such as environmental pollutants, drugs or substances in our diet. Some of these molecules, known as endocrine disruptors, are strongly suspected of interacting inappropriately with regulatory proteins in our cells, and inducing numerous physiological or metabolic disorders (cancers, obesity, diabetes, etc.). Moreover, the combination of these molecules in complex mixtures with which we are in routine contact might exacerbate their toxicity.

In an article to be published in Nature Communications, researchers have unveiled a mechanism that might contribute to this effect of mixing, for which no rational explanation has been offered until now. They show that some oestrogens such as ethinyloestradiol (one of the active ingredients of contraceptive pills) and organochlorine pesticides such as trans-nonachlor, although very weakly active on their own, have the ability to bind simultaneously to a receptor located in the cell nucleus, and to activate it synergistically.

Analyses at molecular level indicate that the two compounds bind cooperatively to the receptor, i.e. binding of the first molecule promotes binding of the second. This cooperativity is due to strong interactions at the level of the receptor binding site, so that the binary mixture induces a toxic effect at substantially lower concentrations than the individual molecules.

These results obtained in vitro constitute a proof of concept that opens the way to a wide field of study. There are actually about 150,000 compounds in our environment that could have unexpected effects on human health through combined action, given their recognised or assumed safety as isolated substances. If these studies are confirmed in vivo, important consequences are expected in the areas of endocrine disruption, toxicology, and the assessment of risks associated with the use of chemicals.

http://www.eurekalert.org/pub_releases/2015-09/uoih-kom090815.php

Keeping older muscles strong

University of Iowa scientists discover cause of and potential treatment for muscle weakness and loss due to aging

As we grow older, we lose strength and muscle mass. However, the cause of age-related muscle weakness and atrophy has remained a mystery.

Scientists at the University of Iowa have discovered the first example of a protein that causes muscle weakness and loss during aging. The protein, ATF4, is a transcription factor that alters gene expression in skeletal muscle, causing reduction of muscle protein synthesis, strength, and mass. The UI study also identifies two natural compounds, one found in apples and one found in green tomatoes, which reduce ATF4 activity in aged skeletal muscle. The findings, which were published online Sept. 3 in the Journal of Biological Chemistry, could lead to new therapies for age-related muscle weakness and atrophy.

"Many of us know from our own experiences that muscle weakness and atrophy are big problems as we become older," says Christopher Adams, MD, PhD, UI professor of internal medicine and senior study author. "These problems have a major impact on our quality of life and health."

Previously, Adams and his team had identified ursolic acid, which is found in apple peel, and tomatidine, which comes from green tomatoes, as small molecules that can prevent acute muscle wasting caused by starvation and inactivity. Those studies set the stage for testing whether ursolic acid and tomatidine might be effective in blocking the largest cause of muscle weakness and atrophy: aging.

In their latest study, Adams' team found that ursolic acid and tomatidine dramatically reduce age-related muscle weakness and atrophy in mice. Elderly mice with age-related muscle weakness and atrophy were fed diets lacking or containing either 0.27 percent ursolic acid, or 0.05 percent tomatidine for two months. The scientists found that both compounds increased muscle mass by 10 percent, and more importantly, increased muscle quality, or strength, by 30

percent. The sizes of these effects suggest that the compounds largely restored muscle mass and strength to young adult levels.

"Based on these results, ursolic acid and tomatidine appear to have a lot of potential as tools for dealing with muscle weakness and atrophy during aging," Adams says. "We also thought we might be able to use ursolic acid and tomatidine as tools to find a root cause of muscle weakness and atrophy during aging."

Adams' team investigated the molecular effects of ursolic acid and tomatidine in aged skeletal muscle. They found that both compounds turn off a group of genes that are turned on by the transcription factor ATF4. This led them to engineer and study a new strain of mice that lack ATF4 in skeletal muscle. Like old muscles that were treated with ursolic acid and tomatidine, old muscles lacking ATF4 were resistant to the effects of aging.

"By reducing ATF4 activity, ursolic acid and tomatidine allow skeletal muscle to recover from effects of aging," says Adams, who also is a member of the Fraternal Order of Eagles Diabetes Research Center at the UI and a staff physician with the Iowa City Veterans Affairs Medical Center.

The UI study was done in collaboration with Emmyon, Inc., a UI-based biotechnology company founded by Adams, that is now working to translate ursolic acid and tomatidine into foods, supplements, and pharmaceuticals that can help preserve or recover strength and muscle mass as people grow older.

In addition to Adams, the UI team included Michael Dyle, Steven Bullard, Jason Dierdorff, Daryl Murry, Daniel Fox, Kale Bongers, Vitor Lira, and David Meyerholz, as well as Scott Ebert and John Talley at Emmyon, Inc.

The study was funded by a Small Business Innovation Research (SBIR) grant to Emmyon, Inc. from the National Institute on Aging, as well as grants from the Department of Veterans Affairs and the Fraternal Order of Eagles Diabetes Research Center at the University of Iowa.

http://www.eurekalert.org/pub_releases/2015-09/smu-ndc090815.php

New drug-like compounds may improve odds of men battling prostate cancer, researchers find

New drug-like compounds have low toxicity to noncancerous cells, but inhibit the human protein often responsible for chemotherapy failure

Researchers at Southern Methodist University, Dallas, have discovered three new drug-like compounds that could ultimately offer better odds of survival to prostate cancer patients.

The drug-like compounds can be modified and developed into medicines that target a protein in the human body that is responsible for chemotherapy resistance in cancers, said biochemist Pia D. Vogel, lead author on the scientific paper reporting the discovery.

So far there's no approved drug on the market that reverses cancer chemotherapy resistance caused by P-glycoprotein, or P-gp for short, said Vogel, a biochemistry professor at SMU.

One potential drug, Tariquidar, is currently in clinical trials, but in the past, other potential drugs have failed at that stage.

"The problem when a person has cancer is that the treatment itself is composed of cellular toxins - the chemotherapeutics that prevent the cells from dividing. Usually upon the first chemo treatment the cancer responds well, and initially goes away.

Ideally it doesn't come back," said Vogel, who is director of SMU's Center for Drug Discovery, Design, and Delivery.

"Sometimes, however, the cancer returns," she said. "The reason often is that some of the cancer cells "learn," after the first rounds of chemotherapy, how to make a lot of this P-gp pump.

The normal function of P-gp is to pump toxins from cells, so it has evolved to protect cells against a large variety of toxins, including almost all currently available chemotherapeutics.

After initial exposure, the cells surviving the chemo make so much P-gp that it allows the cells to pump the chemotherapy drugs straight back out of the cells during subsequent rounds of treatment."

As a result, P-gp causes resistance of the diseased cells to a majority of drugs currently available for the treatment of cancer, as well as drugs used for treatment of infectious diseases like HIV/AIDS.

Using computer-generated model speeds up the drug discovery process

The new drug-like compounds discovered by Vogel and her co-authors offer hope that using a computer-generated P-gp model, explained here http://bit.ly/1LVmR7a, developed to accurately mimic the physical, chemical and biological functions of the protein in the human body, will speed up the drug discovery process and work in real life as well.

"These are not drugs yet. We still have to develop them before they can go in the clinic," Vogel said.

"But what we know now is that they're not toxic - they have low toxicity to noncancerous cells, so that's a pretty good predictor that they may be good candidates for drug development.

But we need to do much more work."

A pharmaceutical hit compound, like those discovered by Vogel and her co-authors, is a compound that is a promising candidate for chemical modification so it can eventually be delivered to patients as a therapeutic drug.

In the case reported here, the compounds were commercially available for testing. The timeline from drug discovery to development to clinical trials and approval can take a decade or more.

Vogel and her co-authors, SMU biologist John G. Wise, and doctoral candidates Courtney A. Follit and Frances K. Brewer, reported their findings in the journal Pharmacology Research & Perspectives.

The article, "In silico identified targeted inhibitors of P-glycoprotein in culture," is published online at http://bit.ly/1JjFizg.

The research was funded in part by the National Institutes of Health. The lab was recently awarded a second grant from the Institute.

Researchers virtually screened 15 million drug-like compounds via SMU supercomputer

The SMU researchers discovered the three hit compounds after virtually screening more than 15 million small drug-like compounds made publically available in digital form from the pharmacology database Zinc at the University of California, San Francisco.

Using SMU's ManeFrame high performance computer, Wise ran the compounds through a computer-generated model of P-gp.

The virtual model, designed and built by Wise, is the first computational microscope of its kind to simulate the actual behavior of P-gp in the human body, including interactions with drug-like compounds while taking on different shapes.

The ultra-high throughput computational searches by ManeFrame led the researchers to 300 compounds that looked like they may inhibit P-gp.

The researchers then tested 38 of those in their physical lab and found four that inhibited the biochemical function of P-gp, stopping it in its action.

Each of the four compounds was then tested in the lab to see how it would affect a line of prostate cancer cells relatively sensitive to the chemotherapeutic Paclitaxel, commonly used to treat prostate cancer patients.

Also, each was tested on a companion cell line already multi-drug resistant, as if the patient already had undergone chemotherapy using Paclitaxel.

The researchers found that with three of the four compounds, they were able to push back the sensitivity of the resistant cancer line to the level of the non-resistant one.

"So the compounds re-sensitized the cancer cell lines to a really high degree, just as if the cancer was seeing the chemotherapy for the first time," Vogel said.

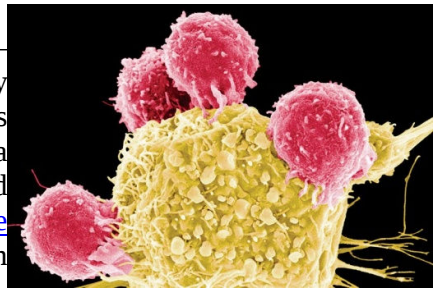
About 14 percent of men will be diagnosed over their lifetime with prostate cancer, according to the National Cancer Institute.

Survival is highest if diagnosed early before it has spread, the institute reports.

http://bit.ly/1UDsyye

Cancer trap grabs wandering tumour cells to warn of early spread

Small implant traps cancer cells as they migrate through blood may become a lifesaving early-detection system



Find wandering cells earlier **Image: Steve Gschmeissner/SPL**

The trouble with cancer is it spreads – sometimes even before someone knows they are ill. A small implant that traps cancer cells as they migrate through the blood could make a lifesaving early-detection system. “This could be the canary in the coal mine,” says Lonnie Shea of the University of Michigan at Ann Arbor, one of the developers.

So far the idea has been tested in mice. If it translates to people, then once it is in place the implant could be scanned for cancer cells while inside the body – either by doctors, or one day perhaps just with a smartphone. “That’s the fantasy,” says Shea.

Shea devised the approach along with Jacqueline Jeruss, a breast cancer surgeon. Jeruss had noticed how common it was for her patients’ first symptom to be breathlessness – as the cancer had already spread to their lungs.

They and their colleagues devised an implant made from an inert porous material already used in medical devices, and loaded it with a signalling molecule called CCL22. This attracts certain immune cells, which encourages cancer cells to follow suit.

They implanted the device under the skin of mice with a version of breast cancer – and found tumour cells in it after two weeks. In experiments on other mice, the team showed that cancer cells could be detected in the implant while it was still in place, via a new scanning system called optical coherence tomography (OCT).

This technique, which can penetrate living tissue by a few millimetres, involves measuring the way light is scattered off large molecules and structures inside cells. Cancer cells can be detected because they are denser internally. Various firms are developing devices that would let OCT be done with a smartphone.

In mice, the implants cut the number of tumour cells that migrated to secondary sites like the lungs.

They probably wouldn’t trap enough cells to work as an anti-cancer therapy, says Shea, but the implant could boost people’s chances of survival by identifying

early on that cancer cells are on the move – allowing the patient to begin chemotherapy right away.

The main challenge, says Shea, will be getting the OCT scanner to penetrate human skin, which is thicker than rodent skin.

Other groups are investigating tumour traps that attract certain types of cancer cells via different, more specific, chemical signals.

The new implant should in theory attract a wide range of cancer cells – although so far the team have only shown it works for one tumour type other than breast cancer, in unpublished work. They envisage first using the trap in women at a high risk of breast cancer, such as those who have already had surgery to remove a tumour and might experience a recurrence.

If a scan reveals that cancer cells are present, the implant could even be removed and the cells analysed to see which cancer drugs they are most susceptible to.

Gerhardt Attard of the Institute of Cancer Research in London says there is growing interest in personalising cancer treatments by testing cancer cells in the blood. "This could be a very powerful way of risk stratifying patients for treatment," he says.

Journal reference: Nature Communications, DOI: 10.1038/ncomms9094

http://bit.ly/1EXDrn3

HIV may kill most cells by a method overlooked for years

T cells can be destroyed by an invading HIV army that is transferred directly into the cell

It's the world's most studied virus, but HIV can still take us by surprise. It turns out that the virus can infect and kill immune cells by being pumped directly from one cell into another, during brief connections made between the two.

Until recently, we thought that HIV particles circulating in the blood were largely to blame for infecting and destroying crucial immune cells called CD4 T cells. According to this classic model, after a single virus has infected a T cell, it hijacks the cell's machinery to build hundreds of copies of itself, which bud off into the blood and eventually wear out and kill the host cell.

This thinking was based on research using blood, a relatively easy way to study the virus. But work with newer tools suggests that this is only part of the story. Using tissue-culture methods, a team led by Warner Greene at the Gladstone Institute of the University of California, San Francisco, has shown that in fact large numbers of virus particles are often pumped directly from one CD4 T cell into another.

And it seems that this process may kill the vast majority of CD4 cells – not infection by single viruses.

Blocking transmission

HIV armies storm neighbouring T cells by hijacking yet another cell system, the immunologic synapses. These are short-term connections between immune cells that allow them to send chemical messages between themselves, which HIV uses to flow from an infected CD4 cell to an uninfected one.

Evidence suggests that this process is hundreds, possibly thousands, of times more efficient than the traditional mode of external infection. Greene says that 95 per cent of the CD4 cells they studied died by this process, rather than from infection by free-floating particles.

This new understanding could open up ways to target the virus, as well as influencing what drugs we choose to treat the disease. Walther Mothes has been studying cell-to-cell HIV transmission at Yale University, and he says that although most antiretroviral drugs work against both forms of infection, the much higher efficiency of pumping viruses directly into a cell can overwhelm some of these drugs, making them less effective.

But the finding may open the way for new treatments. The monkey version of HIV can also be transmitted directly from cell to cell, but monkeys may be able to tolerate this process.

Unlike their human equivalents, monkey CD4 cells manage to survive being inundated with virus particles, and Greene thinks that they have evolved a way to avoid self-destructing. He hopes that anti-inflammatory drugs could be used to mimic this effect in human CD4 cells. One potential drug candidate, VX-765, looks promising in the lab.

Hunt for a vaccine

A better understanding of how the virus spreads directly between cells is probably an important part of the HIV puzzle, says Kenneth Mayer at the Fenway Institute in Boston. He suggests that neglecting to take this mode of transmission into account may at least partly explain the failure of recent vaccine research.

HIV vaccines would work by generating antibodies to fight the virus. But research suggests that different types of antibodies would be needed to kill viruses that are inside cells and viruses that are free-floating in the body.

Viruses hiding out inside cells may be more likely to escape destruction, and could perhaps find it easier to evolve resistance to antibodies.

Carl Dieffenbach of the US National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, says that to better understand how to protect against cell infection, we need better vaccine candidates. "Is cell-to-cell transmission going to torpedo a vaccine? We don't know the answer to this because we don't have a safe, effective and durable HIV vaccine to understand the exact mechanisms," he says. *Journal reference: Cell Reports, DOI: 10.1016/j.celrep.2015.08.011*

http://www.eurekalert.org/pub_releases/2015-09/uobc-mmi090915.php

Metal-eating microbes in African lake could solve mystery of the planet's iron deposits

Microbes metabolize iron and grow at high rates indicating their ancient equivalents deposited some of the world's largest sedimentary iron ore deposits

An isolated, iron-rich bay in the heart of East Africa is offering scientists a rare glimpse back into Earth's primitive marine environment, and supports theories that tiny microbes created some of the world's largest ore deposits billions of years ago.

According to University of British Columbia (UBC) research published this week in Scientific Reports, 30 per cent of the microbes in the Democratic Republic of the Congo's Kabuno Bay grow by a type of photosynthesis that oxidizes (rusts) iron rather than converting water into oxygen like plants and algae.

"Kabuno Bay is a time machine back to the Earth's early history when iron-rich ocean chemistry prevailed," said Marc Llirós of the University of Namur, first author of the paper.

"The bay is giving us real-world insight into how ancient varieties of photosynthesis may have supported Earth's early life prior to the evolution of the oxygen producing photosynthesis that supports life today," said UBC geomicrobiologist Sean Crowe, senior author of the study.

While iron-respiring bacteria were discovered in 1993, the new Scientific Reports study provides evidence that microorganisms could have been directly involved in depositing the Earth's oldest iron formations.

Before 2.3 billion years ago, there was little oxygen in the atmosphere but plenty of dissolved iron and many organisms like bacteria derived energy by metabolizing the metal. Many researchers believe iron-metabolizing microbes might have turned plentiful dissolved iron into minerals, which then settled out of seawater and deposited along the ocean floor.

The UBC study of the Kabuno Bay iron microbes supports that theory. The microbes metabolize iron and grow at rates high enough to indicate their ancient equivalents were capable of depositing some of the world's largest sedimentary iron ore deposits, known as banded iron formations.

By oxidizing iron, these microorganisms likely helped shape the chemistry of the Earth over billions of years, ultimately leading to the evolution of more complex life such as plants and animals.

This study was a collaboration between an international team of researchers from Canada, Belgium, Spain and Denmark that examined the remarkable iron-rich conditions of Kabuno Bay, a part of Lake Kivu in the Democratic Republic of the Congo.

http://www.eurekalert.org/pub_releases/2015-09/oupu-nss090915.php

New study shows smoking doesn't always mean a shortened life span or cancer

Not all smokers experience early mortality and some survive to extreme ages

Smoking has been shown to have drastic consequences for lifespan and disease progression, and it has been suggested that cigarette exposure may impact the risk of death and disease via its acceleration of the aging process.

Not all smokers experience early mortality, however, and a small proportion manage to survive to extreme ages.

Using long-lived smokers as their phenotype, the authors of a study published today in The Journals of Gerontology, Series A: Biological Sciences & Medical Sciences identified a network of SNPs (a DNA sequence variation occurring commonly within a population) that allow certain individuals to better withstand environmental damage (like smoking) and mitigate damage.

Collectively, these SNPs were strongly associated with high survival rates.

Morgan E. Levine, corresponding author of the study, said: "We identified a set of genetic markers that together seem to promote longevity. What's more, many of these markers are in pathways that were discovered to be important for aging and lifespan in animal models.

There is evidence that these genes may facilitate lifespan extension by increasing cellular maintenance and repair.

Therefore, even though some individuals are exposed to high levels of biological stressors, like those found in cigarette smoke, their bodies may be better set up to cope with and repair the damage."

These findings suggest that longevity, rather than being entirely determined by environmental factors, may be under the regulation of complex genetic networks which influence stress resistance and genomic stability.

Therefore, there is reason to believe that long-lived smokers represent a biologically distinct group, endowed with genetic variants allowing them to respond differentially to environmental stressors.

Genomic instability also happens to be one of the hallmarks of cancer pathogenesis, and so the same genes that may promote survival among smokers may also be important for cancer prevention.

This is consistent with the findings of the study, which showed that the genes identified were associated with a nearly 11% lower cancer prevalence.

The full report, "A Genetic Network Associated with Stress Resistance, Longevity, and Cancer in Humans" is available online here:
http://biomedgerontology.oxfordjournals.org/content/early/2015/09/08/gerona.glv141.full

http://www.eurekalert.org/pub_releases/2015-09/acoc-my090315.php

Michigan 'See You in 7' program helps reduce heart failure readmissions

ACC program encourages early follow up after hospital discharge

Michigan hospitals participating in the American College of Cardiology's "See You in 7" program demonstrated important reductions in 30-day readmission rates for Medicare heart failure patients when compared to non-participating hospitals despite only modest increases in seven-day follow-up appointments, according to a study today in JACC: Heart Failure.

"See You in 7" is part of the ACC's Hospital-to-Home initiative, a national quality improvement program aimed at reducing heart disease-related hospital readmissions and improving the transition from hospital to home. "See You in 7" challenges hospitals to ensure all discharged heart failure and heart attack patients have a follow-up appointment scheduled within seven days of hospital discharge.

"Readmissions of heart failure patients remain one of the most important clinical challenges today," said JACC: Heart Failure Editor-in-Chief Christopher O'Connor, M.D., FACC. "Transitional care programs may represent our best opportunity to reduce the burden on patients and health systems."

Researchers looked at the seven-day follow-up and 30-day readmission rates for Medicare heart failure patients at 10 hospitals in the Southeast Michigan "See You in 7" Collaborative and compared them to non-participating hospitals both before joining the "See You in 7" program and after one year of participation.

The one-year program included three phases: implementation, intervention and evaluation periods. During implementation, hospitals selected at least one metric from the "See You in 7" toolkit to focus their efforts and measure progress.

Metrics included:

identify heart failure patients prior to discharge;

schedule and document a follow-up visit with a cardiology or primary care doctor within seven days of discharge;

provide patients with documentation of scheduled follow up;

identify and address barriers to keeping appointment;

ensure patients arrive at scheduled follow up appointment; and

make discharge summary available to follow-up health care providers.

At the end of the program, both participating and non-participating hospitals' seven-day follow-up rates increased but remained low - 31 to 34 percent for participating hospitals and 30 to 32 percent for non-participating hospitals. However, adjusted 30-day readmission rates decreased substantially in participating hospitals compared to non-participating hospitals. Participating hospitals saw readmissions decrease 2.6 percent, while non-participating hospitals saw a 0.6 percent reduction.

"Our study clearly shows there are challenges in coordinating early follow-up care, since increases in seven-day post-discharge follow up were modest. However, despite this, hospitals in the program stepped up to address deficiencies in post-hospital care and reduce 30-day readmissions," said Sandra Marie Oliver-McNeil, DNP, ACNP-BC, a study author and assistant professor of nursing at Wayne State University. "Through collaboratively addressing the 'See You in 7' goals, hospitals participating in this program learned from each other when helping their patients transition from hospital to home, and they should serve as an encouraging example for other regional hospitals to share best practices."

According to the study, participating hospitals designated a staff member to document successful seven-day follow-up visits or investigate why the visits did not take place, leading to more engaged patients and caregivers and giving both sides a better understanding of barriers to care. These efforts may have led to the reduced 30-day readmission rates.

Medicare payments per patient also decreased in participating hospitals. Combined payments for inpatient and 30 days of post-discharge care decreased by $182 in participating hospitals and $63 in non-participating hospitals.

http://www.eurekalert.org/pub_releases/2015-09/spmd-rrs090815.php

Researchers reawaken sleeping HIV in patient cells to eliminate the virus

An emerging class of drugs called Smac mimetics may lead to a safe and effective treatment to eradicate HIV

LA JOLLA, Calif. - A consortium of investigators led by scientists at Sanford Burnham Prebys Medical Discovery Institute (SBP) have found that a new class of drugs may be used to purge pockets of dormant HIV from a patient's body, eliminating the virus once and for all. Since these agents are already being explored in clinical trials for treating cancer, the route to approval for treating HIV may be significantly shorter than usual.

Antiretroviral therapies have made it possible for people to live with HIV for decades. However, patients continue to harbor small and persistent reservoirs of cells that hide the virus. That is, HIV's genes live in the cells, but its genetic code is never read to make protein, and so the virus goes undetected by the immune system.

"If you take people off their antiretroviral therapies, some of these dormant cells reawaken to make more virus and re-establish disease," said lead author Lars Pache, Ph.D., a postdoctoral fellow in the lab of Sumit Chanda, Ph.D., director of

the Immunity and Pathogenesis Program at SBP. "The key for a cure for HIV is to purge these cells that have dormant HIV."

Reactivating latent HIV-infected cells so that they can be killed off is called a shock-and-kill approach. The approach has remained elusive so far, because candidate drugs that reawaken the virus, known as latency reversing agents (LRAs), appear to lack sufficient potency, or alternatively, could trigger massive immune system activation, which itself could be deadly.

The new study, published September 9 in the journal Cell Host & Microbe, "uses a class of drug called Smac mimetics to tap into a molecular backdoor, a cell pathway that can be used as an intense alarm to wake up the virus, but doesn't appear to activate the immune system," Chanda said.

The study started with a broad search of genes within the host cells that help suppress the virus. They found that the absence of one gene in particular, BIRC2, boosted the activity of HIV, and Smac mimetics - already proven safe in early-stage clinical trials for cancer - work by inhibiting BIRC2 and related molecules.

"These experiments led us to develop a strategy of using Smac mimetics to reawaken dormant HIV so that it can be detected by the immune system and purged," explained Chanda.

Chanda's colleague at SBP, Nicholas Cosford, Ph.D., professor in the Cell Death and Survival Networks Program, had recently identified a potent BIRC2 inhibitor, SBI-0637142. "Although there are clinical- stage Smac mimetics available, they were not specifically developed for HIV-1 treatment. Our internal drug possesses about 10-100 times more potent LRA activity than the small molecules currently in clinical development, making it a promising next-generation candidate to tackle HIV latency," says Chanda.

Part of the reason that HIV's genes stay hidden in its host is that they cover themselves with tightly wound DNA. A class of drugs called histone deacetylase inhibitors, which unfurls the DNA, is used to treat a variety of conditions. Although most of these inhibitors haven't thus far worked well on their own to reactivate latent HIV, they might work well with Smac mimetics including SBI-0637142, Chanda's group reasoned.

The key question was whether they could reactivate the virus in cells from HIV-infected patients undergoing antiretroviral therapy. They combined SBI-0637142 with a histone deacetylase inhibitor (panobinostat) and saw signs that the virus had reawakened without triggering immune activation.

"We anticipated that we would see a synergy because the drugs work along parallel pathways. What we didn't expect was the level of activation and the efficacy with which we were able to reverse latency in patient samples," Chanda said.

They saw similar results in patient cells treated with a combination of LCL161 - a Smac mimetic that is already in phase 1 and 2 trials for treating cancer - and panobinostat. "This is a one-two punch for HIV," said Chanda, adding that ultimately, a cocktail of drugs will likely be necessary to cure HIV.

The scientists hope to partner with a pharmaceutical company to develop these molecules for evaluation in clinical models of HIV latency and then move them into human testing if they meet the safety and efficacy criteria.

In addition to SBP, the study consortium included the University of Utah School of Medicine, The Salk Institute for Biological Studies, the Perelman School of Medicine at the University of Pennsylvania, the Icahn School of Medicine at Mount Sinai, the Paul-Ehrlich-Insitut, and the German Center for Infection Research.

This study was supported by NIH grants P01AI090935 to the HIV Immune Networks Team (HINT.org); R01 DA033773, R01 AI087508 and the James B. Pendleton Charitable Trust

http://www.eurekalert.org/pub_releases/2015-09/uom-fii090915.php

Finding iconicity in spoken languages

Researchers show that iconicity is spread across the vocabulary of spoken languages, suggest that iconicity plays key role in word learning

CORAL GABLES, Fla. - Have you ever wondered why we call a dog a dog and not a cat? Is this an arbitrary decision, or is it based on iconicity - the resemblance between word structure and meaning? New research shows that for Indo-European languages, like English and Spanish, iconicity is more common than previously believed.

The results are important for understanding the nature of human language, explains Lynn Perry, assistant professor of psychology in the University of Miami College of Arts & Sciences and co-lead author of the study.

"Many linguists are trained to believe that languages are arbitrary." Perry said. "But sometimes what we as scientists accept as fact leads us to miss out the rich details of experiences," she said. "We treat learning as this impossibly difficult process because we assume languages are completely arbitrary, but it turns out there's a lot of structure and information in the language itself that could be making learning easier."

The study is the first to show that iconicity is prevalent across the vocabulary of a spoken language, explained Marcus Perlman, postdoctoral research associate in the University of Wisconsin-Madison Department of Psychology and co-lead author of the study. "It is the nail in the coffin for the theory that languages are essentially arbitrary," Perlman said.

Most people are familiar with onomatopoeia, words that imitate a sound; for example, boing - the sound of a bounce, and zip - the sound of moving at high speed. However, words can be imitative or iconic of many different kinds of

meanings, not just sounds. For instance, the vowels in the word "tiny" sound small compared to the vowel in "huge," which sounds big.

"Scientists have known for a while that people are sensitive to iconicity," Perry said. "If you show people a novel pointy object and a novel round object, and ask them 'which of these is a 'kiki' and which is a 'bouba," they are more likely to say that a pointy object is called 'kiki' and the round one is called 'bouba,' because they sound more pointy and round, respectively."

Yet, many researchers believe that unlike signed languages, most spoken languages, especially English, are essentially arbitrary. But no one had actually tested this. The current study set out to test this assumption in a rigorous, comprehensive way. The findings show that in spoken languages, iconicity is not just present in some words and not in others. Instead, it appears in different levels throughout the vocabulary.

The findings also show that words learned in childhood are the most iconic, suggesting that iconicity plays an important role in helping children to grasp the concept of a word.

"Young children face the very considerable challenge of figuring out that all these vocalizations that the people around them are making mean something, and further, that they mean very particular things," Perlman said. "When words are iconic, the sound of the word instinctively primes its meaning, and this helps children to understand that the sound is a word with a particular meaning, and that words in general have meanings."

The study provides new information for professionals in the field of language pathology. "Once we better understand why there's a relationship between a word's iconicity and the age at which it's acquired, our results could also have implications for interventions for children with language delays," Perry said.

For the study, the researchers developed three experiments in English and two in Spanish, where native speakers were asked to rate the iconicity of about 600 words in their respective language. The findings show that iconicity in English and Spanish varied with grammatical category. For instance, adjectives were rated as more iconic than nouns and functional words, in both languages.

Interestingly, English verbs were relatively iconic compared to Spanish verbs. The researchers attribute the disparity to semantic differences between the two languages. Many English verbs contain manner information, which predisposes them to be more iconic than Spanish verbs, which do not. For example, in English you'd say "The bottle floated into the cave," and the verb floated describes how something moved, but in Spanish you'd say "La botella entró a la cueva flotando" (or "The bottle entered [into] the cave floating") and the verb "entró" doesn't describe how.

The study is titled "Iconicity in English and Spanish and its relation to lexical category and age of acquisition," published online by the journal PLOS ONE. Gary Lupyan, assistant professor of psychology at the University of Wisconsin-Madison, is also a co-author of the study.

"There are roughly 7,000 languages spoken and signed around the world, and these languages have been evolving for at least tens of thousands of years, if not many more - and we are just taking a little snap shot of two of them," Perlman said. "But this snap shot suggests that even modern spoken languages are iconic in important ways."

The findings have opened up new areas of inquiry. In the future, the researchers would like to understand why some words sound more like what they mean than others and how the iconicity of words evolves and changes over time, among other subjects.

http://www.eurekalert.org/pub_releases/2015-09/slu-rst090915.php

Routinely screen those older than 70 for brain health, world expert panel advises

Saint Louis University geriatrician and lead author says clinicians seek guidance in caring for older adults

ST. LOUIS - A panel of world experts in aging convened at Saint Louis University recommended that everyone 70 and older should have their memory and reasoning ability evaluated annually by a doctor or health care provider.

This is the first time routine brain health screenings have been recommended for patients, starting at age 70. Patients found to have cognitive problems also should be screened for physical frailty, and vice versa, suggested the panel.

Published in the September issue of JAMDA, the recommendation for brain health comes in light of numerous studies, including those in The Lancet and New England Journal of Medicine, that suggest 30 percent of those older than 70 have memory problems. Approximately 16 percent of this group has mild cognitive impairment, while 14 percent has dementia, which includes Alzheimer's disease.

"This is an important step in toward enhancing brain health for aging populations throughout the world," said John Morley, M.D., director of geriatric medicine at Saint Louis University and lead author of the consensus paper. "The ability to learn, solve problems and remember is a key to successful health and aging."

Some causes of early cognitive disorder, can be reversed and treated when caught early. These include depression, hypothyroidism, sleep apnea, problems with sight and hearing, and treatments of multiple health conditions with medications. "You can actually fix some of these issues, which is one reason why it's critical to

identify a problem and try to find a root cause," said Morley, who also is a SLUCare Physician Group geriatrician.

The progression of cognitive impairment sometimes can be slowed through a series of lifestyle changes, the panel said.

They endorsed changes suggested in FINGER, a Finnish geriatric study published in The Lancet, which found those who ate a healthy diet, exercised, trained their memories and managed cardio-vascular risks were less likely to develop cognitive decline and memory problems than older adults who did not.

"There are things you can do to slow down the progression of not thinking well," Morley said.

The panel endorsed a Mediterranean-type diet - packed with fruits and vegetables, fish twice a week, olive oil, nuts, legumes and whole grains - for patients who have early cognitive problems. Further, because population-based studies show brain health as well as physical well-being is connected to exercise, they encouraged physical exercise that can include resistance training and Tai Chi. The panelists also noted that population-based studies show those who dance, engage in intellectual activity and play a musical instrument have less mental decline than those who not pursue these hobbies. And video games can improve reasoning, memory, reaction time and attention in older adults.

Physicians need to know if their patients are not remembering or thinking clearly because they might not be able to follow doctors' orders for medical problems, such as diabetes or heart disease.

"If you have diabetes and are not thinking as well as the general population, you might forget how to do the required daily finger prick to determine your blood sugar levels, which would compromise your health," Morley said.

"However, if your doctor knows you have difficulty remembering, someone in his or her office can make sure you understand exactly how to check your glucose levels and give you written instructions as a ready reference. It's a simple common sense thing that can make a huge difference in your health."

Finally, for those patients whose reasoning and memory problems likely will worsen, knowing in advance can help them plan for the future. They can begin considering tough questions, such as when to stop driving or remove dangerous tools from their homes, and set up advanced directives for health, financial and legal matters. They can identify sources of support like family members or friends and organizations such as the Alzheimer's Association.

Information is power, Morley said.

"Our recommendations are going to shape clinical practice in a big way," Morley said. "Physicians are hungry for this information to help their patients, and as the message gets out, patients will request screenings."

Members of the consensus panel were geriatricians, neurologists, psychiatrists, social workers and psychologists who specialized in caring for older adults. They represented institutions around the world including Saint Louis University; Washington University in St. Louis; University Hospital of Toulouse in France; Alzheimer's Association; Mayo Clinic; University of California Los Angeles; Alzheimer Center in Amsterdam; Albert Einstein College of Medicine in New York; Oxford Institute of Population Ageing in the United Kingdom; Center for Alzheimer Research in Sweden; Chinese University of Hong Kong; University of Washington in Seattle; Indiana University; University of Pittsburgh; and Salpetriere Hospital in Paris.

http://www.bbc.com/news/health-34184470

'Transmittable Alzheimer's' concept raised

People may be able to contract Alzheimer's during certain medical procedures in the same way as the brain disease CJD, say researchers.

By Michelle Roberts Health editor, BBC News online

Contaminated surgical instruments or injections, such as human growth hormone, may pose a rare but potential risk, they speculate in Nature.

The theoretical hunch comes from post-mortem brain studies in eight patients.

The UK experts stress that their findings are inconclusive and do not mean Alzheimer's is infectious. People cannot catch Alzheimer's from coming into contact with other people with the condition.

Brain changes

Alzheimer's is a type of dementia that is more common with increasing age. People with a family history of the condition are also at increased risk of developing it. In Alzheimer's, brain cells die off and, over time, the brain shrinks, affecting many of its functions.

There are two telltale signs - abnormal clusters of protein fragments, called amyloid plaques, and tangles of another protein known as tau.

It was when Dr John Collinge and colleagues from University College London were studying the brains of recently deceased CJD (Creutzfeldt-Jakob disease) patients that they stumbled across one of these Alzheimer-like signs.

Seven of the eight patients they studied had amyloid deposits in the brain, which was surprising given their relatively young ages (between 31 and 51) and the fact that they had no family history of Alzheimer's.

All of the deceased had caught their CJD from contaminated human growth hormone injections, given to them as children.

Animal studies

This treatment was withdrawn in the UK in 1985 once the risk of CJD infection became clear. Extra checks and measures, such as using disposable surgical instruments, are now carried out in NHS hospitals to minimise the risk.

Dr Collinge believes amyloid could be spread accidentally during medical and surgical procedures in the same way as CJD, via contaminating protein "seeds" or prions that grow in the brain. Animal studies support this idea, but caution is needed. None of the eight autopsy patients had full-blown Alzheimer's disease and it is not clear if they would ever have developed dementia.

There is no proof that the growth hormone injections were the cause of the amyloid.

Analysis

Perhaps research papers like this one should come with their own health warning: "may cause unnecessary alarm". That's not to discredit their scientific worth, the findings are interesting and important for furthering understanding. But they must be interpreted with caution.

There are too many 'ifs' to draw any firm conclusions. The observations are from a small number of deceased patients who had a treatment that hasn't been used for years.

Although it's still not clear exactly why some people develop Alzheimer's while others do not, experts agree that you can't "catch it" like a cold.

Dr Collinge says more research is needed. He has already contacted the Department of Health to see if it has any old stocks of human growth hormone that he can check for the presence of amyloid "seeds". He said: "I do not think there is any cause for alarm. No-one should delay or not go for surgery because of this."

The chief medical officer for England, Prof Dame Sally Davies, added: "I can reassure people that the NHS has extremely stringent procedures in place to minimise infection risk from surgical equipment, and patients are very well protected."

Dr Eric Karran, director of research at Alzheimer's Research UK, said: "While the findings sound concerning, it's important to remember that human-derived hormone injections are no longer used and were replaced with synthetic forms since the link to CJD was discovered in the 1980s."

Jump media player

"Current measures in place to limit contamination with the prion protein and minimise CJD risk from hospital procedures are very rigorous and the risk of developing CJD from surgical contamination is extremely low.

"The biggest risk factor for Alzheimer's is age, along with genetic and lifestyle factors. If further research was to confirm a link between historical tissue contamination and Alzheimer's, it would only likely be relevant to a tiny proportion of the total number of people affected."

http://www.bbc.com/news/science-environment-34203797

Ceres' bright spots in sharp detail

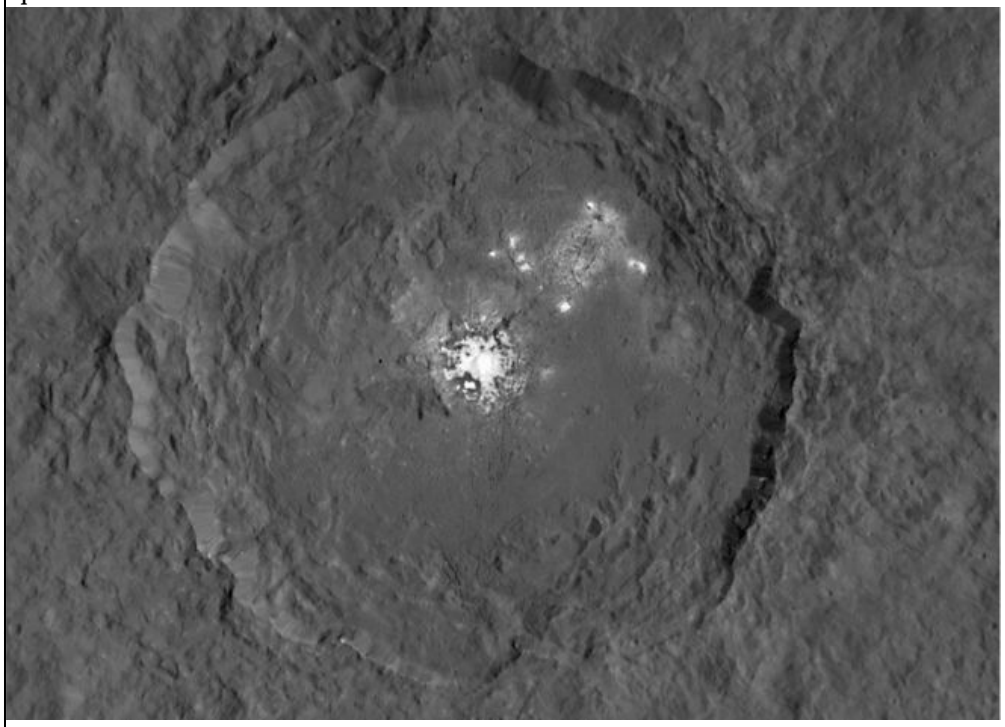
The US space agency's Dawn satellite has returned its best view yet of the enigmatic bright spots on the dwarf planet Ceres.

By Jonathan Amos BBC Science Correspondent

The features sit inside a crater called Occator, and the new image reveals their structure in very fine detail.

To produce the picture, scientists have had to combine two separate exposures: one for the bright spots and one for the darker, surrounding terrain. From an orbital altitude of 1,470km, Dawn sees 140m in every pixel.

But the mission team is still not ready to come forward with an explanation for the spots, with ideas variously floated that they might incorporate significant quantities of ice or salt.



"Dawn has transformed what was so recently a few bright dots into a complex and beautiful, gleaming landscape," Marc Rayman, Dawn's chief engineer and mission director, said in a Nasa release.

Occator is about 90km across: This is a composite of exposures to handle the differences in surface brightness **NASA/JPL-Caltech/UCLA/MPS/DLR/IDA**

"Soon, the scientific analysis will reveal the geological and chemical nature of this mysterious and mesmerising extraterrestrial scenery."

Dawn arrived at Ceres in March this year, and has steadily lowered its orbit since. The pictures it is returning now are nearly 10 times better than the initial observations. With a diameter of 950km, Ceres is the largest object in the asteroid belt between Mars and Jupiter.

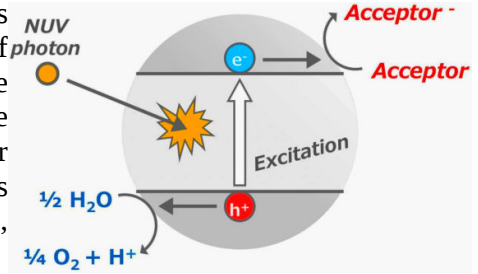
http://www.eurekalert.org/pub_releases/2015-09/nion-oin090915.php

Oxygen is not definitive evidence of life on habitable extrasolar planets

It could be possible for planets to have large quantities of abiotic (non-biologically produced) oxygen

This news release is available in Japanese.

The Earth's atmosphere contains oxygen because plants continuously produce it through photosynthesis. This abundant supply of oxygen allows life forms like animals to flourish. Therefore, oxygen had been thought to be an essential biomarker for life on extrasolar planets. But now, a research assistant professor Norio Narita of the Astrobiology Center of National Institutes of Natural Sciences (NINS), which was founded in April 2015, and an associate professor Shigeyuki Masaoka, of the Institute of Molecular Science of NINS, have presented a novel hypothesis that it could be possible for planets to have large quantities of abiotic (non-biologically produced) oxygen. This study is a good example of interdisciplinary studies that combine knowledge from different fields of science to promote astrobiology in the search for life on extrasolar planets. The study is published in *Scientific Reports* on Sep 10, 2015.



Abiotic oxygen can be produced from water in the presence of titanium oxide and an electron acceptor under UV light. Our report suggests that this photocatalytic reaction can supply significant amount of abiotic oxygen on habitable extrasolar planets.

National Institutes of Natural Sciences (NINS)

Until now, it had been thought that if a planet has oxygen, that must mean that some form of plants are producing it through photosynthesis. Therefore, it had been assumed that when searching for signs of life on habitable extrasolar planets, the presence of oxygen in the atmosphere could be considered a definitive biomarker. However, non-biological chemical reactions can also affect atmospheric compositions of extrasolar planets. Now, the research team led by Dr. Narita has shown that, abiotic oxygen produced by the photocatalytic reaction of titanium oxide, which is known to be abundant on the surfaces of terrestrial planets, meteorolites, and the Moon in the Solar System, cannot be discounted.

For a planet with an environment similar to the Sun-Earth system, continuous photocatalytic reaction of titanium oxide on about 0.05 % of the planetary surface could produce the amount of oxygen found in the current Earth's atmosphere. In addition, the team estimated the amount of possible oxygen production for habitable planets around other types of host stars with various masses and temperatures. They found that even in the least efficient production case of a low-temperature star, the photocatalytic reaction of the titanium oxide on about 3% of the planetary surface could maintain this level of atmospheric oxygen through abiotic processes. In other words, it is possible that a habitable extrasolar planet could maintain an atmosphere with Earth-like oxygen, even without organisms to perform photosynthesis.

Dr. Narita said, "To search for life on extrasolar planets through astronomical observation, we need to combine the knowledge from various scientific fields and to promote astrobiology researches to establish the decisive signs of life. Although oxygen is still one of possible biomarkers, it becomes necessary to look for new biomarkers besides oxygen from the present result."

Title: Titania may produce abiotic oxygen atmospheres on habitable exoplanets
Authors: Norio Narita1,2,3, Takafumi Enomoto3,4, Shigeyuki Masaoka3,4, Nobuhiko Kusakabe2
Affiliation: 1. Astrobiology Center, 2: National Astronomical Observatory of Japan, 3: SOKENDAI (The Graduate University for Advanced Studies), 4:Institute for Molecular Science Scientific Reports, *2015 Sep 10*

http://nyti.ms/1KKcyWq

A Squeeze Down a Narrow Crack, and Then an Amazing Discovery

Jagged rocks hooked into Steven Tucker's overalls as he squeezed through a crack deep in a subterranean cave.

By THE ASSOCIATED PRESS SEPT. 10, 2015, 11:55 A.M. E.D.T.

MAGALIESBURG, South Africa - Upon emerging at the other end, he saw he was in a chamber dripping with stalactites. Then his headlamp shone onto a bone. Then more bones, and half of a skull.

It was the night of Sept. 13, 2013, and Tucker and his caving partner had just discovered the remains of what scientists would later determine to be a new member of the human family tree. The announcement of the discovery was made by scientists on Thursday, with Tucker looking on.

Tucker was only trying to get out of fellow caver Rick Hunter's way, inching to the side, on a different intended route when he stepped into the crack in the

network of caves known as Rising Star. He'd heard of the crack before, but despite having been down this cave more than 20 times before, he had never noticed it, nor known of any other caver who had ventured down it.

He shone his headlamp down the dark crevice, and couldn't see where it ended. He knew of at least one other caver who also stared down the crack, and decided it was too dangerous. He began to lower himself, feet-first, into the narrow vertical opening.

"It's exciting to find something new," Tucker, now 27, told The Associated Press on Thursday, trying to explain why he took the risk.

Tucker, just wiry enough to fit, followed the crack deeper into the earth for nearly 13 yards (12 meters).

"It's 18 centimeters (7.1 inches) wide, with these jagged rocks, sticking into you from all sides. And suddenly at the bottom, it opens up into a large chamber with really stunning stalactites hanging from the ceiling," Tucker said, hunching his shoulders and jutting his elbows out as he re-enacted the descent.

The 50,000-hectare (123,550-acre) area of hilly grasslands where the two were spelunking is recognized as the Cradle of Humankind, featuring a network of caves that has yielded nearly 40 percent of known hominid fossils, according to the University of the Witwatersrand in Johannesburg. But the bones in this particular chamber had apparently remained undiscovered until Tucker entered it.

Inside what is now known as the Dinaledi chamber, Tucker's headlamp illuminated pure white rock formations. Tucker and Hunter, who also braved the narrow chute, were excited to find new caving terrain. Then they saw the bones scattered on the chamber floor.

"You could see half of a skull sticking out of the floor," Tucker said. "Of course, at that time we had no idea what we had found. ... What interested us at first was the fact that these were quite large bones. How does something that has no lights, no protective equipment like we had get in here?"

An almost complete mandible told the cavers that they had found something almost human. Their camera battery had died so a week later they made their way through the cave again, and photographed their find. They sent the photos to geologist Pedro Boshoff, who alerted paleontologist Lee Berger, who went onto become the lead paleontologist on the discovery of Homo naledi. It was only when the cavers saw Berger's excitement that they realized just how big their discovery was.

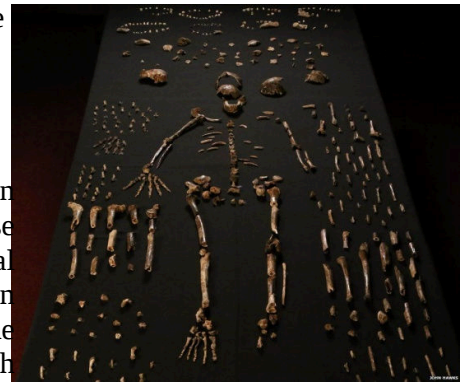
At the press conference announcing the discovery of Homo naledi, a potential new member of the human family tree, Tucker was joined by other cavers who volunteered on the excavation for nearly two years. Berger called them "underground astronauts."

http://www.bbc.com/news/science-environment-34192447

New human-like species discovered in S Africa

Scientists have discovered a new human-like species in a burial chamber deep in a cave system in South Africa.

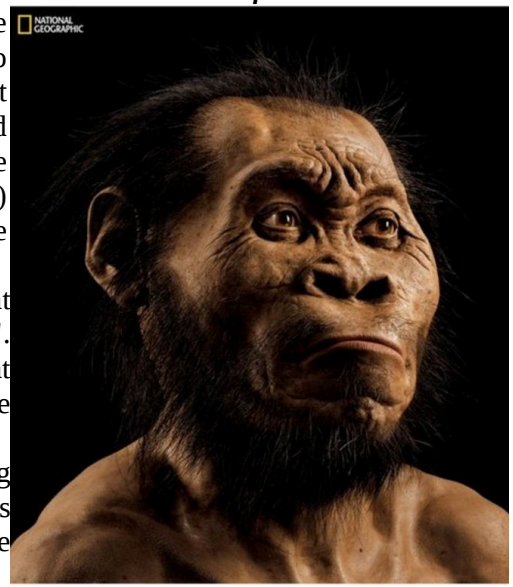
By Pallab Ghosh Science correspondent, BBC News, Johannesburg



The discovery of 15 partial skeletons is the largest single discovery of its type in Africa. The researchers claim that the discovery will change ideas about our human ancestors.

The studies which have been published in the journal Elife also indicate that these individuals were capable of ritual behaviour. The species, which has been named *naledi*, has been classified in the grouping, or genus, *Homo*, to which modern humans belong.

Homo naledi has a mixture of primitive and more modern features **John Hawks**



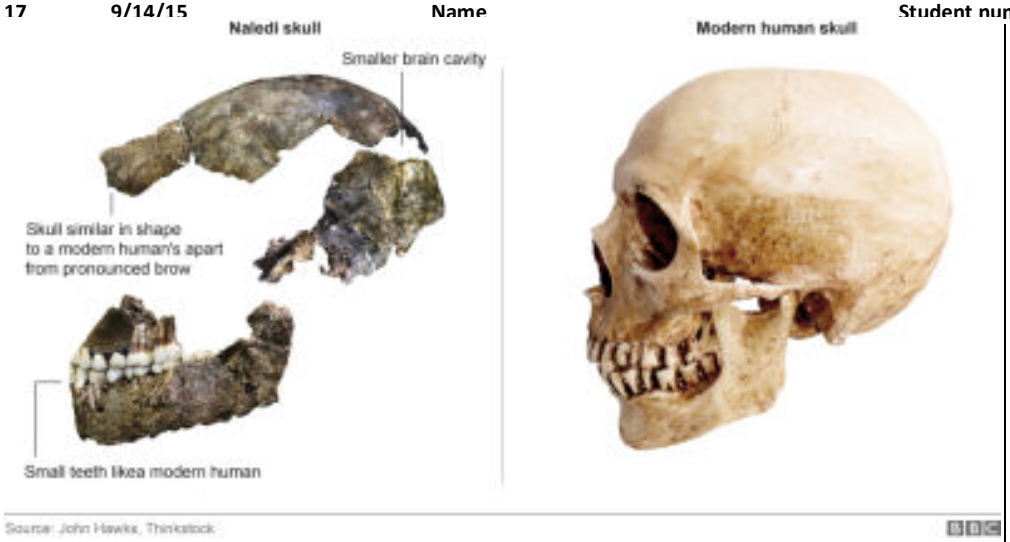
The researchers who made the find have not been able to find out how long ago these creatures lived - but the scientist who led the team, Prof Lee Berger, told BBC News that he believed they could be among the first of our kind (*genus Homo*) and could have lived in Africa up to three million years ago.

Like all those working in the field, he is at pains to avoid the term "missing link". Prof Berger says *naledi* could be thought of as a "bridge" between more primitive bipedal primates and humans.

"We'd gone in with the idea of recovering one fossil. That turned into multiple fossils That turned into the discovery of multiple skeletons and multiple individuals.

Homo naledi may have looked something like this **National Geographic**

"And so by the end of that remarkable 21-day experience, we had discovered the largest assemblage of fossil human relatives ever discovered in the history of the continent of Africa. That was an extraordinary experience."



Prof Chris Stringer of the Natural History Museum said *naledi* was "a very important discovery". "What we are seeing is more and more species of creatures that suggests that nature was experimenting with how to evolve humans, thus giving rise to several different types of human-like creatures originating in parallel in different parts of Africa. Only one line eventually survived to give rise to us," he told BBC News.

I went to see the bones which are kept in a secure room at Witwatersrand University. The door to the room looks like one that would seal a bank vault. As Prof Berger turned the large lever on the door, he told me that our knowledge of very early humans is based on partial skeletons and the occasional skull.

The haul of 15 partial skeletons includes both males and females of varying ages - from infants to elderly. The discovery is unprecedented in Africa and will shed more light on how the first humans evolved.

"We are going to know everything about this species," Prof Berger told me as we walked over to the remains of *H. naledi*.

"We are going to know when its children were weaned, when they were born, how they developed, the speed at which they developed, the difference between males and females at every developmental stage from infancy, to childhood to teens to how they aged and how they died."

A chronology of human evolution

Ardipithecus ramidus (4.4 million years ago) : ***Fossils were discovered in Ethiopia in the 1990s. Pelvis shows adaptations to both tree climbing and upright walking.***

Australopithecus afarensis (3.9 - 2.9 million years ago) : ***The famous "Lucy" skeleton belongs to this species of human relative. So far, fossils of this species have only been found in East Africa. Several traits in the skeleton suggest afarensis walked upright, but they may have spent some time in the trees.***

Homo habilis (2.8 - 1.5 million years ago) : ***This human relative had a slightly larger braincase and smaller teeth than the australopithecines or older species, but retains many more primitive features such as long arms.***

Homo naledi (Of unknown age, but researchers say it could be as old as three million years) : ***The new discovery has small, modern-looking teeth, human-like feet but more primitive fingers and a small braincase.***

Homo erectus (1.9 million years - unknown) : ***Homo erectus had a modern body plan that was almost indistinguishable from ours. But it had a smaller brain than a modern person's combined with a more primitive face.***

Homo neanderthalensis (200,000 years - 40,000 years) ***The Neanderthals were a side-group to modern humans, inhabiting western Eurasia before our species left Africa. They were shorter and more muscular than modern people but had slightly larger brains.***

Homo sapiens (200,000 years - present) ***Modern humans evolved in Africa from a predecessor species known as Homo heidelbergensis. A small group of Homo sapiens left Africa 60,000 years ago and settled the rest of the world, replacing the other human species they encountered (with a small amount of interbreeding).***

I was astonished to see how well preserved the bones were. The skull, teeth and feet looked as if they belonged to a human child - even though the skeleton was that of an elderly female. Its hand looked human-like too, up to its fingers which curl around a bit like those of an ape.

Homo naledi is unlike any primitive human found in Africa. It has a tiny brain - about the size of a gorilla's and a primitive pelvis and shoulders. But it is put into the same genus as humans because of the more progressive shape of its skull, relatively small teeth, characteristic long legs and modern-looking feet.

"I saw something I thought I would never see in my career," Prof Berger told me. "It was a moment that 25 years as a paleoanthropologist had not prepared me for."

One of the most intriguing questions raised by the find is how the remains got there.

I visited the site of the find, the Rising Star cave, an hour's drive from the university in an area known as the Cradle of Humankind. The cave leads to a narrow underground tunnel through which some of Prof Berger's team crawled in an expedition funded by the National Geographic Society.

Small women were chosen because the tunnel was so narrow. They crawled through darkness lit only by their head torches on a precarious 20 minute-long journey to find a chamber containing hundreds of bones.

Among them was Marina Elliott. She showed me the narrow entrance to the cave and then described how she felt when she first saw the chamber.

"The first time I went to the excavation site I likened it to the feeling that Howard Carter must have had when he opened Tutankhamen's tomb - that you are in a very confined space and then it opens up and all of a sudden all you can see are all these wonderful things - it was incredible," she said.

Ms Elliott and her colleagues believe that they have found a burial chamber. The *Homo naledi* people appear to have carried individuals deep into the cave system and deposited them in the chamber - possibly over generations.

If that is correct, it suggests *naledi* was capable of ritual behaviour and possibly symbolic thought - something that until now had only been associated with much later humans within the last 200,000 years.

Prof Berger said: "We are going to have to contemplate some very deep things about what it is to be human. Have we been wrong all along about this kind of behaviour that we thought was unique to modern humans?

"Did we inherit that behaviour from deep time and is it something that (the earliest humans) have always been able to do?"

Prof Berger believes that the discovery of a creature that has such a mix of modern and primitive features should make scientists rethink the definition of what it is to be human - so much so that he himself is reluctant to describe *naledi* as human.

Other researchers working in the field, such as Prof Stringer, believe that *naledi* should be described as a primitive human. But he agrees that current theories need to be re-evaluated and that we have only just scratched the surface of the rich and complex story of human evolution.

http://www.eurekalert.org/pub_releases/2015-09/uow-fta091015.php

Fossil trove adds a new limb to human family tree

The largest, most complete set of hominin remains found to date in Africa

MADISON, Wis. - Working in a cave complex deep beneath South Africa's Malmani dolomites, an international team of scientists has brought to light an unprecedented trove of hominin fossils - more than 1,500 well-preserved bones and teeth - representing the largest, most complete set of such remains found to date in Africa.

The discovery of the fossils, cached in a barely accessible chamber in a subterranean labyrinth not far from Johannesburg, adds a new branch to the human family tree, a creature dubbed Homo naledi. The remains, scientists believe, could only have been deliberately placed in the cave.

So far, parts of at least 15 skeletons representing individuals of all ages have been found and the researchers believe many more fossils remain in the chamber. It is part of a complex of limestone caves near what is called "The Cradle of Humankind," a World Heritage Site in Gauteng province well known for critical paleoanthropological discoveries of early humans, including the 1947 discovery of 2.3 million-year-old Australopithecus africanus.

"We have a new species of Homo, with all of its interesting characteristics," says John Hawks, a University of Wisconsin-Madison paleoanthropologist and one of the leaders of a team that painstakingly retrieved the fossils under excruciatingly cramped and difficult conditions. "We now have the biggest discovery in Africa for hominins."

The find was reported today (Sept. 10, 2015) with the publication of two papers in the open access journal eLife by a group led by paleoanthropologist Lee R. Berger of the University of Witwatersrand. The expedition to retrieve the fossils and their subsequent analysis was supported by the National Geographic Society.

With a small head and brain, hunched shoulders, powerful hands and thin limbs, Homo naledi was built for long-distance walking, says Hawks, an expert on early humans. Fully grown, it stood about five feet tall, was broad chested, walked upright and had a face, including a smile that was probably more human than apelike. Powerful hands imply it was also a climber.

The fossils have yet to be dated. The unmineralized condition of the bones and the geology of the cave have prevented an accurate dating, says Hawks. "They could have been there 2 million years ago or 100,000 years ago, possibly coexisting with modern humans. We don't yet have a date, but we're attempting it in every way we can."

So far, the remains of newborns to the aged have been retrieved from the cave and the researchers expect that many more bones remain in the chamber, which is nearly 100 feet underground and accessible only after squeezing, clambering and crawling 600 feet to a large chamber where the brittle fossils cover the floor.

"We know about every part of the anatomy, and they are not at all like humans," notes Hawks, who co-directed the analysis of the fossils. "We couldn't match them to anything that exists. It is clearly a new species."

The astonishing find was made initially by amateur cavers and thought at the time to be a single hominin skeleton. The fossils were retrieved by a band of diminutive paleoanthropologists, all women, recruited for their size.

"Naledi" means star in the Sesotho language and is a reference to the Rising Star cave system that includes the chamber, known as the Dinaledi Chamber, where the fossils were found. The circuitous and difficult passage to the chamber narrows at one point to a bare seven inches.

In addition to identifying an entirely new species in the genus Homo, the collections of fossils, which bear no marks from predators or scavengers, are strong evidence that Homo naledi was deliberately depositing its dead in the cave, according to Hawks, a UW-Madison professor of anthropology.

"We think it is the first instance of deliberate and ritualized secreting of the dead," says Hawks. "The only plausible scenario is they deliberately put bodies in this place."

The cave, according to Hawks, was likely more accessible to Homo naledi than it is today for modern humans. Geochemical tests, however, show that the cave was never open to the surface, raising intriguing questions about the behavior and technologies available to the creatures.

"We know it was not a death trap," says Hawks, referring to natural features like hidden sinkholes that sometimes trap and doom creatures over long periods of time. "There are no bones from other animals aside from a few rodents. And there are no marks on the bones from predators or scavengers to suggest they were killed and dragged to the chamber. We can also rule out that it was a sudden mass death."

Instead, Hawks, Berger and their colleagues believe the chamber was something like a repository. "It seems probable that a group of hominins was returning to this place over a period of time and depositing bodies," Hawks explains, adding that the supposition is akin to discovering similar behavior in chimpanzees. "It would be that surprising."

The way the bodies are arranged and their completeness suggests they were carried to the cave intact. "The bodies were not intentionally covered and we're not talking about a religious ceremony, but something that was repeated and repeated in the same place. They clearly learned to do this and did it as a group over time. That's cultural. Only humans and close relatives like Neandertals do anything like this." So far, no other organic materials or evidence of fire have been found in the cave complex.

Dating the fossils remains a key problem to solve, says Hawks. "We depend on the geology to help us date things, and here the geology isn't much like other caves in South Africa. And the fossils don't have anything within them that we can date. It's a problem for us."

One hope, he says, is finding the remains of an animal that may have been a contemporary of Homo naledi. The fossils are embedded in a matrix of soft sediment and there are layers that remain unexcavated.

According to Hawks, years of work remain at the site and to document and analyze all of the materials excavated from the Dinaledi Chamber. Plans, he says, include bringing many new technologies to bear on analyzing the fossils to help determine diet, rate of aging and where on the landscape the creatures may have been from.

The project to excavate the fossils and the May 2014 scientific workshop to analyze them were supported by the National Geographic Society, the South African National Research Foundation, the Gauteng Provincial Government, and Wits University. The Wisconsin Alumni Research Foundation also provided support, as did the Texas A&M College of Liberal Arts Seed Grant Program.

Berger led the Rising Star expedition as National Geographic Explorer-in-Residence. The expedition involved an international team of scientists, including six "underground astronauts" who descended into the Dinaledi chamber to excavate and retrieve the fossils of Homo naledi.

http://www.eurekalert.org/pub_releases/2015-09/uom-ncc090915.php

Natural compound could reduce breast cancer risk in some women

Luteolin may inhibit growth of human breast cancer cells in postmenopausal women taking hormone replacement therapy

COLUMBIA, Mo. - More than 100 women die from breast cancer every day in the United States. The odds increase in postmenopausal women who have taken a combined estrogen and progestin hormone replacement therapy; these women also have an increased risk of developing progestin-accelerated breast tumors. Now, University of Missouri researchers have found that luteolin, a natural compound found in herbs such as thyme and parsley as well as vegetables such as celery and broccoli, could reduce the cancer risk for women who have taken hormone replacement therapy.

"In most circumstances, hormone replacement therapies improve the lives of menopausal women and achieve excellent results," said Salman Hyder, the Zalk Endowed Professor in Tumor Angiogenesis and professor of biomedical sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center. "Nevertheless, research has proven that a higher incidence of breast cancer tumors can occur in women receiving therapies that involve a combination of the natural component estrogen and the synthetic progestin.

"Most older women normally have benign lesions in breast tissue," Hyder said. "These lesions typically don't form tumors until they receive the 'trigger' - in this case, progestin - that attracts blood vessels to cells essentially feeding the lesions causing them to expand." His newest study shows that when the supplement luteolin is administered to human breast cancer cells in the lab, benefits can be observed including the reduction of those vessels "feeding" the cancer cells causing cancer cell death.

Hyder's lab has found that as human breast cancer cells develop, they tend to take on stem cell-like properties, which can make them harder to kill. Here, luteolin was used to monitor stem cell-like characteristics of breast cancer cells and his

team saw a vast reduction in this phenomenon, further proving that the natural compound exerts its anti-tumor effects in a variety of ways.

Then, Hyder further tested laboratory mice with breast cancer and found that blood vessel formation and stem cell-like characteristics also were reduced in vivo, or inside the body.

"We feel that luteolin can be effective when injected directly into the bloodstream, so IV supplements may still be a possibility," Hyder said. "But, until the supplement is tested for safety and commercialized, which we hope will happen after further testing and clinical trials, women should continue consuming a healthy diet with fresh fruits and vegetables."

The early-stage results of this research are promising. If additional studies are successful within the next few years, MU officials will request authority from the federal government to begin human drug development (this is commonly referred to as the "investigative new drug" status). After this status has been granted, researchers may conduct human clinical trials with the hope of developing new treatments for breast cancer in women who have taken combined estrogen and progestin hormone replacement therapies.

Researchers involved with the study included Matthew T. Cook, a recent doctoral graduate and research scientist at Dalton Cardiovascular Research Center; Cynthia Besch-Williford, associate professor of veterinary pathobiology; Yayun Liang, a research associate professor of biomedical sciences in the College of Veterinary Medicine at MU; and Sandy Goyette and Benford Mafuvadze, who are graduate students in biomedical sciences. The research recently was published in the journal Springer Plus through the generosity of numerous donors to the Ellis Fischel Cancer Center at MU.

http://bit.ly/1ilBQOa

Early Americans Went to Great Lengths to Get Caffeine

Pottery shards reveal 1,000-year-old traces of caffeine in places where it wasn't readily available

By Erin Blakemore

Many people simply don't feel human without that cup of coffee in the morning - but how far would you go for a bit of caffeine? Probably not as far as people did 1,000 years ago. New analysis of pottery shards from the Southwest shows that people worked hard for a buzz, finding ways to obtain their fix even when they lived in places with no obvious source of caffeine.

The new study, the largest of its kind, looked at caffeine residue found on pottery retrieved from archaeological sites throughout the Southwest and Northern Mexico. Patricia Crown and her team used tools to remove small chunks of the shards, then ground them into a powder before using a liquid chromatography-mass spectrometry technique to figure out whether they contained traces of caffeine. (They even banned caffeine from the lab to prevent potential cross-contamination.)

The results were intriguing, says Crown in a release: 40 of the 177 samples revealed traces of caffeine. The shards show evidence of cacao-based chocolate drinks and something called “black drink,” a holly-derived, tea-like beverage. Since neither holly nor cacao is native to the Southwest, Crown believes the residue points to extensive trade routes with both the southeastern United States and Mexico or South America.

“Any Mesoamerican archaeologist that works on that time period is well aware of that phenomenon: increased trade, increased long-distance trade in more and more products,” Crown tells NPR’s Murray Carpenter. She says that the find “builds the argument even further that there was this vibrant trade going on.”

Since caffeine traces were found on a variety of different types of pottery, the artifacts suggest a variety of ways to make, serve and drink caffeine. In the paper, the team suggests that some drinks were consumed individually, and others shared using straws, dippers or smaller vessels.

Unlike modern-day coffee freaks, though, the caffeine likely wasn’t used for an early morning pick-me-up. The need for caffeine meant that people who lived in areas without the means of getting their fix had to either travel to far-away locations or trade with people from other places, writes Crown and her team. This may have stimulated new trade relationships - and probably meant that caffeine was reserved for political get-togethers and religious rituals.

http://www.medscape.com/viewarticle/849924

FDA Expands Warning on Becton-Dickinson Syringes

Megan Brooks

UPDATED // The US Food and Drug Administration (FDA) has expanded its alert regarding compounded or repackaged drugs stored in Becton-Dickinson general use syringes to include several more syringe sizes.

In a safety alert issued August 18, the FDA said compounded or repackaged drugs that have been stored in 3- and 5-mL syringes manufactured by Becton-Dickinson should not be administered to patients "unless there is no suitable alternative available."

"Preliminary information indicates that drugs stored in these syringes may lose potency over a period of time due to a possible interaction with the rubber stopper in the syringe," the FDA said August 18. On September 8, the FDA expanded this alert to include additional syringe sizes, including 1-, 10-, 20-, and 30-mL Becton-Dickinson syringes, as well as the company's oral syringes.

"This expansion of the alert to additional sizes of syringes is based on Becton-Dickinson reports that an interaction with the rubber stopper in certain lots of these syringes can cause some of the drugs stored in these syringes to lose potency if filled and not used immediately," the FDA said.

According to Becton-Dickinson, the following drugs in particular can be affected by the stoppers, although they do not know whether other drugs can be affected: fentanyl, rocuronium, neostigmine, morphine, midazolam, methadone, atropine, hydromorphone, cisatracurium, and remifentanyl. The company has created a webpage to assist customers in determining whether their lots are affected.

The company has alerted customers to this issue via letter.

In their latest alert, the FDA again said hospital pharmacies and staff should not administer compounded or repackaged drugs that have been stored in any of these syringes unless there is no suitable alternative available.

In their August 18 alert, the FDA said these syringes have been approved as medical devices for general purpose fluid aspiration and injection only. "These syringes were not cleared for use as a closed container storage system for drug products, and the suitability of these syringes for that purpose has not been established. This issue may extend to other general use syringes made by other manufacturers that were not cleared for the purpose of closed-container storage usage," the FDA said.

The agency has received "several reports" of compounded and repackaged drugs, such as fentanyl, morphine, methadone, and atropine, losing potency when stored in Becton-Dickinson's 3- and 5-mL general purpose syringes. "It is possible that this chemical reaction may affect other compounded and repackaged drugs stored in syringes not FDA cleared for closed-container storage," the FDA said.

These syringes are marked with the BD logo at the base of the syringe.

The FDA said it is unclear how long drugs can be stored in these syringes before degrading. "There is no information to suggest that there is a problem with potency or drug degradation when medication is administered promptly after the syringes are filled."

"This warning does not extend to products approved by FDA for marketing as pre-filled syringes, because as part of the approval process, FDA has determined that these products have been shown to maintain stability in the syringe container through the expiration date on the product," they note.

The FDA is continuing to investigate this issue.

The agency encourages healthcare professionals to report adverse events related to the use of these products to MedWatch, the FDA's safety information and adverse event reporting program, by telephone at 1-800-FDA-1088; by fax at 1-800-FDA-0178; online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm; with postage-paid FDA form 3500, available at http://www.fda.gov/MedWatch/getforms.htm; or by mail to MedWatch, 5600 Fishers Lane, Rockville, Maryland 20852-9787.

http://www.eurekalert.org/pub_releases/2015-09/cp-yht090315.php

You'd have to be smart to walk this lazy... and people are

Your nervous system is subconsciously working against you as you work out

Those of you who spend hours at the gym with the aim of burning as many calories as possible may be disappointed to learn that all the while your nervous system is subconsciously working against you. Researchers reporting in the Cell Press journal Current Biology on September 10 have found that our nervous systems are remarkably adept in changing the way we move so as to expend the least amount of energy possible. In other words, humans are wired for laziness.

The findings, which were made by studying the energetic costs of walking, likely apply to most of our movements, the researchers say.

"We found that people readily change the way they walk - including characteristics of their gait that have been established with millions of steps over the course of their lifetime - to save quite small amounts of energy," says Max Donelan of Simon Fraser University in Canada. "This is completely consistent with the sense that most of us have that we prefer to do things in the least effortful way, like when we choose the shortest walking path, or choose to sit rather than stand. Here we have provided a physiological basis for this laziness by demonstrating that even within a well-rehearsed movement like walking, the nervous system subconsciously monitors energy use and continuously re-optimizes movement patterns in a constant quest to move as cheaply as possible."

There is a bright side to this, lead author Jessica Selinger adds: "Sensing and optimizing energy use that quickly and accurately is an impressive feat on the part of the nervous system. You have to be smart to be that lazy!"

Donelan, Selinger, and their colleagues wanted to understand why people move the way they do, given that there are countless ways to get from point A to point B. This is partly a question of evolution and learning. But, the researchers wanted to know, to what extent can our bodies adapt movement based on real-time physiological inputs?

To find out, the researchers asked people to walk while they wore a robotic exoskeleton. This contraption allowed the researchers to discourage people from walking in their usual way by making it more costly to walk normally than to walk some other way. More specifically, the researchers made it more difficult for participants to swing their legs by putting resistance on the knee during normal walking, whereas the researchers eased this resistance for other ways of walking.

"We think of our experiment like dropping someone into a new world with all new rules," Selinger says. "Any walking strategies that may have developed over evolutionary or developmental timescales are now obsolete in this new world."

This scheme allowed the researchers to test whether people can sense and optimize the cost associated with their movements in real time. And it turns out we can.

The experiment revealed that people adapt their step frequency to converge on a new energetic optimum very quickly - within minutes. What's more, people do this even when the energy savings is quite small: less than 5%. The findings show that the energetic costs of our activities aren't just an outcome of our movements, but in fact play a central role in continuously shaping them.

The researchers say they now plan to explore questions about how the human body measures the energetic costs associated with particular ways of moving. They are also keen to know how the body solves what is a very complex optimization problem.

"Walking requires the coordination of literally tens of thousands of muscle motor units," Donelan says. "How do we so quickly discover the optimal combinations?"

This work was supported by a Vanier Canadian Graduate Scholarship, the Michael Smith Foundation for Health Research, and the U.S. Army Research Office.

Current Biology, Selinger et al.:"Humans Can Continuously Optimize Energetic Cost during Walking" http://dx.doi.org/10.1016/j.cub.2015.08.016

http://www.eurekalert.org/pub_releases/2015-09/qmuo-pcs091015.php

Pancreatic cancer stem cells could be 'suffocated' by an anti-diabetic drug

Not all cancer cells are alike when it comes to metabolism

Cancer cells commonly rely on glycolysis, the type of metabolism that does not use oxygen to generate their energy however, researchers from Queen Mary University of London's Barts Cancer Institute and the Spanish National Cancer Research Centre (CNIO) in Madrid have now found that not all cancer cells are alike when it comes to metabolism.

PancSCs can make use of a more efficient form of metabolism, called oxidative phosphorylation or OXPHOS, which does use oxygen. OXPHOS uses a part of the cell called mitochondria and it is this which can be targeted with anti-diabetic drug, metformin.

Some PancSCs are however able to escape this treatment by being much more flexible in their metabolism, leading to a recurrence of the cancer, but the investigators also found a way to prevent such resistance and force all PancSCs to keep using OXPHOS.

The researchers think that the new discovery could be used to develop treatments that stop the stem cells using oxygen and prevent cancer returning after conventional treatment. A clinical trial is planned for later next year.

Dr Patricia Sancho, first author of the research paper, said:

"We might be able to exploit this reliance on oxygen by targeting the stem cells with drugs that are already available, killing the cancer by cutting off its energy supply.

"In the long term, this could mean that pancreatic cancer patients have more treatment options available to them, including a reduced risk of recurrence following surgery and other treatments."

Pancreatic cancer is still one of the most difficult cancer types to treat, partly because of its tendency to cause symptoms and trigger diagnosis only at a late and advanced stage. Many patients do not live longer than a year post-diagnosis.

These cancers are also becoming more common due to obesity, which causes pancreatic cancer risk factors including metabolic syndrome and diabetes. Limited treatment options and a failure to improve survival rates mean that finding new treatment strategies is a priority.

PancSCs could be an important but as yet overlooked piece of this puzzle. While they make up only a small proportion of the tumour, they have the potential to make new tumours, even if all the other cells are killed, and are prone to spreading around the body (metastasis).

http://nyti.ms/1Nx2oZC

No Surf, but Maybe Dunes in NASA's Latest Pluto Photos

Dunes on Pluto?

By KENNETH CHANG SEPT. 10, 2015

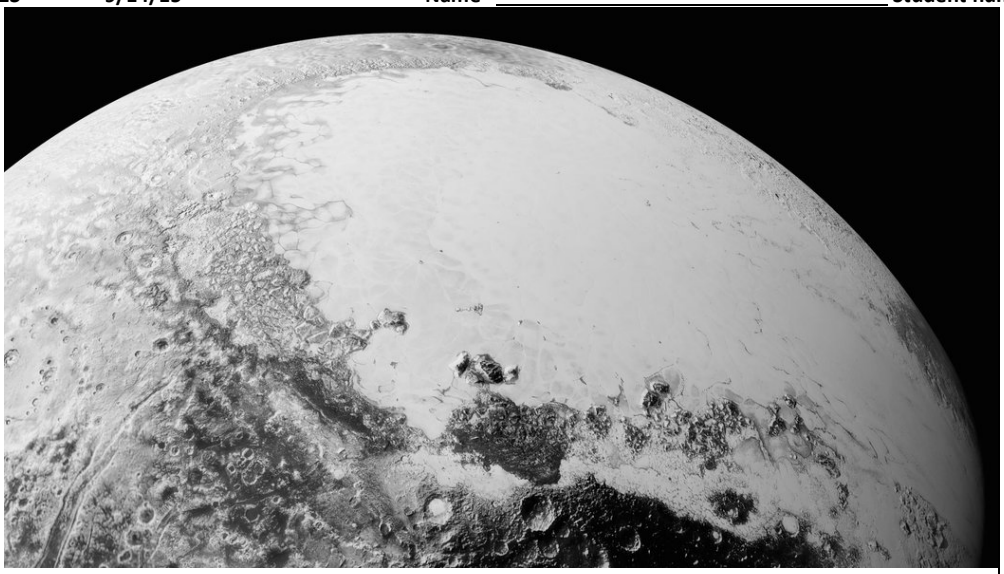
On a landscape that already includes soaring ice mountains, smooth plains and strange polygonal patterns, planetary scientists have found another feature that most did not expect of a frozen world.

"We have detected vast fields of features that look like dunes," said S. Alan Stern, the principal investigator for NASA's New Horizons spacecraft, which flew past Pluto on July 14. "Now we are being careful to say they look like dunes. They may or may not actually be dunes."

That surprise is among several in a new batch of flyby photographs released by NASA on Thursday.

Dunes are undulating ridges of particles piled up by blowing wind, but the air of present-day Pluto is much too thin and weak to sculpt the fields of dunes, some of which stretch for kilometers.

That could suggest that Pluto once possessed a much thicker atmosphere. If they are not dunes, then some force other than wind created them. "Their origin is under debate," Dr. Stern said.

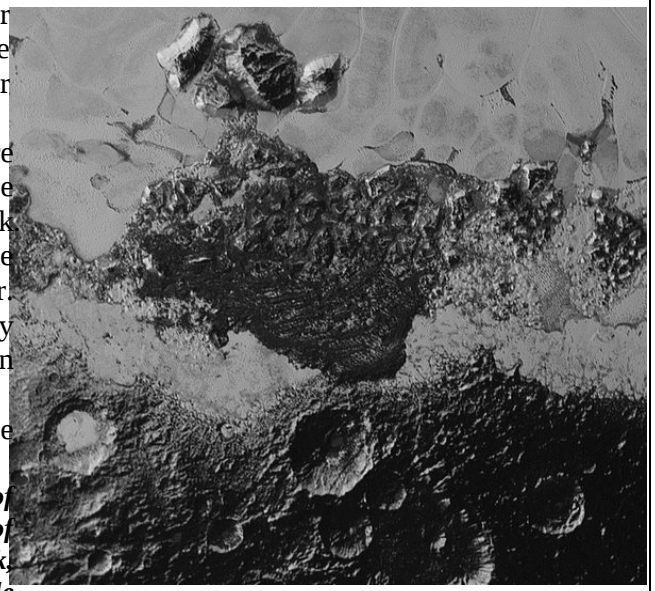


This mosaic of high-resolution images shows what one would see about 1,100 miles above Pluto's equatorial region. **Credit NASA/Johns Hopkins University Applied Physics Laboratory/Southwest Research Institute**

It is also unknown whether the dunelike structures are made of ice particles or sandlike bits of rock.

Some of the structures are fairly bright, reflective as ice might be; others are very dark. "The dunes may all be identical in composition," Dr. Stern said, "but some may have a veneer of dark stuff on them.

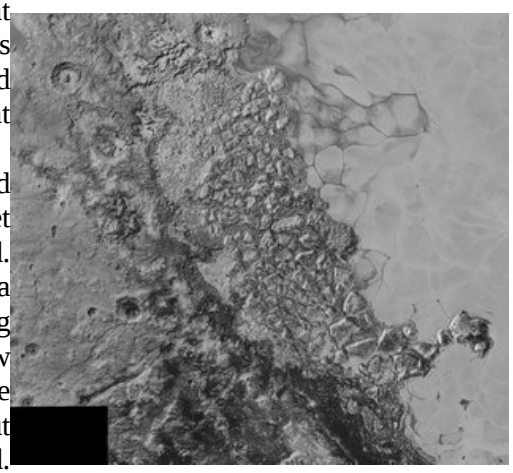
Or they may be different. We just don't know."



A 220-mile-wide close-up of Pluto reveals a diversity of landforms including dark, aligned ridges that resemble dunes. **Credit NASA/Johns Hopkins University Applied Physics Laboratory/Southwest Research Institute**

New Horizons captured a trove of images and data during the flyby, but it will take a year for it to send all that information across the solar system for scientists to study. In August, the spacecraft sent back data from two instruments measuring the dance of charged particles around Pluto and a student experiment that counted dust particles.

The scientists working with the charged particles data say they do not yet understand what they have found. "Because, as you might expect from a first flyby, they found really puzzling things," Dr. Stern said. "They know they got good data, and they see signatures from the Pluto system, but they're not anything like they predicted.



A jumbled, chaotic terrain in the middle of this 300-mile-wide swath of Pluto lies to the left of icy plains known as Sputnik Planum. **Credit NASA/Johns Hopkins University Applied Physics Laboratory/Southwest Research Institute**

Last Friday, the mission team resumed the retrieval of images from New Horizons; it plans to release them weekly. Other photographs in this week's batch show multiple haze layers in Pluto's atmosphere, glacierlike flows of ice and what Dr. Stern described as "a very disorganized region hundreds of miles across where the mountains appear to be chaotically jumbled."

Similar jumbled landscapes have been seen on Jupiter's moon Europa, where the flow of water in an underground ocean may have destabilized the surface.

Dr. Stern said that on Pluto, it is possible that liquid nitrogen below the surface caused the mountains to collapse.

In late October and early November, New Horizons is set to fire its thrusters four times to point itself toward its next destination: a small, icy body designated 2014 MU69, which it will study in 2019 if NASA approves an extension to the mission.

http://www.eurekalert.org/pub_releases/2015-09/sdsu-abc091015.php

A better class of cancer drugs

An SDSU chemist has developed a technique to identifying potential cancer drugs that less likely to produce side effects

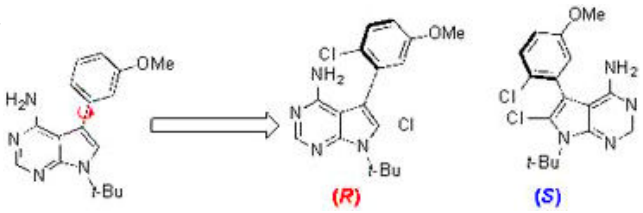
SAN DIEGO - A class of therapeutic drugs known as protein kinase inhibitors has in the past decade become a powerful weapon in the fight against various life-threatening diseases, including certain types of leukemia, lung cancer, kidney cancer and squamous cell cancer of the head and neck. One problem with these

drugs, however, is that they often inhibit many different targets, which can lead to side effects and complications in therapeutic use. A recent study by San Diego State University chemist Jeffrey Gustafson has identified a new technique for improving the selectivity of these drugs and possibly decreasing unwanted side effects in the future.

Why are protein kinase-inhibiting drugs so unpredictable? The answer lies in their molecular makeup.

Many of these drug candidates possess examples of a phenomenon known as atropisomerism. To understand what this is, it's helpful to understand a bit of the chemistry at work. Molecules can come in different forms that have exactly the same chemical formula and even the same bonds, just arranged differently. The different arrangements are mirror images of each other, with a left-handed and a right-handed arrangement. The molecules' "handedness" is referred to as chirality. Atropisomerism is a form of chirality that arises when the spatial arrangement has a rotatable bond called an axis of chirality. Picture two non-identical paper snowflakes tethered together by a rigid stick.

Some axes of chirality are rigid, while others can freely spin about their axis. In the latter case, this means that at any given time, you could have one of two different "versions" of the same molecule.



The left-most molecule shows an unstable atropisomer, its axis of chirality shown by the red arrow. The two on the right are stable "arrangements." **Jeffrey Gustafson**

Watershed treatment

As the name suggests, kinase inhibitors interrupt the function of kinases - a particular type of enzyme - and effectively shut down the activity of proteins that contribute to cancer.

"Kinase inhibition has been a watershed for cancer treatment," said Gustafson, who attended SDSU as an undergraduate before earning his Ph.D. in organic chemistry from Yale University, then working there as a National Institutes of Health poctdoctoral fellow in chemical biology.

"However, it's really hard to inhibit a single kinase," he explained. "The majority of compounds identified inhibit not just one but many kinases, and that can lead to a number of side effects."

Many kinase inhibitors possess axes of chirality that are freely spinning. The problem is that because you can't control which "arrangement" of the molecule is present at a given time, the unwanted version could have unintended consequences.

In practice, this means that when medicinal chemists discover a promising kinase inhibitor that exists as two interchanging arrangements, they actually have two different inhibitors. Each one can have quite different biological effects, and it's difficult to know which version of the molecule actually targets the right protein.

"I think this has really been under-recognized in the field," Gustafson said. "The field needs strategies to weed out these side effects."

Applying the brakes

So that's what Gustafson did in a study recently published in the high-impact journal Angewandte Chemie. He and his colleagues synthesized atropisomeric compounds known to target a particular family of kinases known as tyrosine kinases. To some of these compounds, the researchers added a single chlorine atom which effectively served as a brake to keep the atropisomer from spinning around, locking the molecule into either a right-handed or a left-handed version.

When the researchers screened both the modified and unmodified versions against their target kinases, they found major differences in which kinases the different versions inhibited. The unmodified compound was like a shotgun blast, inhibiting a broad range of kinases. But the locked-in right-handed and left-handed versions were choosier.

"Just by locking them into one or another atropisomeric configuration, not only were they more selective, but they inhibited different kinases," Gustafson explained.

If drug makers incorporated this technique into their early drug discovery process, he said, it would help identify which version of an atropisomeric compound actually targets the kinase they want to target, cutting the potential for side effects and helping to usher drugs past strict regulatory hurdles and into the hands of waiting patients.

http://www.eurekalert.org/pub_releases/2015-09/gumc-ri090415.php

Resveratrol impacts Alzheimer's disease biomarker

The largest nationwide clinical trial to study high-dose resveratrol long-term in people with mild to moderate Alzheimer's disease found that a biomarker that declines when the disease progresses was stabilized in people who took the purified form of resveratrol.

WASHINGTON - Resveratrol is a naturally occurring compound found in foods such as red grapes, raspberries, dark chocolate and some red wines.

The results, published online today in Neurology, "are very interesting," says the study's principal investigator, R. Scott Turner, MD, PhD, director of the Memory Disorders Program at Georgetown University Medical Center. Turner, who treats

patients at MedStar Georgetown University Hospital, cautions that the findings cannot be used to recommend resveratrol. "This is a single, small study with findings that call for further research to interpret properly."

The resveratrol clinical trial was a randomized, phase II, placebo-controlled, double blind study in patients with mild to moderate dementia due to Alzheimer's disease. An "investigational new drug" application was required by the U.S. Food and Drug Administration to test the pure synthetic (pharmaceutical-grade) resveratrol in the study. It is not available commercially in this form.

The study enrolled 119 participants. The highest dose of resveratrol tested was one gram by mouth twice daily - equivalent to the amount found in about 1,000 bottles of red wine.

John Bozza, 80, participated in the study. Five years ago, his wife, Diana, began noticing "something wasn't quite right." He was diagnosed with mild cognitive impairment, but only a year later, his condition progressed to mild Alzheimer's.

Diana, whose twin sister died from the same disease, says there are multiple reasons she and John decided to participate in the resveratrol study, and they now know he was assigned to take the active drug. "I definitely want the medical community to find a cure," she says. "And of course I thought there's always a chance that John could have been helped, and who knows, maybe he was."

Patients, like John, who were treated with increasing doses of resveratrol over 12 months showed little or no change in amyloid-beta40 (Abeta40) levels in blood and cerebrospinal fluid. In contrast, those taking a placebo had a decrease in the levels of Abeta40 compared with their levels at the beginning of the study.

"A decrease in Abeta40 is seen as dementia worsens and Alzheimer's disease progresses; still, we can't conclude from this study that the effects of resveratrol treatment are beneficial," Turner explains. "It does appear that resveratrol was able to penetrate the blood brain barrier, which is an important observation. Resveratrol was measured in both blood and cerebrospinal fluid."

The researchers studied resveratrol because it activates proteins called sirtuins, the same proteins activated by caloric restriction. The biggest risk factor for developing Alzheimer's is aging, and studies with animals found that most age-related diseases - including Alzheimer's - can be prevented or delayed by long-term caloric restriction (consuming two-thirds the normal caloric intake).

Turner says the study also found that resveratrol was safe and well tolerated. The most common side effects experienced by participants were gastrointestinal-related, including nausea and diarrhea. Also, patients taking resveratrol experienced weight loss while those on placebo gained weight.

One outcome in particular was confounding, Turner notes. The researchers obtained brain MRI scans on participants before and after the study, and found that resveratrol-treated patients lost more brain volume than the placebo-treated group.

"We're not sure how to interpret this finding. A similar decrease in brain volume was found with some anti-amyloid immunotherapy trials," Turner adds. A working hypothesis is that the treatments may reduce inflammation (or brain swelling) found with Alzheimer's.

The study, funded by the National Institute on Aging and conducted with the Alzheimer's Disease Cooperative Study, began in 2012 and ended in 2014. GUMC was one of 21 participating medical centers across the U.S.

Further studies, including analysis of frozen blood and cerebrospinal fluid taken from patients, are underway to test possible drug mechanisms.

"Given safety and positive trends toward effectiveness in this phase 2 study, a larger phase 3 study is warranted to test whether resveratrol is effective for individuals with Alzheimer's - or at risk for Alzheimer's," Turner says.

Resveratrol and similar compounds are being tested in many age-related disorders including cancer, diabetes and neurodegenerative disorders. The study Turner led, however, is the largest, longest and highest dose trial of resveratrol in humans to date.

The research was supported by a grant from the National Institute on Aging (U01 AG010483). Turner reports no personal financial interests related to the study.

http://www.eurekalert.org/pub_releases/2015-09/uok-urf091115.php

UK researchers find 'dormant' parasite cysts are actually quite active

A new University of Kentucky study in the journal mBio shows that tissue cysts of the parasite Toxoplasma gondii, long thought to be dormant, are quite active.

LEXINGTON, Ky. - Led by Anthony Sinai, professor at the UK College of Medicine, the study has significant implications on the understanding of chronic toxoplasmosis in the brain, a condition suggested to contribute to a range of neurological diseases including schizophrenia in humans, and the modulation of behavior in rodents.

Toxoplasmosis, which can be acquired from the droppings of infected cats as well as the consumption of tissue cyst contaminated meat, infects roughly one-third of the human population. Infected individuals rarely show symptoms as their immune systems tackle the actively growing parasite.

However, the immune system never clears the parasite. Immunity causes the parasite to morph into the "dormant" tissue cyst form, leading to a life-long chronic infection. Unfortunately, conditions leading to compromised immunity - such as HIV/AIDS, organ transplantation and chemotherapy - can cause reactivation that can be life-threatening. Until this study these enigmatic tissue

cysts remained largely unstudied on account of the technical challenges their study presented.

The study required not only the development of novel methodologies, but also an entirely new mindset toward tackling a problem that remained largely untouched for decades. These approaches include an imaging application developed by the group of UK College of Engineering Professor Abhijit Patwardhan that permitted the actual quantification of individual parasites within cysts for the first time. This advance, together with other experiments, has led to new insights that reveal not only direct evidence for parasite growth, but also a surprising level of coordination of that growth within the cysts.

"This fundamentally alters our understanding of chronic toxoplasmosis," Sinai said.

Ongoing collaboration between the Sinai and Patwardhan groups aims at the refinement of computational approaches to model these newly discovered growth characteristics. These insights will will provide new impetus for drug development against a form of the parasite that has been resistant to all treatments to date.

"We hope that defining parasite growth properties in cysts will allow researchers to begin crafting new targeted therapies clear the parasite burden in immune-compromised patients," said Elizabeth Watts, lead author on the study. "Additionally, this work emphasizes the value of collaboration between different disciplines to make exciting new discoveries."

This study was supported by National Institute of Allergy and Infectious Diseases funding awards R21AI098371 and R21AI099509 awarded to Sinai and does not necessarily represent the views of the National Institutes of Health.

http://bit.ly/1i8atXi

What Makes a Fossil a Member of the Human Family Tree?

The surprising new species Homo naledi raises more questions than answers - for now

By Brian Handwerk

Every family has its oddball aunt or uncle, and our ancient human relations are no exception. The latest branch on the human family tree goes to *Homo naledi*, a species with a surprising - and somewhat contentious - mix of primitive and modern features.

The discovery is unusual because it marks the greatest concentration of ancient human remains found in a single site - a whopping 1,550 bones from about 15 individuals. What's more, the hominids seem to have deliberately placed their dead deep in a South African cave, a behavior that paleontologists say is oddly advanced considering the species' small brain size.

***Meet* Homo naledi*, the newest member of the human family tree.* (University of the Witwatersrand)**

Announcing the find on September 10, paleoanthropologist Lee Berger of the University of the Witwatersrand argued that the fossils represent a previously unknown member of the human genus, one that seems to be in the transition zone between *Homo* and the next closest relative, *Australopithecus*. But other human origins experts are not ready to re-write the textbooks just yet. For instance, *H. naledi* shares a lot of features with *Homo erectus*, another early human species found in the same region.

So while the *H. naledi* fossils undeniably add to the story of human evolution, they also highlight the difficulties of defining exactly what makes a fossil species human in the first place.

According to the fossil record, the genus *Australopithecus* includes the predecessors to our own *Homo* genus, such as the famed "Lucy" fossil, a female *A. afarensis*, found in 1974 in Ethiopia. Members of this genus walked upright regularly but frequently spent time in the trees to feed or avoid predators. Their brain size was equivalent to that of chimpanzees and gorillas.

The most generally accepted evolutionary timelines say these ancient hominids gave way to the genus *Homo* beginning some 2.8 million years ago. *Homo sapiens*, or modern humans, are one of seven known members of the genus - eight now that *H. naledi* has been described. Some of these species are our direct ancestors, while others lived and died on more distant branches of the family tree.

As Berger and his colleagues write in the journal eLife, an adult *H. naledi* would have been about 5 feet tall and would have weighed just 100 pounds, with a brain about the size of an orange. The remains present a complex mix of the characteristics scientists use to differentiate members of the genus *Homo* from earlier relatives - things like tooth and cranial shape, bipedal walking, arboreal living and brain size.

“In terms of a combination of human and more primitive features, the volume of evidence from 15 individual skeletons is so compellingly different from anything that we've seen in other bipedal, upright human-like fossils that I'm completely convinced that it's a new species and part of our human evolutionary tree,” says Rick Potts, director of the Smithsonian's Human Origins Program.

For instance, *H. naledi's* teeth and skull are similar to early members of our genus, like *Homo habilis*. Its feet are also much like those of later humans, as are aspects of its hands.

"But it also has these long, curved fingers that indicate tree living behavior more than anything that we see in *Australopithecus* even," Potts says. The fossils' raised shoulders and rib cage are also more like those seen among the *Australopithecus* group.

However, New York University anthropologist Susan Anton notes that there's no consensus in paleoanthropology about exactly how such comparisons are used to define the genus *Homo*. Some would argue that striding bipedalism is a defining feature, so that being *Homo* means using a specific way of moving around the environment. Other scholars may look more to cranial characteristics as *Homo* family features.

"It's a little more complicated than this of course," she adds of cranial comparisons, "but the simple line is brain size increases, jaw and tooth size decrease and that combination is what gives you *Homo* as opposed to *Australopithecus*."

Which characteristics take precedence depends to some extent on the different philosophies of publishing scientists, says Anton. "The problem with this [*H. naledi*] find is that it seems to show both primitive and more *Homo*-like characteristics," she notes. "And in that I think it highlights that we really need a conversation about what we mean by *Homo* and how we decide which of the different characteristics we are going to give precedence to."

***Fossils of the hand of* Homo naledi *are seen in the Wits bone vault at the Evolutionary Studies Institute at the University of the Witwatersrand in South Africa.* (John Hawks/University of Wisconsin-Madison)**

Complicating matters is the fact that Berger and his team have not yet dated the bones, so we don't know where *H. naledi* belongs on the evolutionary timeline.

"What's important to an evolutionist are the species lineages … when do they arise by branching, and when do they terminate by extinction?" says Tim White of the University of California, Berkeley.

Based on anatomical clues, it's possible *H. naledi* lived about 2.5 million years ago, just before *H. erectus* came on the scene. However, the strange new species could also be less than a million years old, which means it may have shared the landscape with a handful of other human species, including a few evolutionary dead-ends as well as the earliest members of *Homo sapiens.*

"It has a combination of A*ustralopithecus* and *Homo*-like traits, so Berger and his team are guessing that it's related to the transition between those two groups, which was a time when different populations lived under varying survival pressures that led to very different evolutionary experiments and different combinations of *Australopithecus* and *Homo* traits in different areas across Africa," Potts says.

"But it's hard to know without a date whether it's from that period, as one of those experiments that then went nowhere, or whether it's in fact much less than one million years old. In that case, we could be talking about something that also didn't go anywhere and was just an isolated, probably very small population that persisted for a long time in splendid isolation."

"We're talking about the origins of *Homo* because of the presumed age for this thing, but I have no idea how old this thing is," Anton says. "It's not clear to me from the anatomy that this has anything to do with the origin of *Homo*. Because the way that it's combining primitive and *Homo*-like characteristics is at least not the way that early *Homo* in East Africa does it. If it's either much earlier or much later in time, that to me makes it less weird."

For his part, White sees no new branch forming with *H. naledi*, and he thinks its skull suggests that the fossil find is simply an early member of a previously known genus: "When you compare so-called *H. naledi* with the *Homo* skull SK 80/847 from the Swartkrans site 800 meters [2,625 feet] away, you say wow, this looks awfully similar. This is what an early, small *H. erectus* looks like."

H. erectus was an extremely successful *Homo* species that abandoned arboreal living and not only survived from about 1.9 million years ago to around 100,000 years ago, but also spread across Africa and Eurasia. White suggests that the *H. naledi* skull also looks a lot like a 1.8-million-year-old *Homo* skull found in Dmanisi, Georgia, which combines features of several early lineages.

"If you took the 1000-year-old skull of a San Bushman from South Africa and compared it to some Caucasian in what would become Georgia, their skulls would be more different than *H. naledi* and Dmanisi - which is pretty amazing when you think about the distance between those two sites," says White.

"I'm not saying this is not a major discovery," he adds. "I'm saying it's a major discovery whose significance is unknown until more than a test pit has been dug, dating has been completed, and a proper anatomical comparison between this and previously known fossils has been done."

Even the physical location of the find has sparked debate - how did the bodies get into a remote pit deep in a dark cave? The bones were found in an isolated

chamber that could only be accessed through a seven-inch-wide gap. Berger and his colleagues characterize this as a deliberate funerary behavior previously seen only in modern humans.

Potts describes it as more of a mystery: “There is no evidence of material culture, like tools, or any evidence any kind of symbolic ritual that we almost always associated with burial," he says. "These bodies seem to have simply been dropped down a hole and disposed of, and that really brings up a whodunit.”

Berger and his team held off on dating the bones because the process requires destroying some of the physical remains. Now that all the fossils have been described in the formal literature, scientists will try and place *H. naledi* on the timeline. Even then, experts will likely spend many years striving to put these fossils in the proper context.

For Potts, the find will remain fascinating wherever they end up on our family tree - even if on an oddball, cutoff family branch.

“We've made a transition in the field from always wanting to find the ancestor of human beings to now understanding that the evolutionary process had all of this creative variation, especially when you look at it in the context of changing environmental and survival pressures,” he notes.

“So it's really cool to be able to learn from these kinds of finds not only that we have a new relative, which is really cool in itself, but also to learn more and more about the evolutionary process and how dynamic it really is.”

http://bit.ly/1KLujEH

Can red wine and chocolate really stave off Alzheimer’s disease?

A study suggests that a chemical in dark chocolate and red wine can slow the progression of Alzheimer’s disease. But how conclusive is the data, and does this mean we should all drink more wine?* New Scientist *looks at the evidence.

What is resveratrol?

Found in grapes, red wine and dark chocolate, many claims have been made about resveratrol. It has been touted as a potential panacea for a range of age-related disorders, including cancer, diabetes and neurological problems, but so far most of the data supporting these claims has come from lab studies and work in animals. There have been only a few, small studies in humans.

How might resveratrol protect us from age-related illness?

Extremely calorie-restricted diets greatly reduce age-related diseases in lab animals. This is thought to happen through the activation of a group of enzymes called sirtuins, which seem to affect gene expression and protect against the effects of stress, including a poor diet.

The hope is that resveratrol activates sirtuins to get the same benefits – like preventing the onset of age-related diseases, including Alzheimer’s – without having to stick to such a low-energy diet. But some experiments have suggested slowed ageing from caloric restriction may not be down to sirtuins after all.

What does the latest study show?

To see if resveratrol could delay the progression of Alzheimer’s disease in people , Scott Turner at Georgetown University Medical Centre in Washington DC and his team gave 119 people with mild to moderate symptoms of the disease either a gram of synthesised resveratrol twice a day in pills for a year, or a placebo. Over the course of the study, those in the placebo group showed typical signs of Alzheimer’s progressing, including a decline in the level of amyloid beta protein in their blood – thought to be a sign that this compound was being taken from their blood and deposited in their brains. Those taking resveratrol, however, showed little or no change in amyloid beta levels in their blood.

Did the resveratrol make any difference to brain function?

This study was designed to test the safety of taking large doses of resveratrol, rather than look at whether it works. As such, the study is too small to detect any meaningful effect that it might have had on brain function. But Turner says they did see a slight improvement in one measure of cognitive function, although this wasn’t statistically significant. A larger study may find a stronger result.

Is amyloid a good indicator of Alzheimer’s disease?

Alzheimer’s is typically characterised by the build-up of amyloid plaques in the brain, so it is often used as a biomarker for the disease. But questions remain over the role of amyloid in the disease – does it cause the condition or is it just a symptom? We won’t know how informative amyloid levels are until we find a successful way of stopping or slowing Alzheimer’s, says Neil Buckholtz of the NIH National Institute on Aging in Bethesda, Maryland, which funded this study.

Does this mean we should drink more wine?

“You can’t possibly consume enough resveratrol from food sources to reach the doses that were used in the study,” says James Hendrix, a scientist with the US charity Alzheimer’s Association. Turner estimates someone would have to drink 1000 bottles of red wine a day to even come close.

Natural supplements are problematic, too. Plants produce resveratrol in response to stress, such as a fungal infection, cold or drought, and the level of the compound in a plant can vary tremendously. The only way to guarantee the dose is with a synthesised product.

“Nature did not design resveratrol to treat Alzheimer’s disease, it designed it for some other reason that only a grape knows,” says Hendrix. But the molecule is a

good starting point, he says. Chemists should be able to tweak the structure to make more of the chemical reach the brain and to reduce the dose and side effects. Until then, it's probably best to think of resveratrol and other dietary molecules as counteracting poor diet rather than preventing Alzheimer's.

Journal reference: *Neurology, DOI: 10.1212/WNL.0000000000002035*

http://www.bbc.com/news/health-34222023

Target of four-week cancer diagnosis

The government has given more details of a package of measures to improve cancer treatment in England.

It includes a target that 95% of people should be given a cancer diagnosis or the all-clear within 28 days of being referred by a GP, by 2020. Implementing it will cost £300m a year until then. Faster diagnosis could save up to 11,000 lives a year, according to an Independent Cancer Taskforce report. The health secretary said the measure was a "simple promise".

Jeremy Hunt said the UK lagged behind other western European countries in cancer survival rates and the new measures would help "close the gap". "We know that the biggest single factor that means that our cancer survival rates lag those of France, Germany and other European countries is the fact that we have too much late diagnosis; we don't get an answer to people quickly enough," he said.

"And what we're saying here is a very simple promise to all NHS patients by 2020 that if your GP has a concern that you may have cancer, we will get you an answer - either a cancer diagnosis or an all-clear within 28 days - that will be one of the fastest diagnosis rates anywhere in the world."

Speeding up diagnosis would require more cancer consultants, specialist nurses, staff trained in endoscopies and diagnostic tests, he added.

Currently 280,000 people in England are diagnosed with cancer each year - with half surviving for at least 10 years. Patients are meant to see a specialist within two weeks of a GP referral under existing targets but may then face a long wait for test results, meaning a growing number of patients do not get their treatment started within the recommended 62 days. Cancer patients will also get online access to their test results if they choose, under the new measures.

Ambition

Harpal Kumar, chief executive of Cancer Research UK and chairman of the Independent Cancer Taskforce, said services for diagnosing cancer were under immense pressure, which is why increased investment and extra staff were so important. "Introducing the 28-day ambition for patients to receive a diagnosis will maximise the impact of this investment which, together with making results available online, will spare people unnecessary added anxiety and help cancer patients to begin treatment sooner," he said.

The announcement comes after a cross-party group of MPs warned that cancer services had "lost momentum" in the past two years. The health service has been struggling to meet waiting times and seen resources reduced, the Public Accounts Committee warned.

Juliet Bouverie of Macmillan Cancer Support, said: "We desperately need to see continued action from the government and the NHS to ensure that all the recommendations laid out in the recently published Cancer Strategy for England are fully funded and implemented."