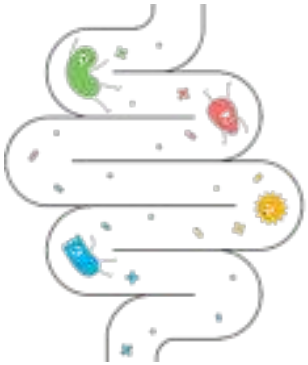


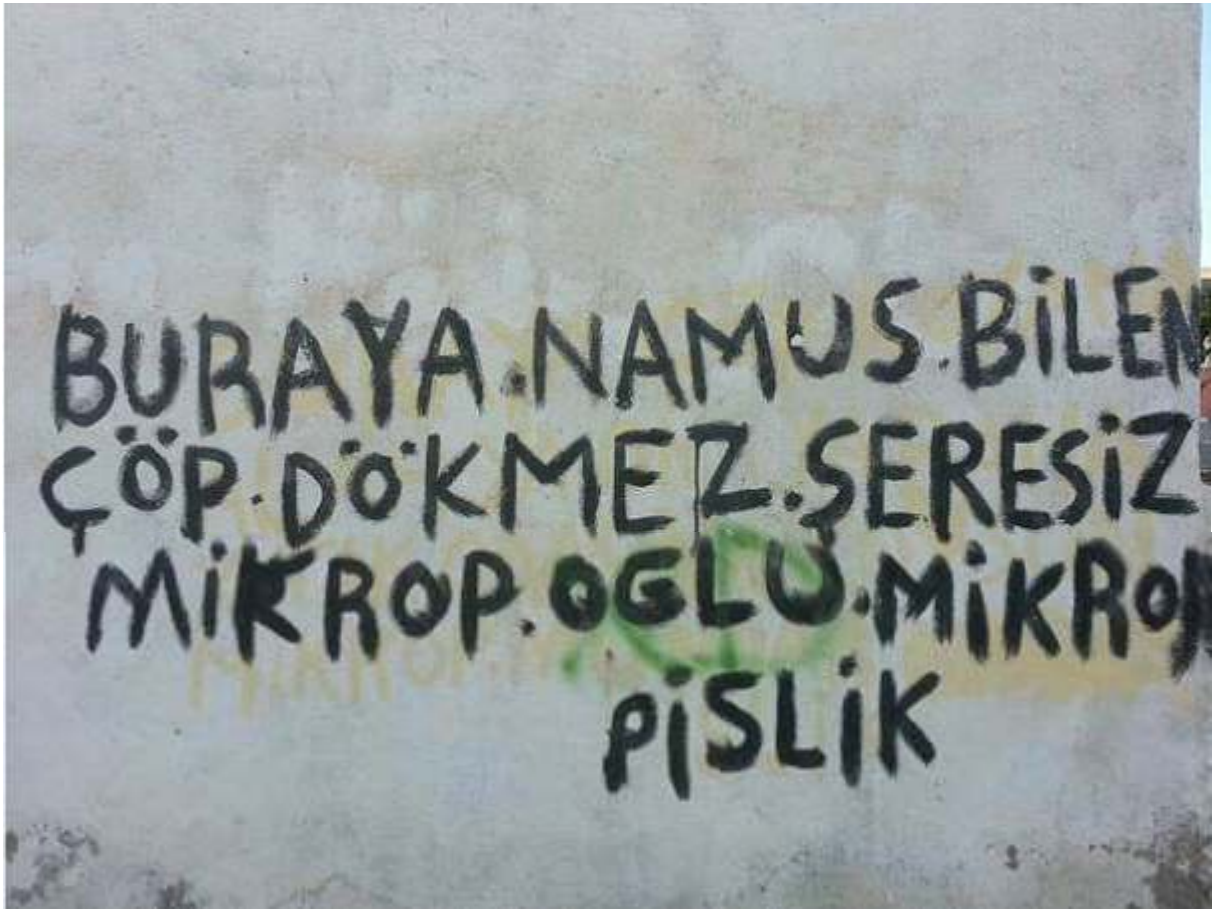
Mikroorganizmalarla Tanışma:

Mikropların Dünyası, Antimikrobiyal Direnç ve Mikrobiyota

Barış Otlu
İnönü Üniversitesi Tıp Fakültesi
Tıbbi Mikrobiyoloji Anabilim Dalı, Malatya

Mikrop algısı

- Mikrop oğlu mikrop pislik….



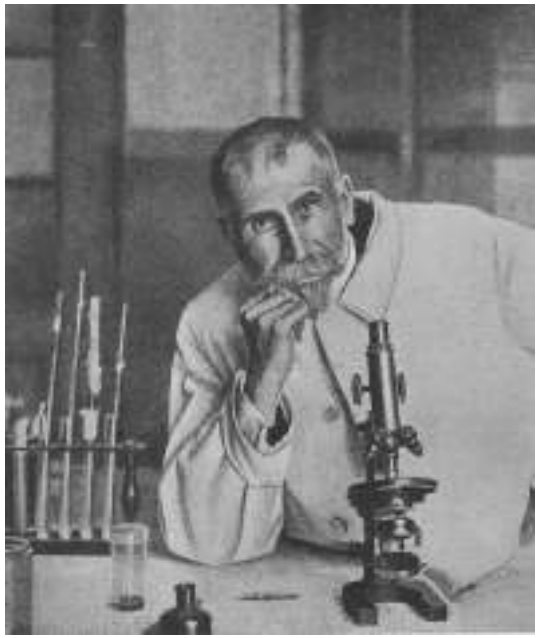
Mikrop algısı

- Mikrop oğlu mikrop pislik….

Mikrop oğlu mikroplar

- Kötüyüm ben kötüyüm kötüyüm kötüyüm herkesi hasta ederim ederim ishal yapar kustururum, bezdiririm….

Mikrop Avcıları



Pierre Paul Emile Roux
(1926 Microbe Hunters)

Mikropların yuvası…..

HASTANE DEĞİL MİKROP YUVASI!

LEFKOŞA DEVLET HASTANESİNİN HAVALANDIRMA SİSTEMİ BAKIMSIZLIKTAN MİKROP YUVASINA DÖNDÜ

yıllardır temizlenmeyen havalandırma sistemindeki birikmiş siyah küfler görenleri şaşkına çeviriyor.

İnsan hayatı için büyük tehlikeli olan birikmiş siyah küfler insanların ölümüne kadar neden olabilirken sağlık merkezi olan bir kurumda mikrop yuvasının olması devletin de bu konudaki sorumsuzluğunu gözler önüne seriyor.

Cebimizde "mikrop yuvası" taşıyoruz !

Mikropların yuvası…..

Mikropların yuvası.....

Evdeki Tehlike: Koronavirüs için Mikrop Yuvası!

Türkiye Halı Yıkamacılar Konfederasyon Genel Başkanı, "Mikrobu en çok barındıran yerler halılardır." dedi.

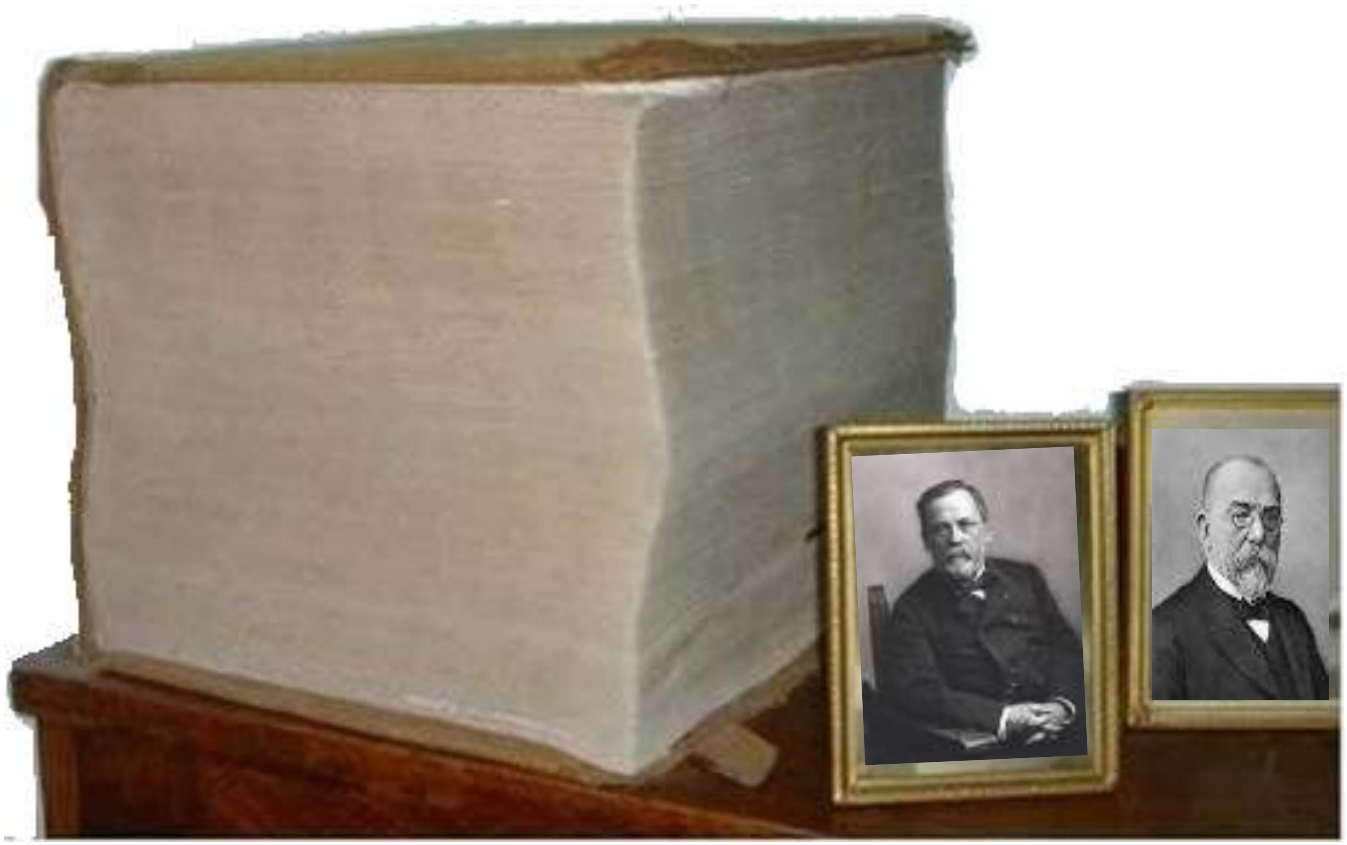
Ulusal Gündem · 21 Mart 2020 Cumartesi 12:36 · Burcu Keskin

Mikropların yuvası neresi?

- Mikropların dünyasında yaşıyoruz.

Mikroplar bir dünya tarihi kitabı yazsa….

- İnsanoğlu kitabın son sayfasında yer alır



1674 - Mikroorganizma Sonrası; 0. zaman

- Mikroorganizmalarla ilk tanışma

1680

1800’li Yıllara Kadar - Miasma Teorisi

- Ortaçağ'da ortaya çıkmış ve yüzyıllarca devam etmiştir.

1850 - Hotel Dieu

- Ampütasyonlardan ölüm oranı %60

  salgın sırasında lohusalık hummasından ölüm oranı 19/20

1850 - Mikroorganizma Sonrası; 176. yıl

- Ignaz Semmelweis'ın

  1841-1850 yılları arasında Avusturya ve Viyana'da iki farklı doğum hastanesindeki gözlemleri

1850

Ignaz Semmelweis

1854-Mikrop Teorisi

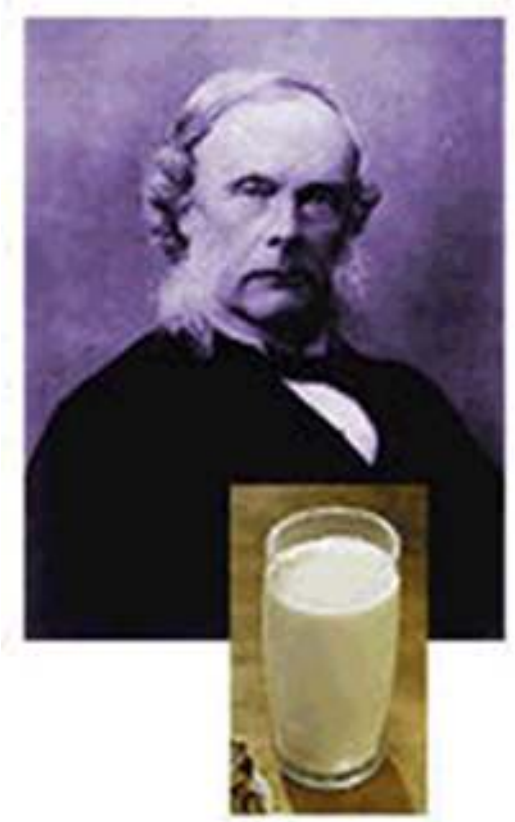
- Pasteur, mikrop tehdit;

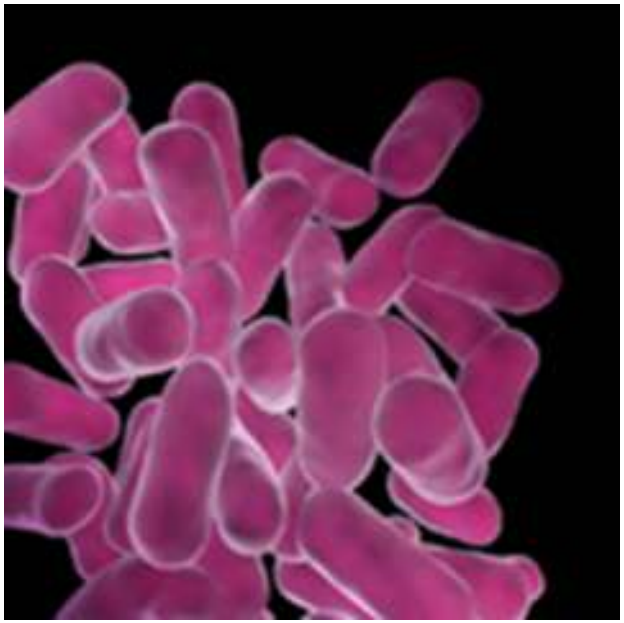
  her mikrop bir hastalığa neden olur (Miasma Teorisinin Sonu)

**“Mikrop hiçbir şeydir,
savunma ise her şey.”**

1877 – Bir bakteri ilk kez saf olarak izole edildi 203. yıl

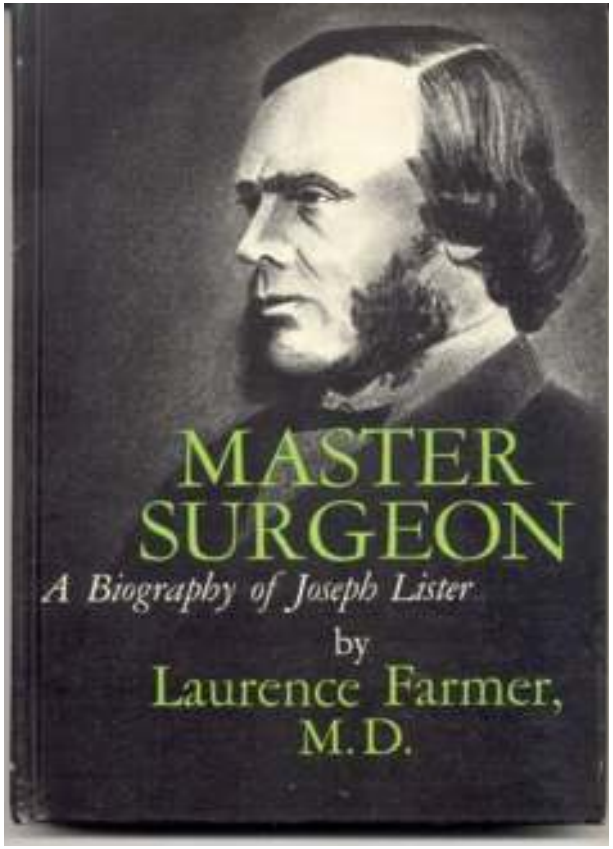
- Joseph Lister (1827-1912)





1877 - Antisepsi

- Joseph Lister (1827-1912)



1877 - Antisepsi

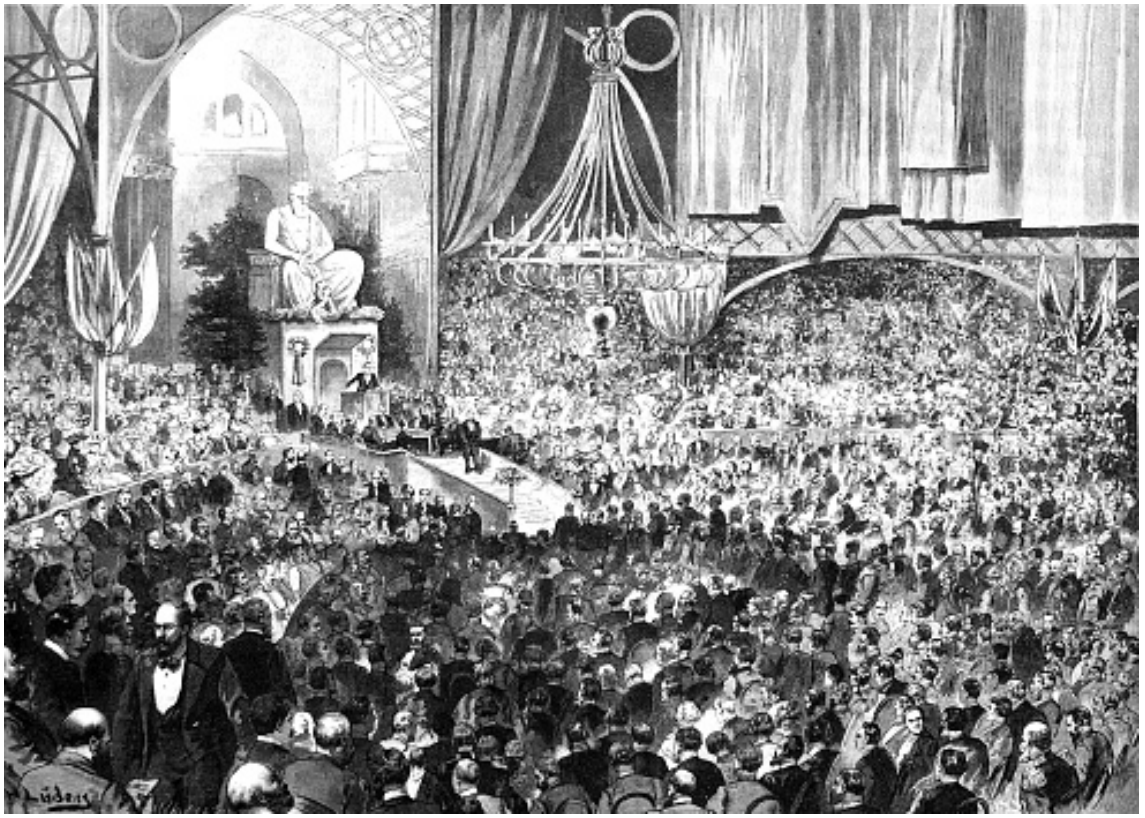
- Joseph Lister (1827-1912)

  "the father of modern antisepsis"

The Lister antiseptic carbolic spray.

1890 – Koch Postülatı

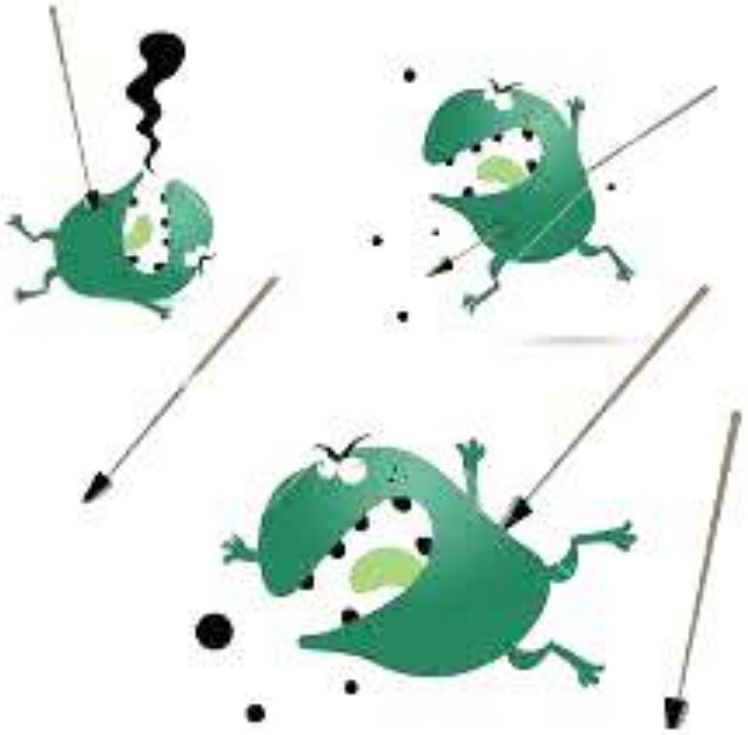
- Koch, bir mikroorganizma ve bir hastalık arasında nedensel bir ilişki kurmak için tasarlanmış dört kriter yayınladı.



Mikroorganizma Sonrası; 216. yıl

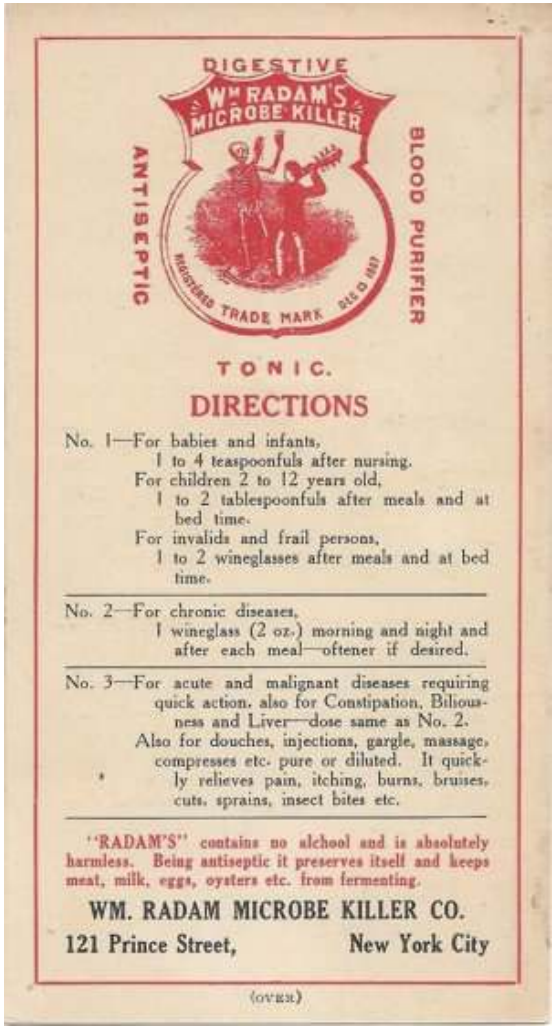
- Bu tarihten sonra mikroorganizmalar ve insanoğlu arasındaki savaş başlamış ve "mikrobu bul, mikrobu yok et" sloganı yıllar boyu sürecek mücadelenin ana fikri olmuştur.

" mikrobu bul, mikrobu yok et"



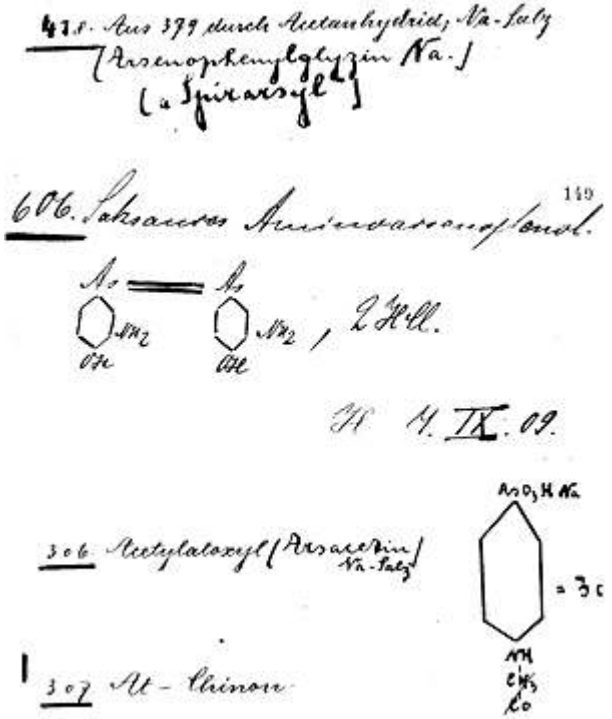
Mikroorganizma Sonrası; 216. yıl

- Mikrop katilleri



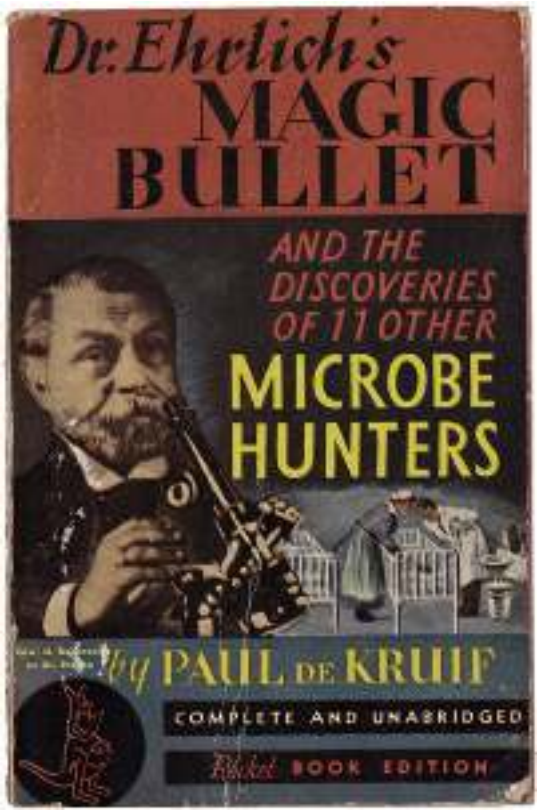
1910 - Mikroorganizma Sonrası; 236. yıl

- Paul Ehrlich'in geliştirdiği "sihirli mermi" kavramı sonucunu vermiş ve bir arsenik türevi olan arsphenamine (salvarsan) ile mikrop katliamına başlanmıştır.



1924 - Mikroorganizma Sonrası; 250. yıl

- Poul de Kruif tarafından 1924 yılında yazılan "Microbe Hunters" kitabında, mikroplarla savaşan cesur ve korkusuz "ölüm savaşçıları" olarak anlatılmaktadır.



Spallanzani

Koch

Paul Ehrlich

Pasteur

Metchnikoff

Mikroorganizmlar yaşam destek sistemimiz

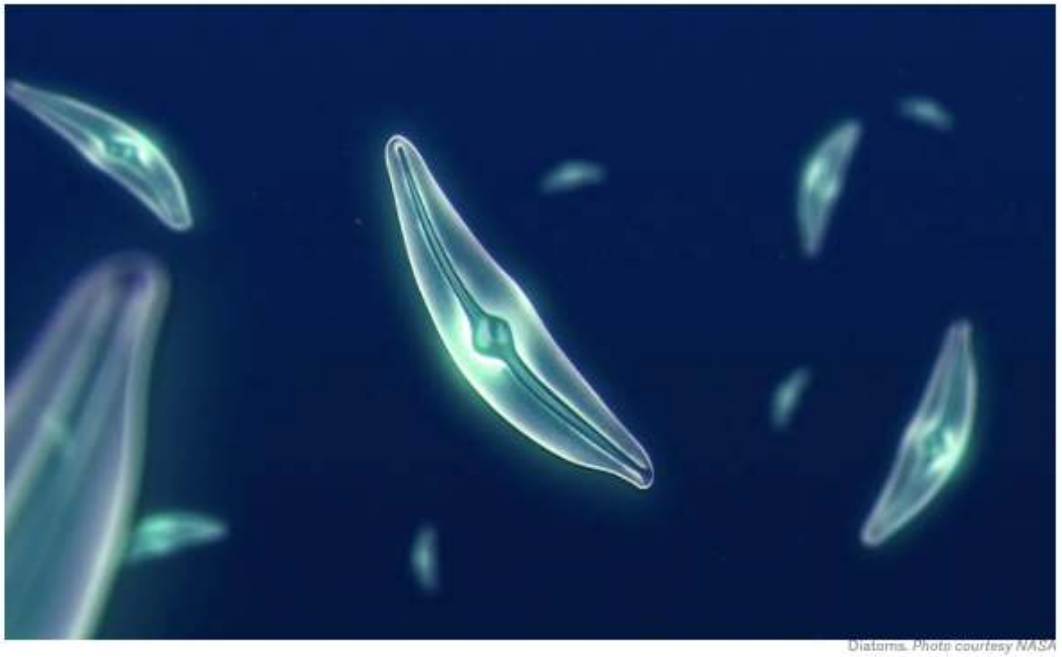
- Dünyamızı yaşanılabilir bir yer haline getirmeleri 2.5 milyar yıllarını aldı…
- Hayatı işgal etmek yerine onu besleyip korurlar.

Sayıca çok üstünler

- 1 gr toprakta 1-10 milyar bakteri

There are more microbial species on Earth than stars in the galaxy

When microorganisms are taken into account, recent studies suggest that Earth might be home to a staggering 1 trillion (10^{12}) species. If true, then the grand effort to discover Earth's biodiversity has only come within a 1,000th of 1 per cent of all species on the planet.



Mikrobiyal Kara Madde

- 10^4 kültürü yapılanlar
  - 10^5 sekansı bulunanlar
    - 10^7 *Earth Microbiome* projesinde kataloglananlar
      -

nature

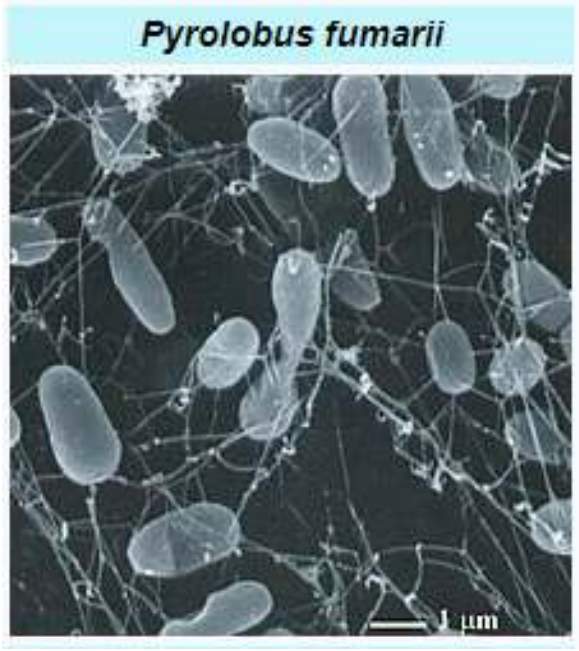
TECHNOLOGY FEATURE | 08 June 2020

The search for microbial dark matter

Researchers are developing technologies to find and grow microbes that biologists have struggled to culture in the lab.

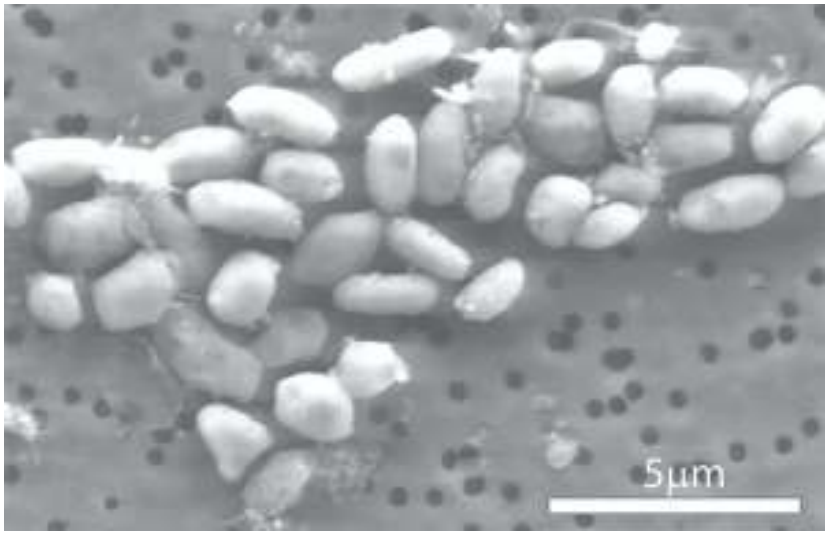
Dayanıklıdırlar

- Ekstremofiller, yüksek basınç ve sıcaklık altında "aşırı ortamlarda" yaşayan organizmalardır.



Dayanıklıdırlar

- Ekstremofiller: Dünyadaki en tuhaf yaşam şekli



Using a Poison to Turn Sunlight into Food

Bacteria from a hot spring in California conduct photosynthesis with arsenic--and suggest a process that might have predated typical photosynthesis

By David Biello

Arsenic, a deadly poison, kills by blocking the ability of cells to produce and consume energy. Yet, some red and green slime mats in briny hot springs in Mono Lake, Calif., use the potent compound rather than water to carry energy during photosynthesis (the process used by bacteria and plants that converts sunlight into food) new research in *Science* reveals.

The newly discovered microbes steal two electrons from the arsenic in the spring water, turning it into so-called arsenate, and use the energy to transform carbon dioxide into food. This only happens in the presence of light, which provides the energy to initiate the process, according to microbiologist Ronald Oremland of the U.S. Geological Survey, who led the discovery.

POISON PHOTOSYNTHESIS: This red slime mat is made up of an extremophile bacteria that uses arsenic to power photosynthesis. *Image: COURTESY OF SCIENCE*

SCIENTIFIC AMERICAN FSG Books

The Best Science Writing Online 2012

Dayanıklıdırlar

- Uçak yakıtını besin kaynağı olan bakteriler yakıt tankında korozyona neden olurlar.

Microbiological Contamination in Aircraft Fuel Tanks

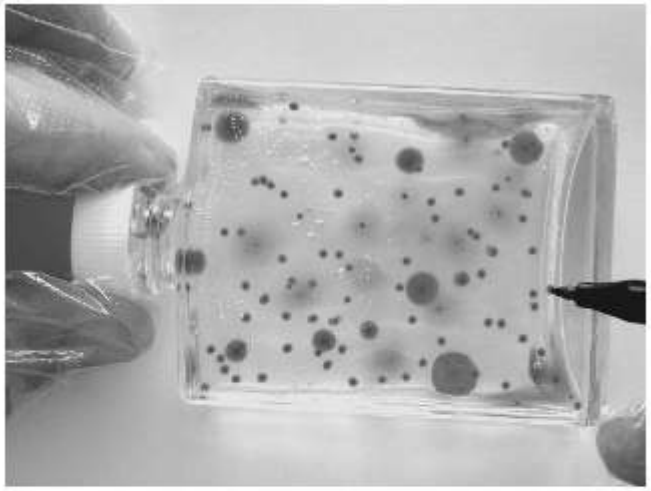
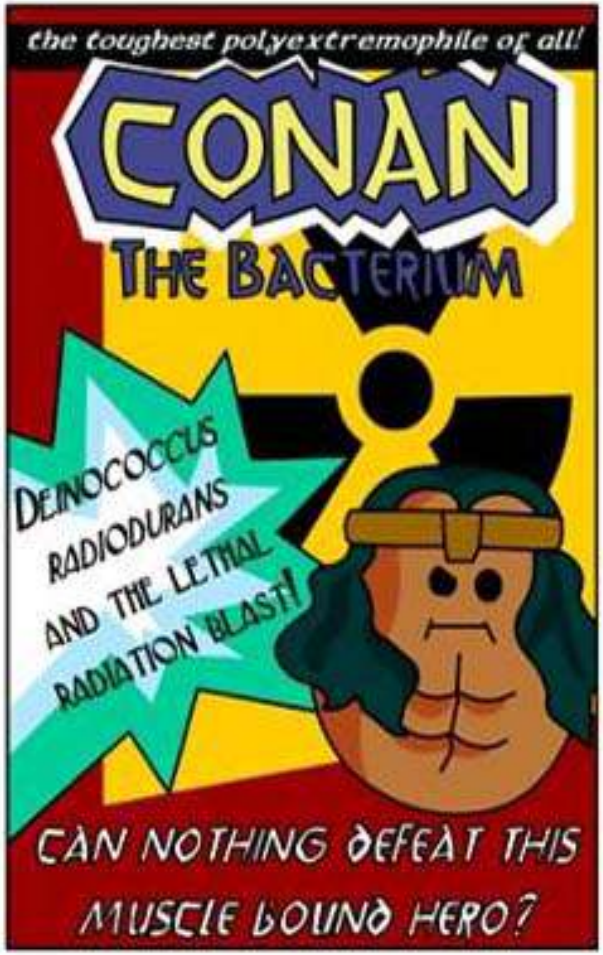
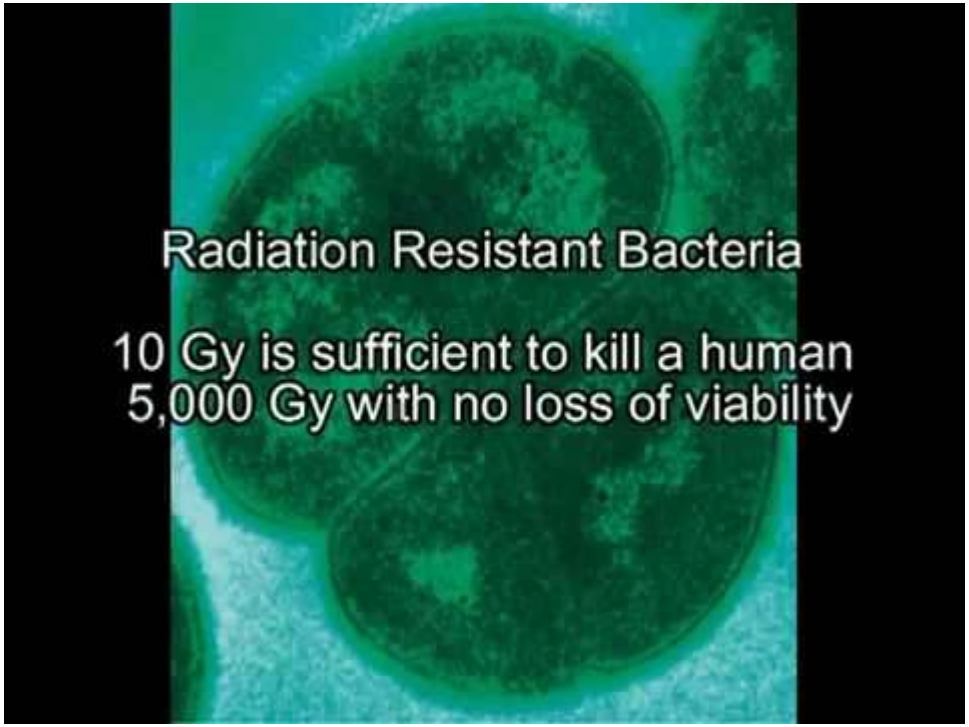


Figure 3

Counting "colonies" of microbes in fuel that have grown in a MicrobMonitor^2 test

Dayanıklıdırlar





DEINOCOCCUS RADIODURANS

Not many bacteria have a nickname, but *D. radiodurans* has earned its moniker, Conan the Bacterium. It is one of the most radiation-resistant organisms on Earth, able to withstand 10,000Gy (measurement unit for absorbed radiation) of ionising radiation. In contrast, just 5Gy can kill a human. *D. radiodurans* is also able to deal with UV radiation, desiccation and extreme cold. Like any true hero, its power is now being used for good: *D. radiodurans* and other bacteria from the same genus are now being engineered to help clean up radioactive sites left over from the Cold War.

Dayanıklıdırlar

Mariana Çukur 10.994 m

Stratosfer'de üç yeni mikroorganizma keşfedildi

Hintli bilim insanları Stratosfer'in üst kısımlarında, üç yeni bakteri türü keşfetti.

Hintli bilim insanları, Atmosferin 12 ile 50km yükseklik arasında bulunan Stratosfer tabakasının üst kısımlarında, yeryüzünde şu ana kadar görülmemiş ultraviyole ışınlara dayanıklı üç yeni tür bakteri türü keşfetti.

Keşfedilen yeni bakterilere astrofizikçi Fred Hoyle'nin anısına Janibacter Hoylei, balonun yürüttüğü deneye katkılarından ötürü ISRO'nun şerefine Bacillus Isronensis ve Hindistan'ın eski astronomlarından Aryabhata'nın anısına Bacillus Aryabhata isimleri verildi.

Haydarabad'da bulunan Milli Balon Üssü'nden havalanan 736 bin 238 metreküplük balonun taşıdığı bilimsel kargo içinde bulunan 38 kilogramlık likit neon içinde tutulan örnekler, 20 kilometre ve 41 kilometre arasında değişen irtifalarda toplandı.

Tüm deney tüplerinin yeryüzüne dönmesinin ardından açılması üzerine, toplamda 12 bakteri ve 6 mantar kolonisi keşfeden bilim insanları, bunların dokuzunun 16S RNA sıralamasında olduğunu belirledi. Bu sıralamanın Dünya üzerinde bulunan mikroorganizma çeşitlerinin %98'inden fazlasıyla benzer olduğu belirtiliyor. Ancak ilk olarak PVAS-1, B3 W22 ve B8 W22 olarak adlandırılan örneklerin tamamiyle farklı türler olduğu keşfedildi. Bu üç türün ortak özelliği çok yüksek UV ışınlarına karşı dayanıklı olmaları.

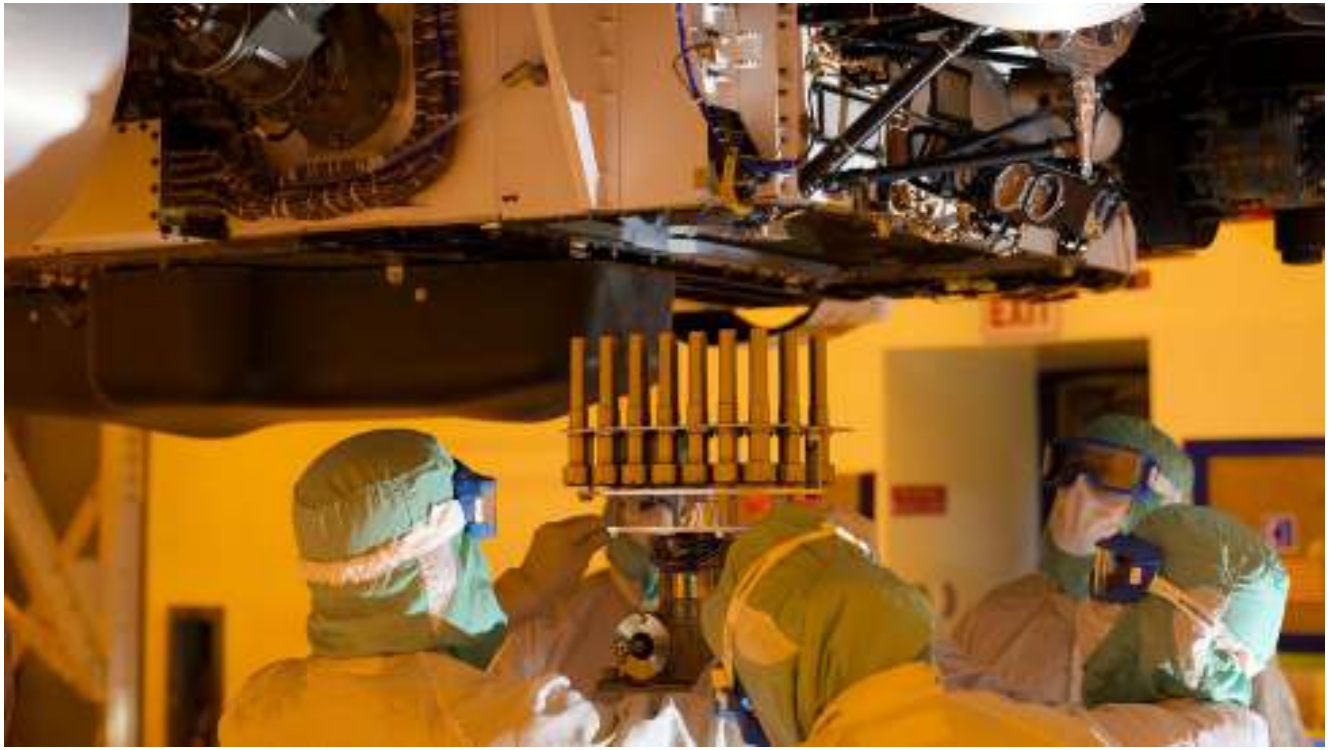
Dayanıklıdırlar

- Uluslararası Uzay İstasyonunda yaşayan dört yeni tür bakteri bulundu

Dayanıklıdırlar

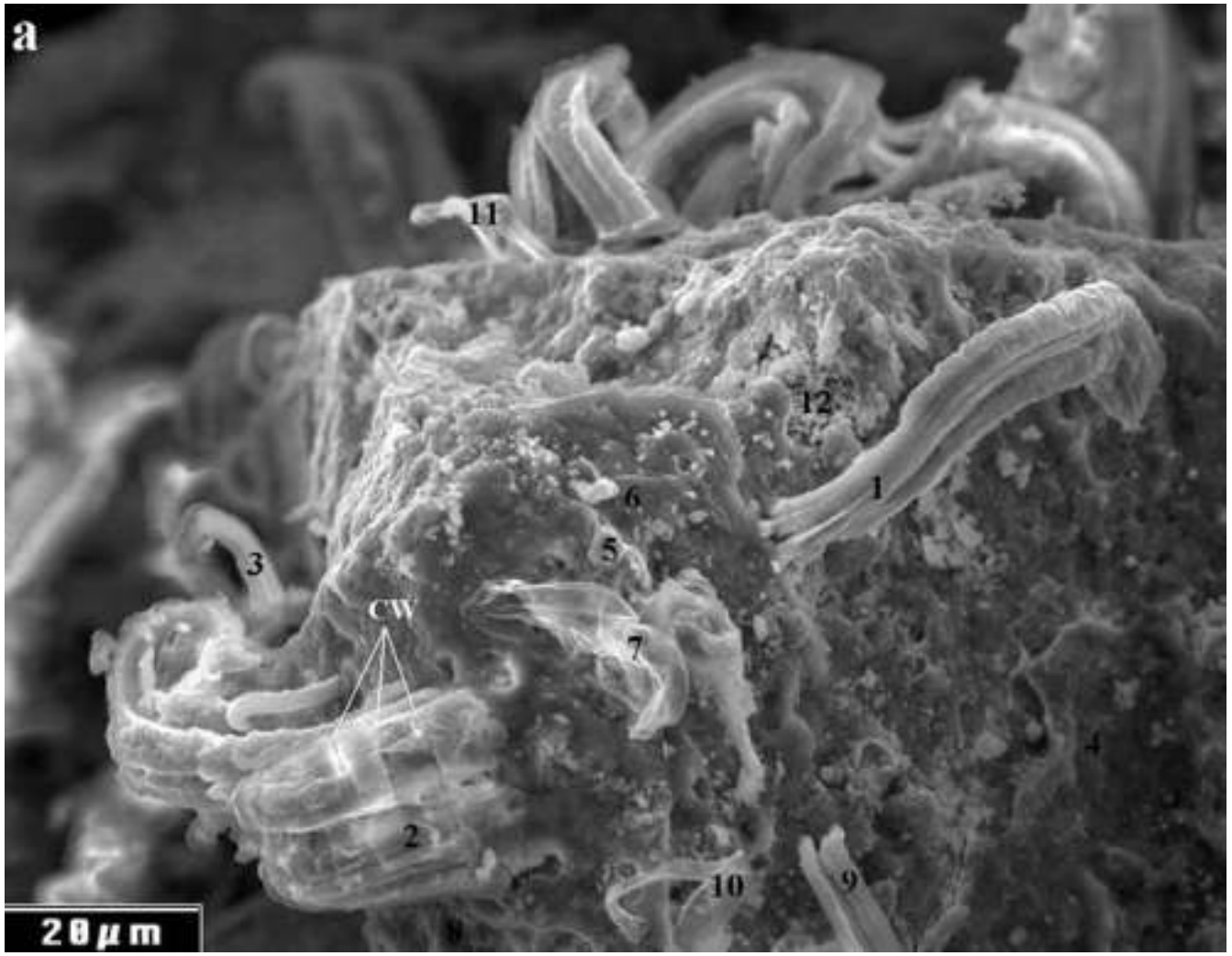
- Kızıl Gezegene bugüne kadar 30 uzay aracı gönderildi.

Could humans have contaminated Mars with life?



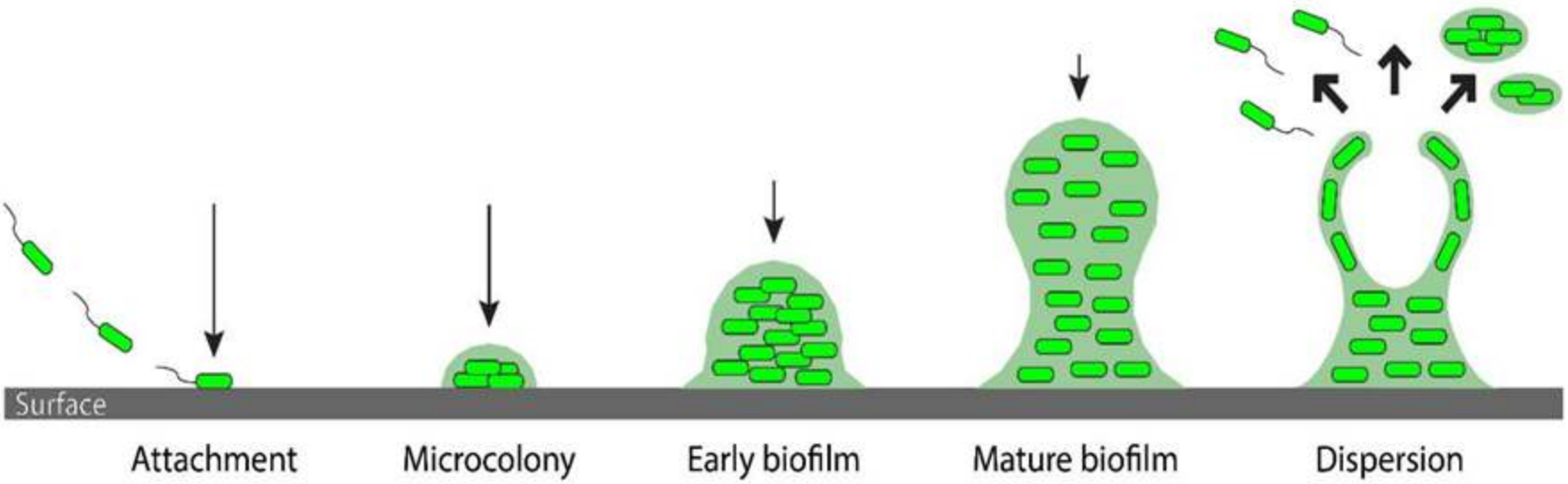
Mikrop varsa hayat var

- Martian meteorite ALH84001, Antartika



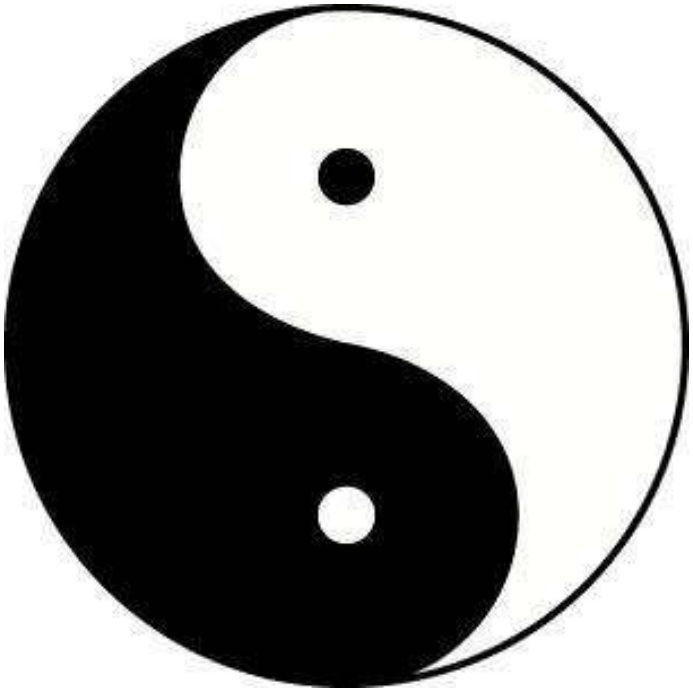
Mükemmel Zamanlama

Mükemmel Zamanlama



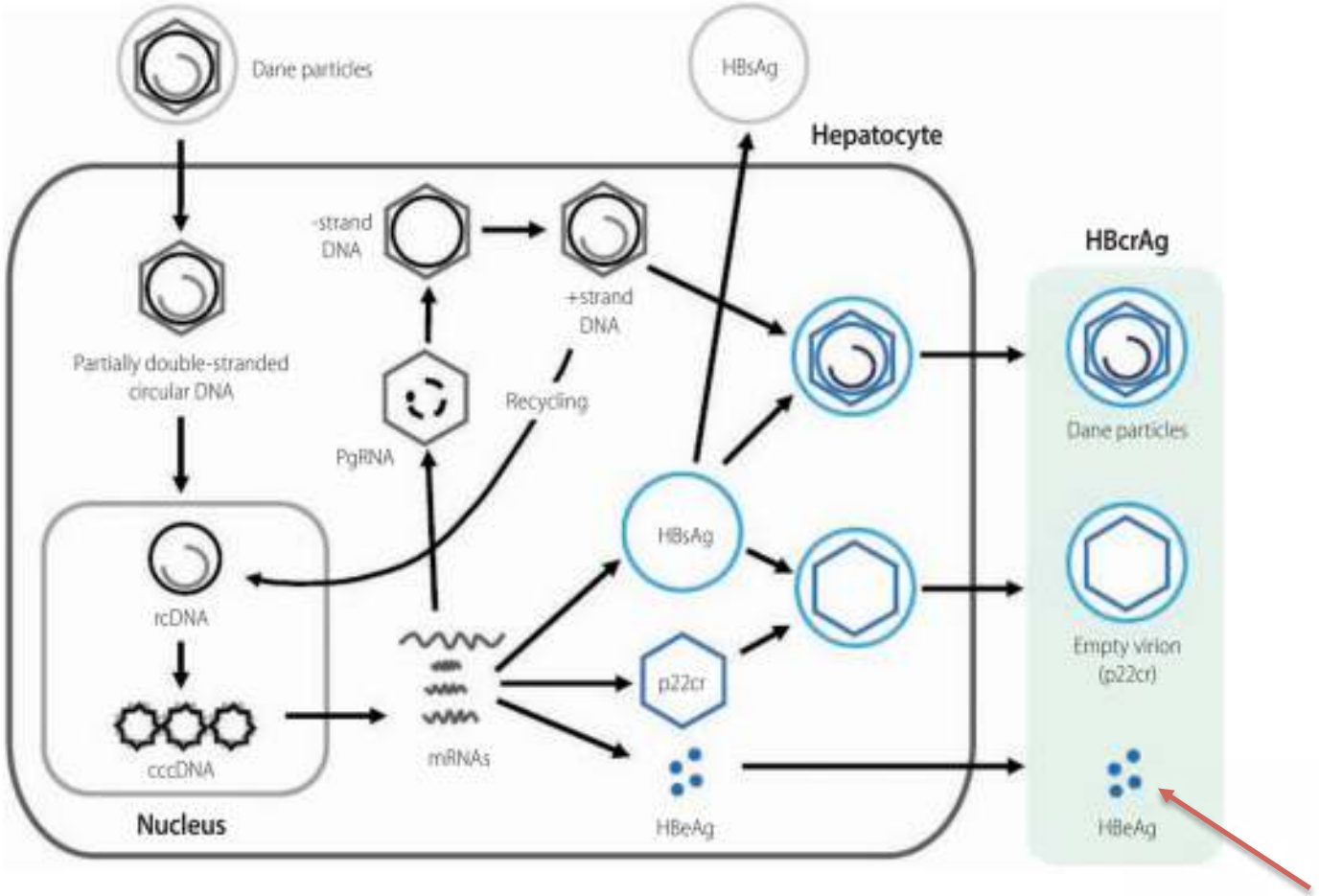
Potansiyelinin Farkında Olma

- /Dengesiz Patojen

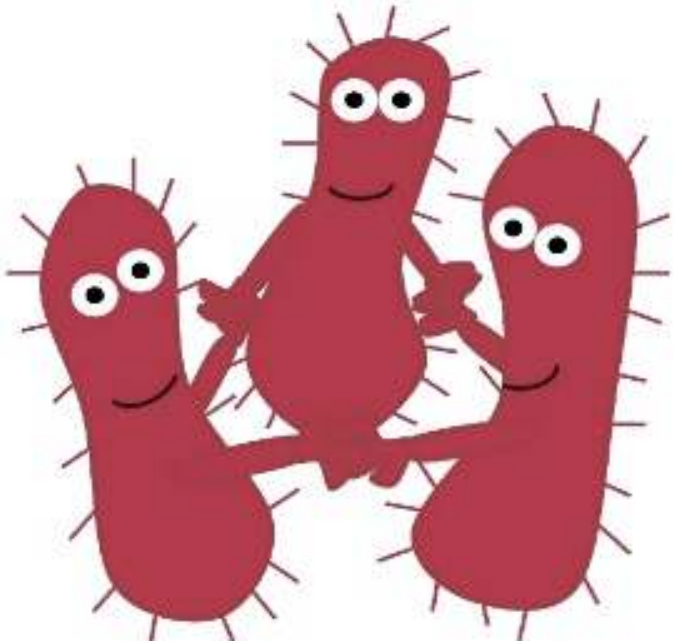


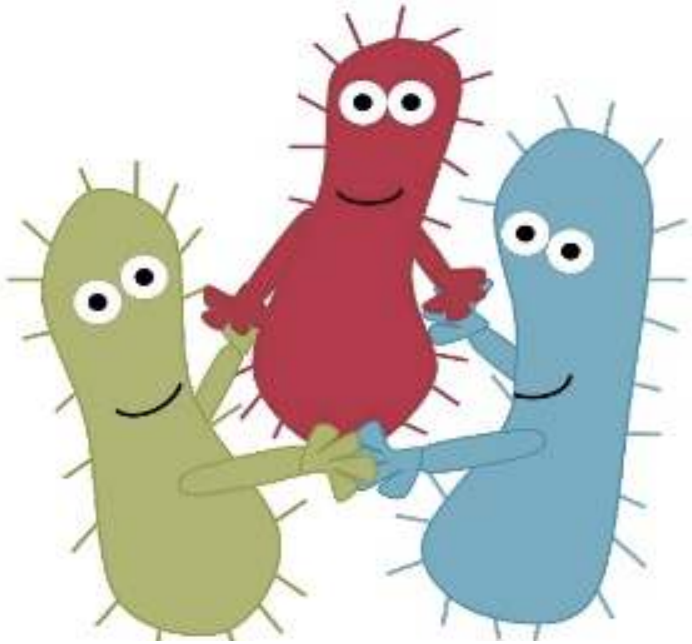
Potansiyelinin Farkında Olma

- /Dengesiz Patojen



Yardımlaşma ve haberleşme





Yardımlaşma ve haberleşme

Yardımlaşma ve haberleşme

Teaching bacteria a new language

Yoram Gerchman* and Ron Weiss*†‡
*Departments of *Electrical Engineering and †Molecular Biology, Princeton University, Princeton, NJ 08544*

In the nascent field of synthetic biology (1), the engineering of novel cell–cell communication capabilities will become critical. Synthetic biology involves the creation of artificial gene and metabolic networks to program new cell and organism behaviors. Recent accomplishments have demonstrated that cells can be engineered to carry out novel tasks (refs. 2–10; R.W. and S. Basu, www.hpcaconf.org/hpca8), and hint that someday we will be able to program cell behaviors with the same ease and capability that we now program computers. However, to achieve

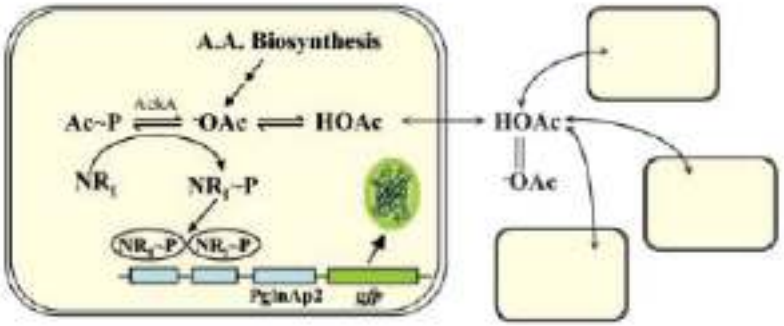
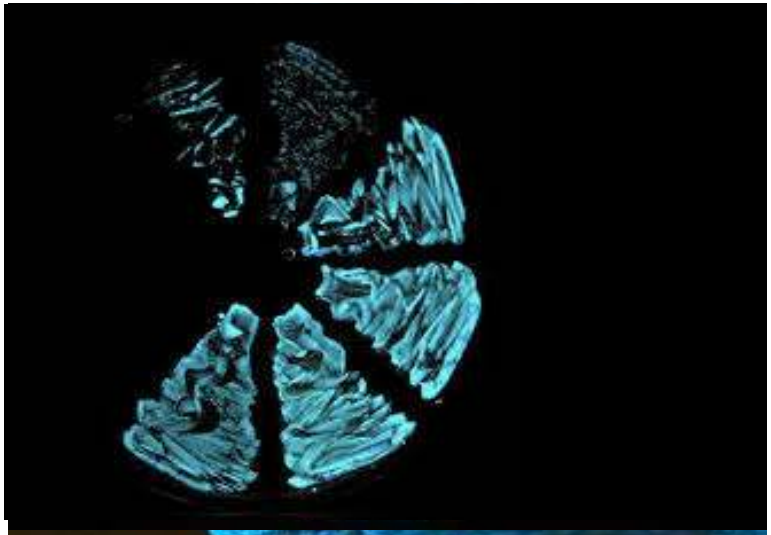
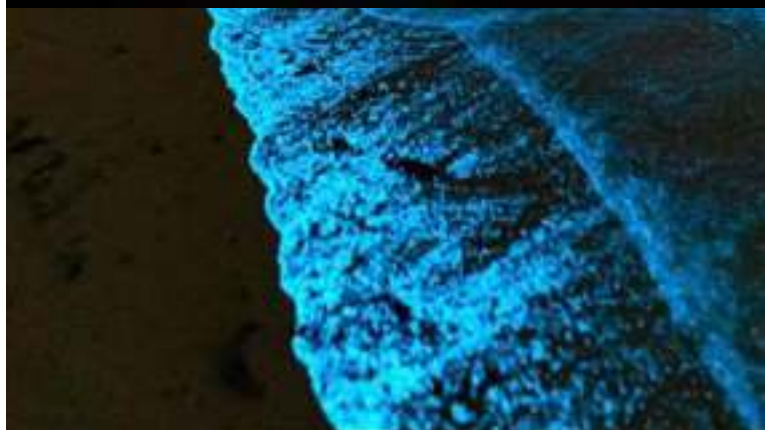


Fig. 1. Basic operation of the engineered acetate QS circuit. Ac~P, acetyl phosphate; ⁻OAc, acetate; HOAc, acetic acid; A.A., amino acid; NR_I, nitrogen regulator protein I; *gfp*, gene for green fluorescent protein; AckA, acetate kinase; PglnAp2, glnAp2 promoter.

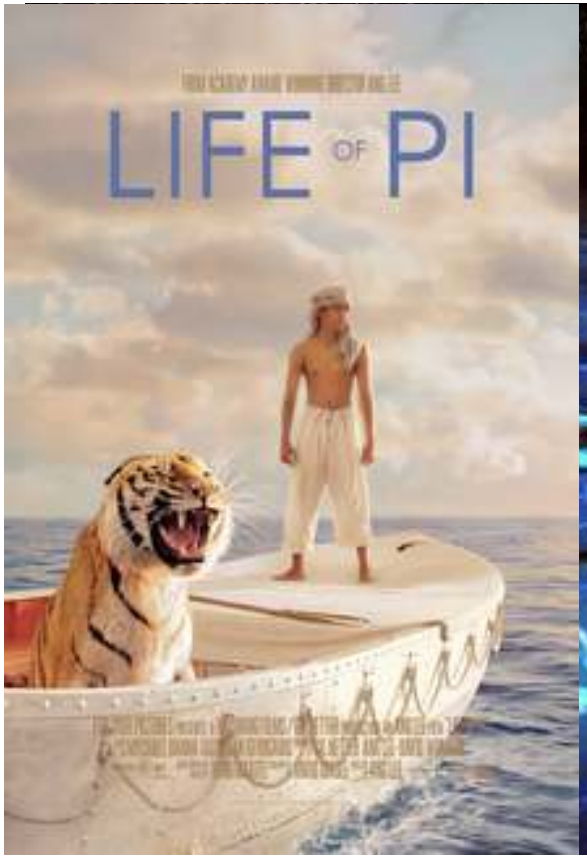
Yakamoz

- *Vibrio fischeri*'nin biyolüminesans

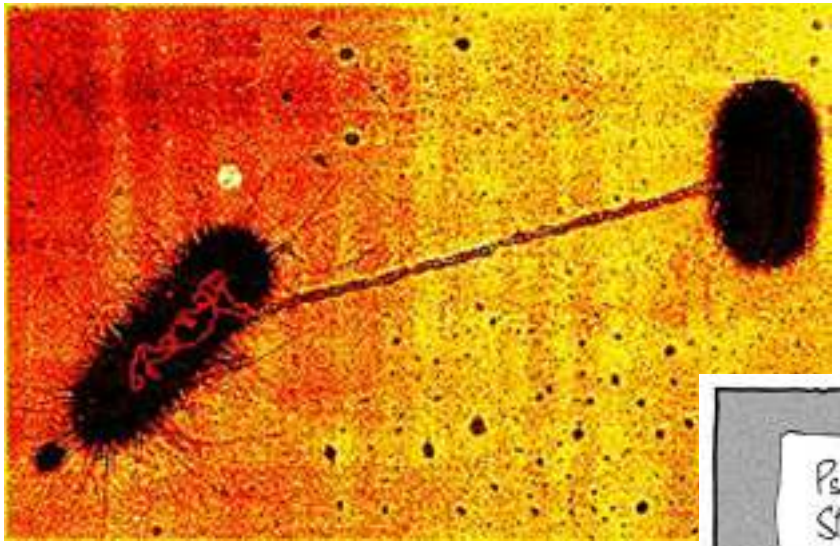




Yakamoz

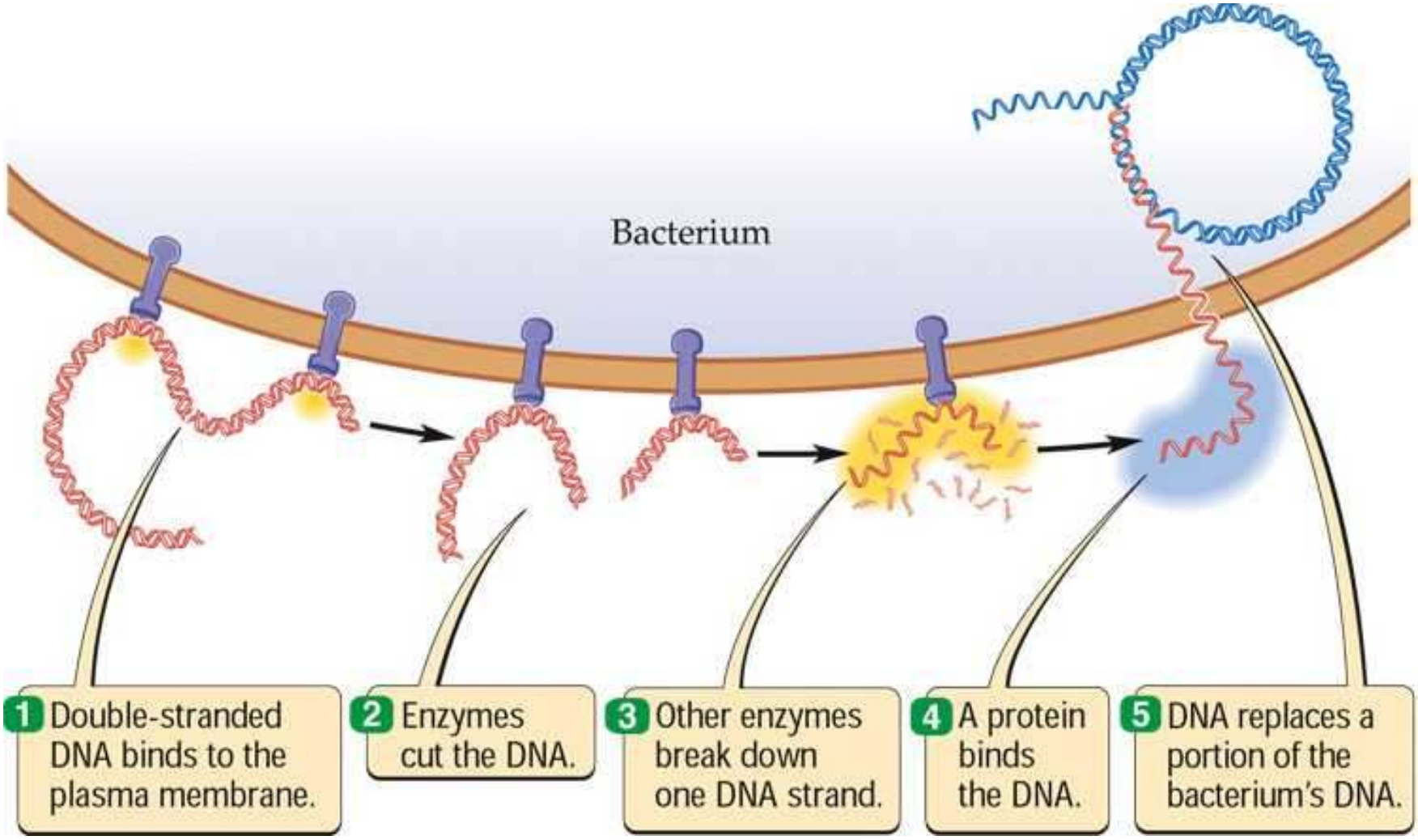


Paylaşıyorlar



Paylaşıyorlar

- Ölen bakterilerin işe yarar DNA'ları boşa gitmiyor.



Koşullara uyum sağladılar

- Yeryüzünde yaşamış canlıların %99'u yok oldular.

Koşullara uyum sağladılar

- *Bacillus marismortui*

nature
International weekly journal of science

Access
To read this story in full you will need to login or make a payment (see right).

nature.com • Journal home • Table of Contents

Letters to Nature

Nature 407, 897-900 (19 October 2000) | doi:10.1038/35038060; Received 15 November 1
Accepted 4 July 2000

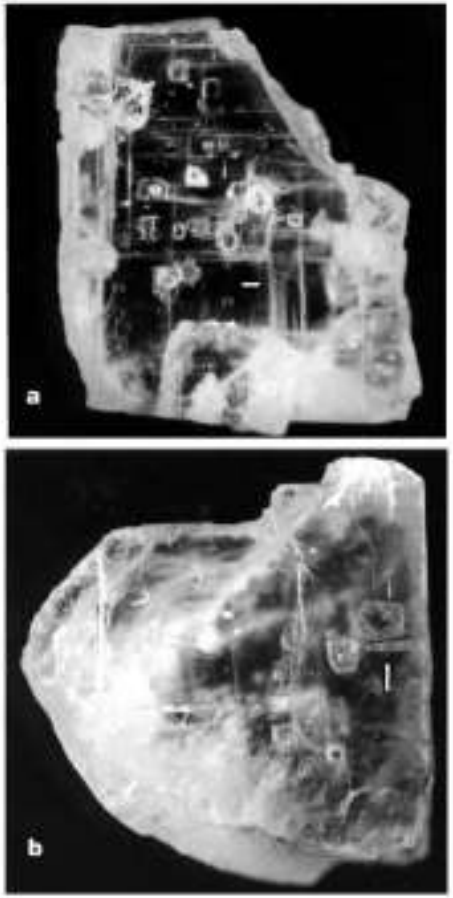
Isolation of a 250 million-year-old halotolerant bacterium from a primary salt crystal

Russell H. Vreeland[1], William D. Rosenzweig[2] & Dennis W. Powers[3]

1. Department of Biology, West Chester University, West Chester, Pennsylvania 19383, USA
2. Consulting Geologist, Box 27, Archery, Texas 79021, USA

Correspondence to: Russell H. Vreeland[1]. Correspondence and requests for materials should be addressed to R.H.V. (e-mail: [illegible]).

Bacteria have been found associated with a variety of ancient samples[1], however few studies are generally accepted due to questions about sample quality and contamination. When Cano and Borucki[2] isolated a strain of Bacillus sphaericus from an extinct bee trapped in 25–30 million-year-old amber, careful sample selection and stringent sterilization techniques were the keys to acceptance. Here we report the isolation and growth of a previously unrecognized spore forming bacterium (Bacillus species, designated 2-9-3) from a brine inclusion within a 250 million-year-old salt crystal from the Permian Salado Formation. Complete gene sequences of the 16S ribosomal DNA show that the organism is part of the lineage of Bacillus marismortui and Virgibacillus pantothenticus. Delicate crystal structures and sedimentary features indicate the salt has not recrystallized since formation. Samples were rejected if brine inclusions showed physical signs of possible contamination. Surfaces of salt crystal samples were sterilized with strong alkali and acid before extracting brines from inclusions. Sterilization procedures reduce the probability of contamination to less than 1 in 10[-3].



Oldest bacteria ever found (BBC Online image)

Yönlerini bulabilirler

- *Magnetospirillum magnetotacticum*
- Sitoplazmasında manyetik nano partiküller (magnetozom) içeren granüllere sahip bu gram negatif, spiral bakteri dünyanın manyetik alanına göre kendini konumlandırabiliyor.

International Journal of *Molecular Sciences*

MDPI

Article

The Magnetosome Protein, Mms6 from *Magnetospirillum magneticum* Strain AMB-1, Is a Lipid-Activated Ferric Reductase

Dilini Singappuli-Arachchige [1,2], Shuren Feng [1,3,†], Lijun Wang [1,3], Pierre E. Palo [1], Samuel O. Shobade [1,3], Michelle Thomas [1] and Marit Nilsen-Hamilton [1,2,3,*]

Görebilirler

- Proteorhodopsin
- Bakterinin yüzeyinde bir güneş paneli gibi yer alır.
- İnsan retinasındaki “OPSİN” homologlarıdır. Bu bakterilerin de “duyusal fonksiyonlara” sahip olduğu anlamına gelebilir.

1950 - Mikrobiyom kavramı

- Mikrobiyom:

  bir mikrobiyom, mikropların toplamı, genetik elementleri (genomları) ve belirli bir ortamdaki çevresel etkileşimlerdir.

World Microbiome Day | 27th June

2022 theme

"Celebration of The Microbial World"

Mikrobiyom

- Mikrobiyom terimi Nobel Ödülü sahibi Joshua Lederberg tarafından üretildi.

Joshua Lederberg (1925-2008)

Ester Lederberg (1922-2006)

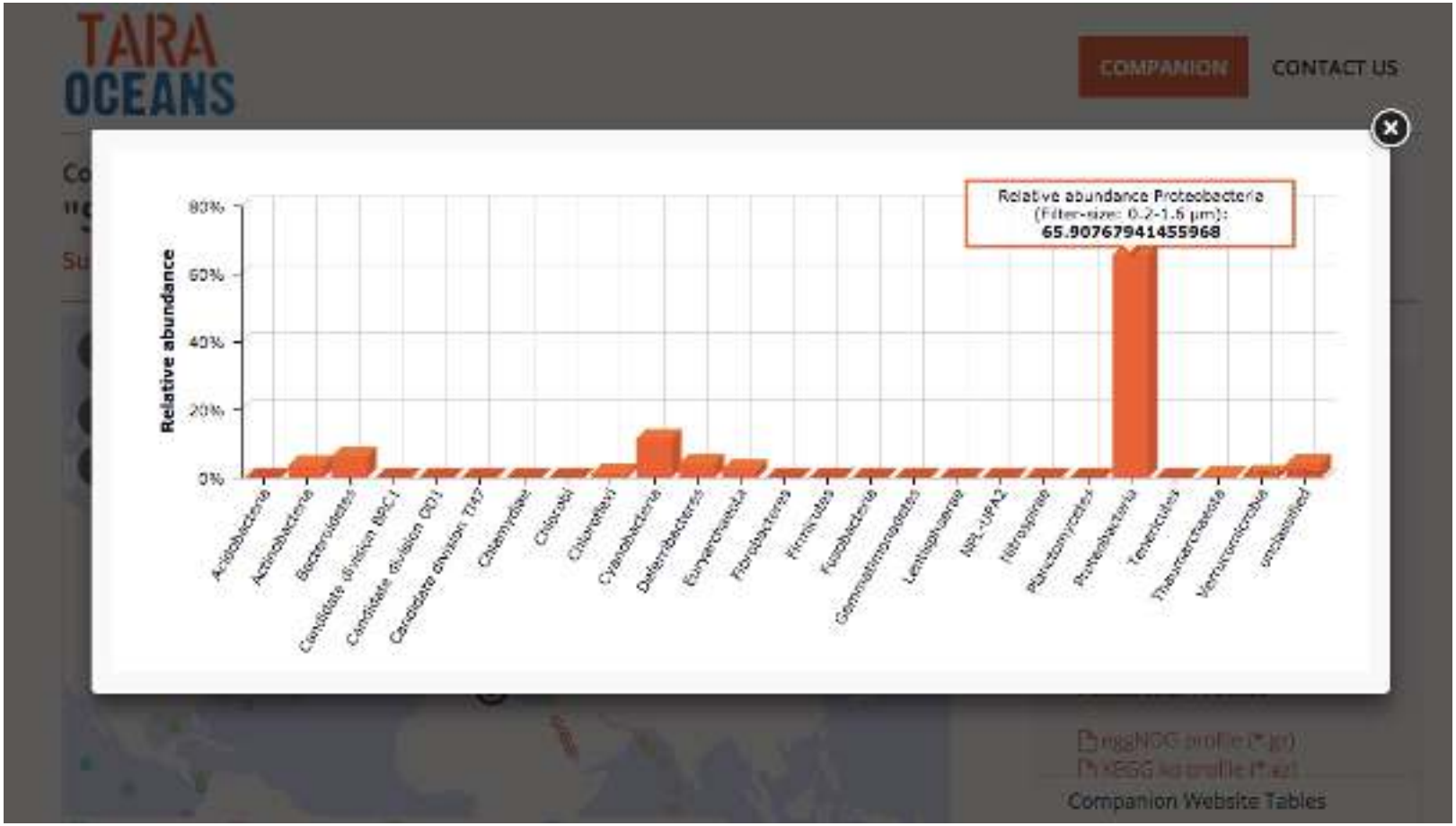
"mikrobiyom" terimini , insan vücudunda bulunan ortak, simbiyotik ve belki de patojenik mikroorganizmalardan oluşan ekolojik bir sistemi tanımlamak için kullanmıştır

Mikrobiyom

- 1958, Nobel Ödülü

Mikrobiyom

- Deniz/okyanus mikrobiyomu



Mikrobiyom

- Toprak mikrobiyomu

Mikrobiyom

- Dünya mikrobiyom projesi

Mikrobiyom

- Dünya mikrobiyom projesi

Earth Microbiome Project: Mapping the microbiome of... everything

November 1, 2017, University of California - San Diego

Earth Microbiome Project collaborators collect and analyze samples from diverse environments around the world. Top left: Hiking through the rain forest of Puerto Rico to sample soils with students (credit: Krista McGuire, University of … more

2007 - İnsan Mikrobiyom Projesi

2007 - İnsan Mikrobiyom Projesi

Four Sequencing Centers

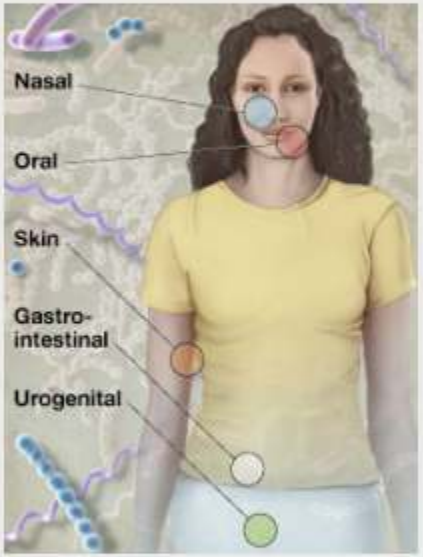
BCM
Baylor College of Medicine

J. Craig Venter INSTITUTE

BROAD INSTITUTE

Washington University in St. Louis

300 'Healthy' People/ 15(18) Body Sites



Evolving Technologies

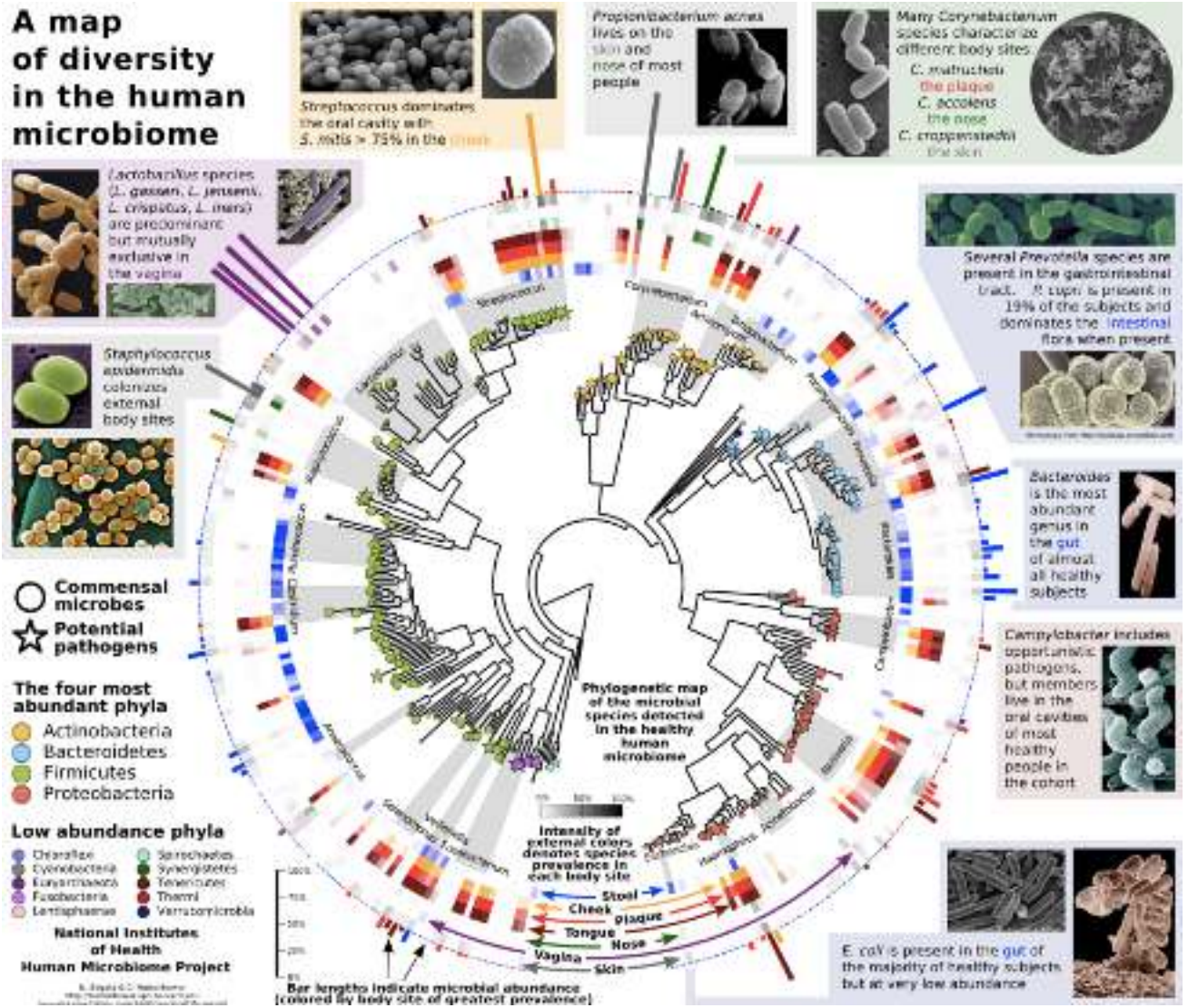
Sanger
30cm
50cm

454
FLX
Titanium

illumina
GAII
HiSeq

12,000 samples collected over 2 years

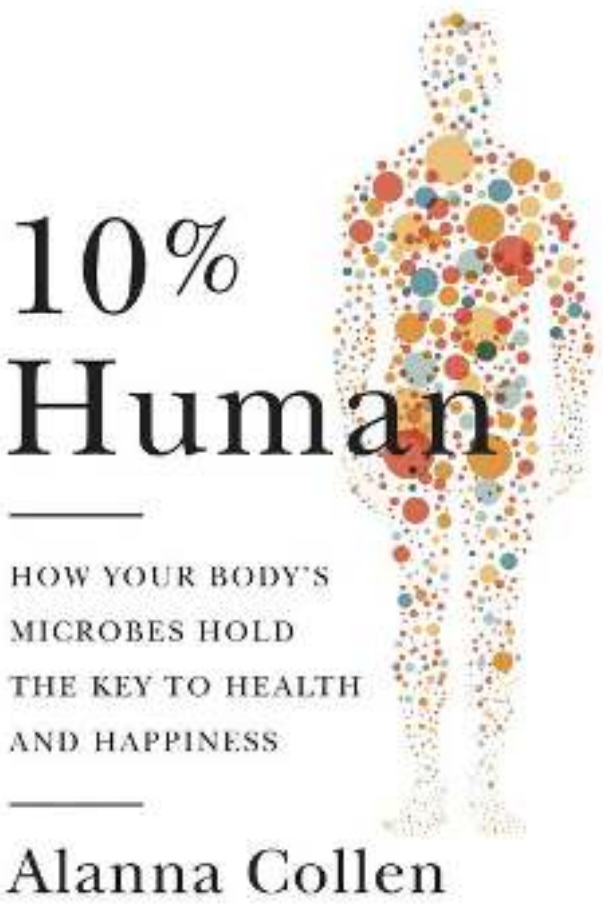
2007 - İnsan Mikrobiyom Projesi



2008 - İnsan Mikrobiyom Projesi

- İlk hesaplamalara göre;

  10 katrilyon insan hücresine karşılık, 100 katrilyon bakteri hücresi



Her yerimiz mikroplarla kaplı

- Muhteşem çeşitlilik

araştırılan 60 farklı göbek deliğinde, 2400 bakteriyel filotip tespit edildi

OPEN ACCESS Freely available online

PLOS ONE

A Jungle in There: Bacteria in Belly Buttons are Highly Diverse, but Predictable

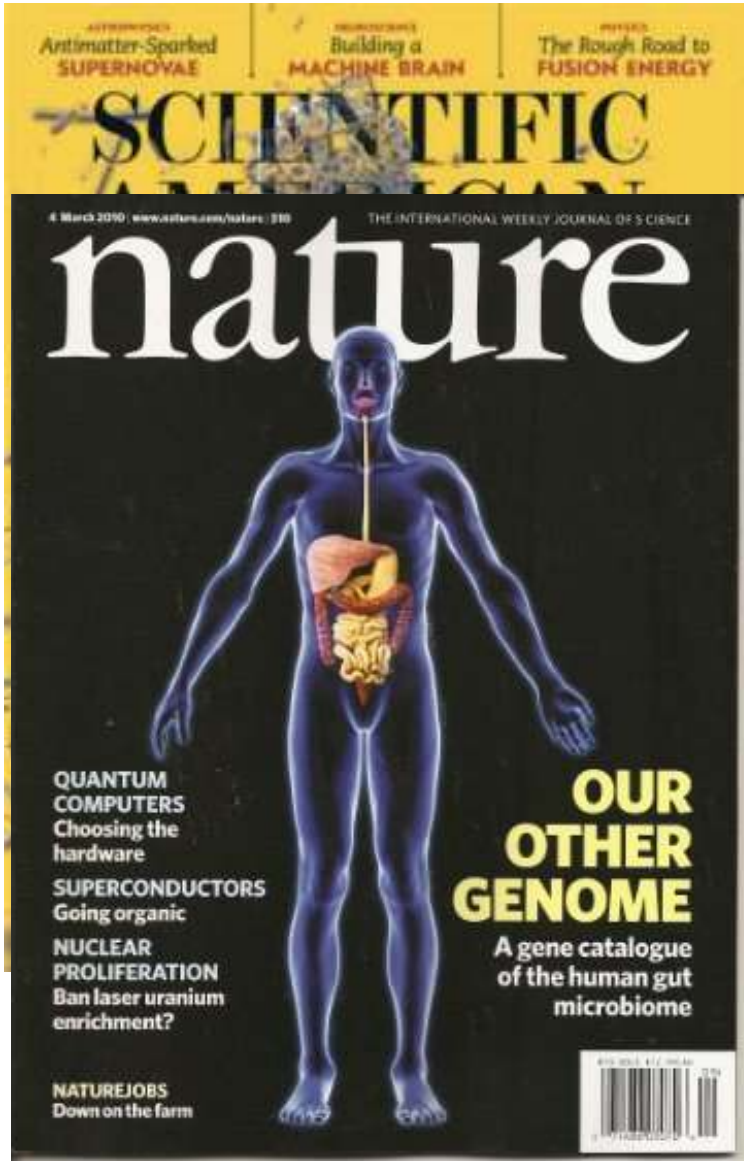
Jiri Hulcr[1,2], Andrew M. Latimer[3], Jessica B. Henley[4], Nina R. Rountree[2], Noah Fierer[4,5], Andrea Lucky[2,6], Margaret D. Lowman[1,7], Robert R. Dunn[2]*

1 School of Forest Resources and Conservation, University of Florida, Gainesville, Florida, United States of America, 2 Department of Biology and Keck Center for Behavioral Biology, North Carolina State University, Raleigh, North Carolina, United States of America, 3 Department of Plant Sciences, University of California Davis, California, United States of America, 4 Cooperative Institute for Research in Environmental Sciences, University of Colorado, Boulder, Colorado, United States of America, 5 Department of Ecology and Evolutionary Biology, University of Colorado, Boulder, Colorado, United States of America, 6 Department of Entomology, University of Florida, Gainesville, Florida, United States of America, 7 North Carolina Museum of Natural Sciences, Raleigh, North Carolina, United States of America

Abstract

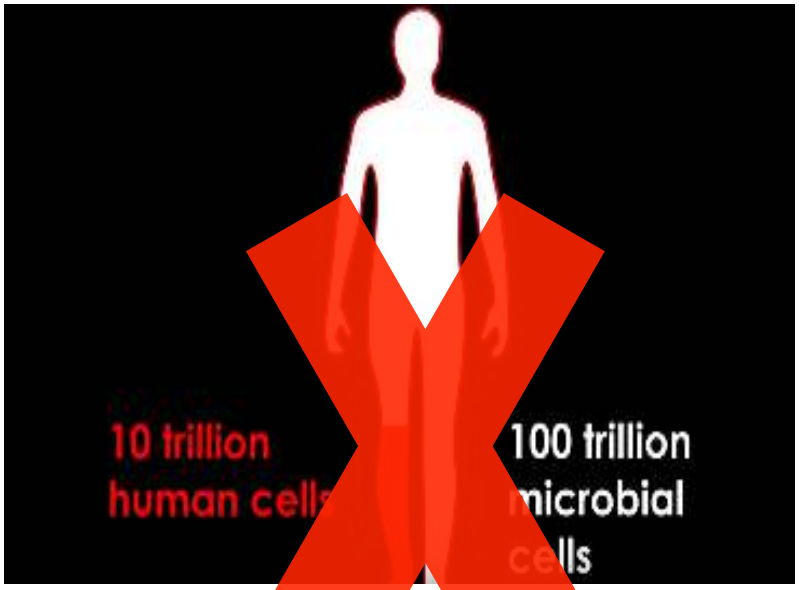
The belly button is one of the habitats closest to us, and yet it remains relatively unexplored. We analyzed bacteria and archaea from the belly buttons of humans from two different populations sampled within a nation-wide citizen science project. We examined bacterial and archaeal phylotypes present and their diversity using multiplex pyrosequencing of 16S rDNA libraries. We then tested the oligarchy hypothesis borrowed from tropical macroecology, namely that the frequency of phylotypes in one sample of humans predicts its frequency in another independent sample. We also tested the predictions that frequent phylotypes (the oligarchs) tend to be common when present, and tend to be more phylogenetically clustered than rare phylotypes. Once rarefied to four hundred reads per sample, bacterial communities from belly buttons proved to be at least as diverse as communities known from other skin studies (on average 67 bacterial phylotypes per belly button). However, the belly button communities were strongly dominated by a few taxa: only 6 phylotypes occurred on >80% humans. While these frequent bacterial phylotypes (the archaea were all rare) are a tiny part of the total diversity of bacteria in human navels (<0.3% of phylotypes), they constitute a major portion of individual reads (~1/3), and are predictable among independent samples of humans, in terms of both the occurrence and evolutionary relatedness (more closely related than randomly drawn equal sets of phylotypes). Thus, the hypothesis that "oligarchs" dominate diverse assemblages appears to be supported by human-associated bacteria. Although it remains difficult to predict which species of bacteria might be found on a particular human, predicting which species are most frequent (or rare) seems more straightforward, at least for those species living in belly buttons.

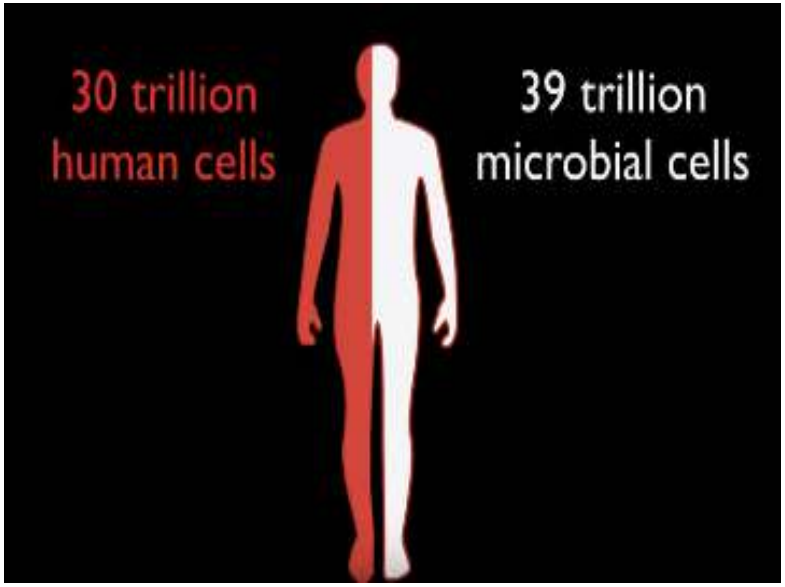
Mikrobiyota



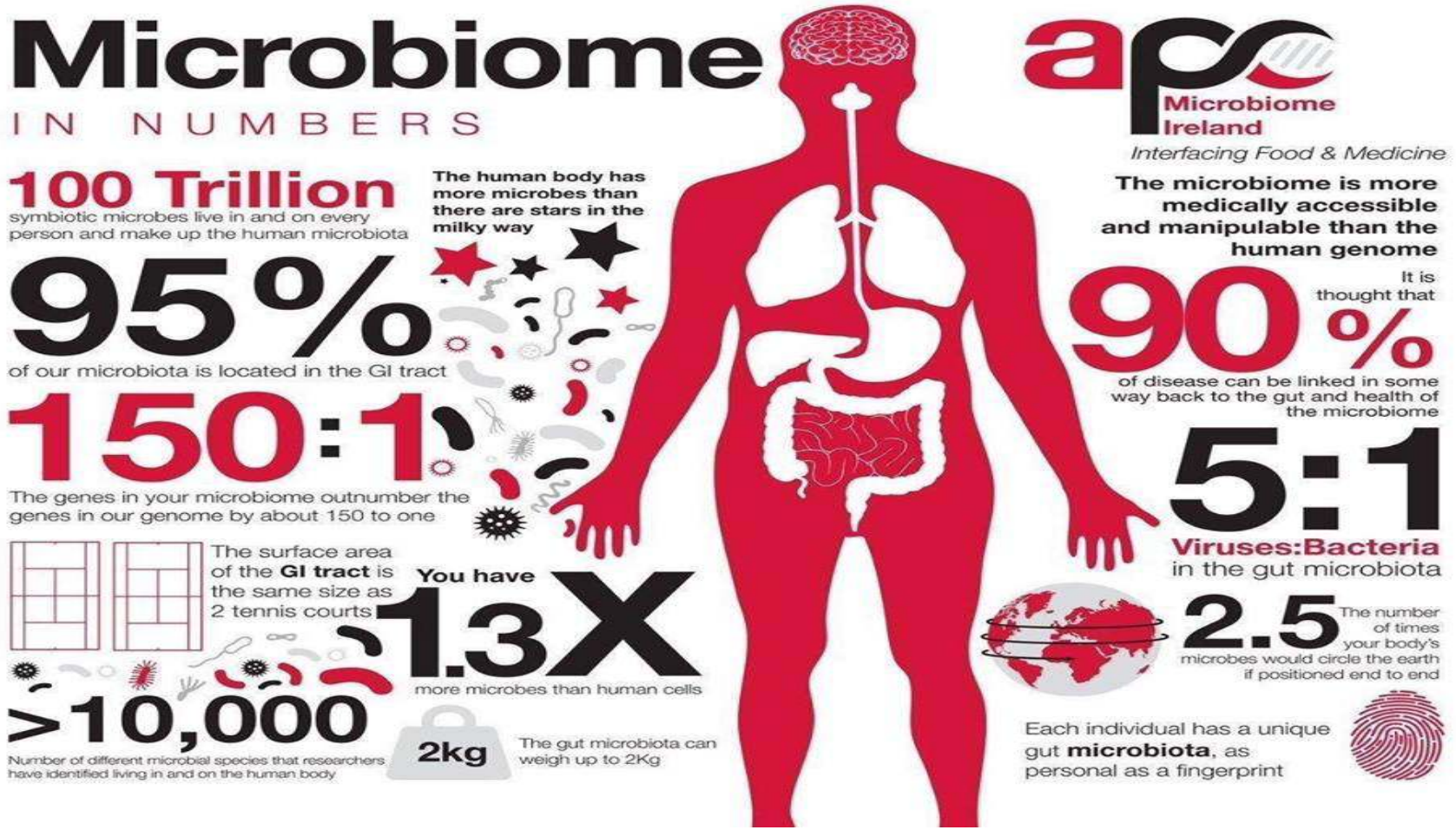
Mikroorganizma/insan hücresi oranı güncellendi!

- %99 insan olarak doğuyoruz, %57 mikroorganizma olarak ölüyoruz!





İnsan Mikrobiyom Projesi-2012'de tamamlandı



Doğumdan ölüme mikrobiyota

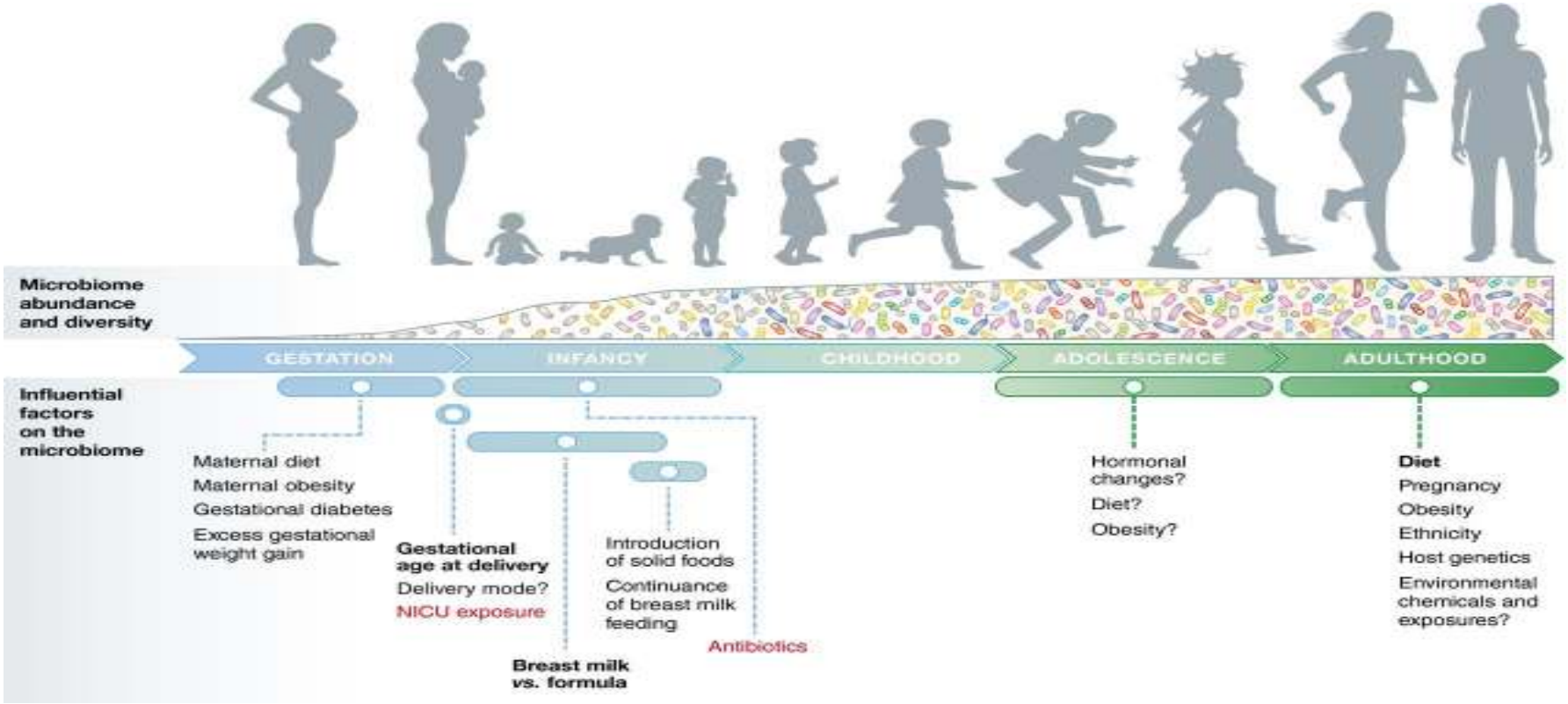
Science & Society

Open Access

Una destinatio, viae diversae

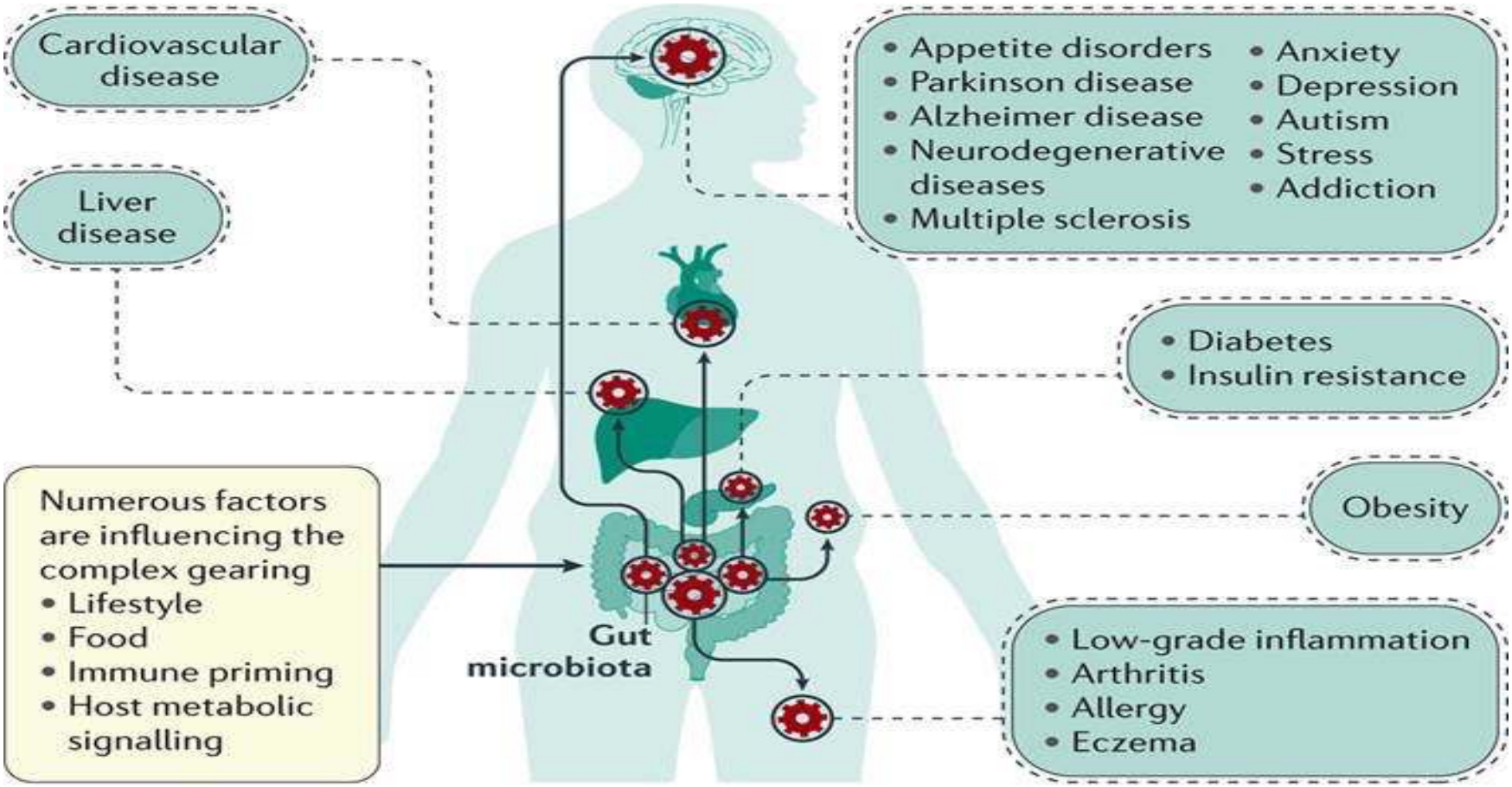
Does exposure to the vaginal microbiota confer health benefits to the infant, and does lack of exposure confer disease risk?

Kjersti Aagaard, Christopher J Stewart, Derrick Chu



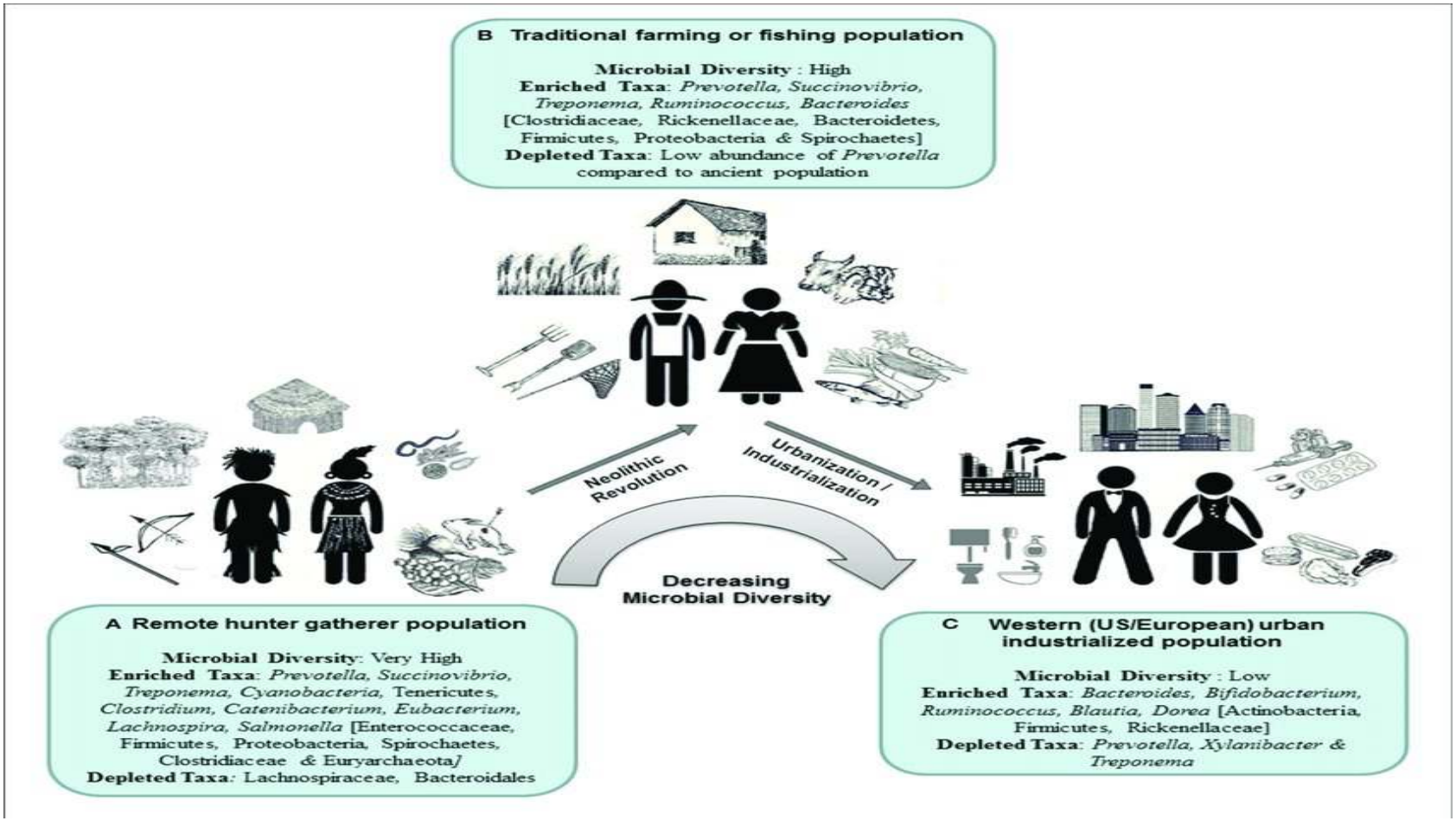
Disbiyozis

- Herhangi bir nedenle mikrobiyotanın dengesinin bozulmasıdır.



Mikrobiyal çeşitlilik

- Mikrobiyal çeşitlilik modern dünyada giderek azalıyor.



Mikrobiyal Çeşitlilik

- Mikrobiyal çeşitlilik modern dünyada giderek azalıyor.

Mikrobiyal Çeşitlilik

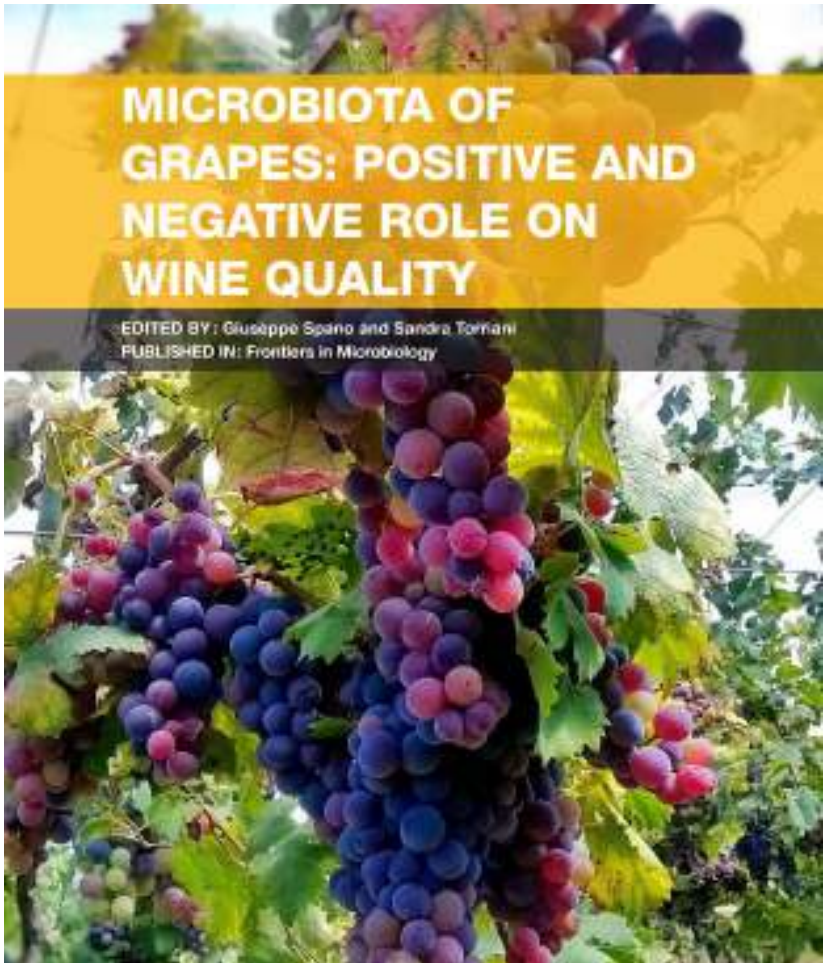
- Mikrobiyal çeşitlilik modern dünyada giderek azalıyor.

Mikrobiyal Çeşitlilik

- Mikrobiyal çeşitlilik modern dünyada giderek azalıyor.

Mikrobiyota ve lezzet

- Kaliteli şarap, sirke bölgenin mikrobiyotası ile ilişkili



Mikrobiyota ve lezzet

FOOD FOR THOUGHT

Sourdough Hands: How Bakers And Bread Are A Microbial Match

November 12, 2018 · 11:37 AM ET

LINDSAY PATTERSON

"Our data suggests that something about baking seems to be changing the hands of the people who do the baking," says ecologist Rob Dunn.

Rick Gayle/Getty Images

Mikrobiyota ve lezzet

That's the surprising finding from a sourdough bake-off experiment, coordinated by ecologists Rob Dunn and Anne Madden. Fifteen sourdough experts from around the world arrived at a Belgian baking center with brand-new homemade starters, fed from the exact same ingredients sent from Dunn's lab. But before the bakers could get their hands into the dough, they held them out to Madden for bacterial swabbing.

Partnered with analysis of the starter's microbial ecosystem, Dunn and his collaborators were able to draw a close connection between bread, bakers and their bacterial species.

"It's a reminder that we have a really intimate relationship with our food," says Dunn. "Not only do we impact the species in our food, but the species in our food impacts the species on or in our bodies."

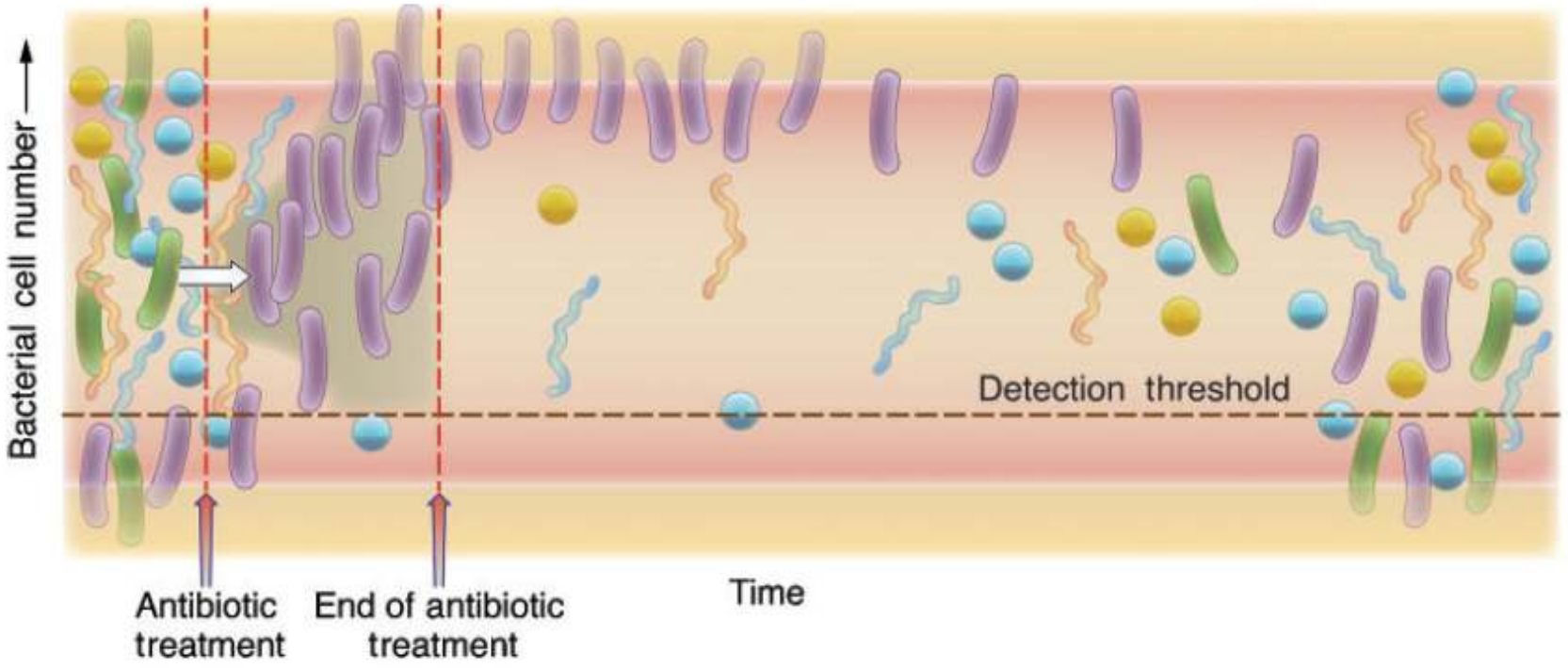
Author and scientist Rob Dunn helped conduct an experiment to explore the microbial interaction between bakers and sourdough bread.

Lauren Nichols/NPR

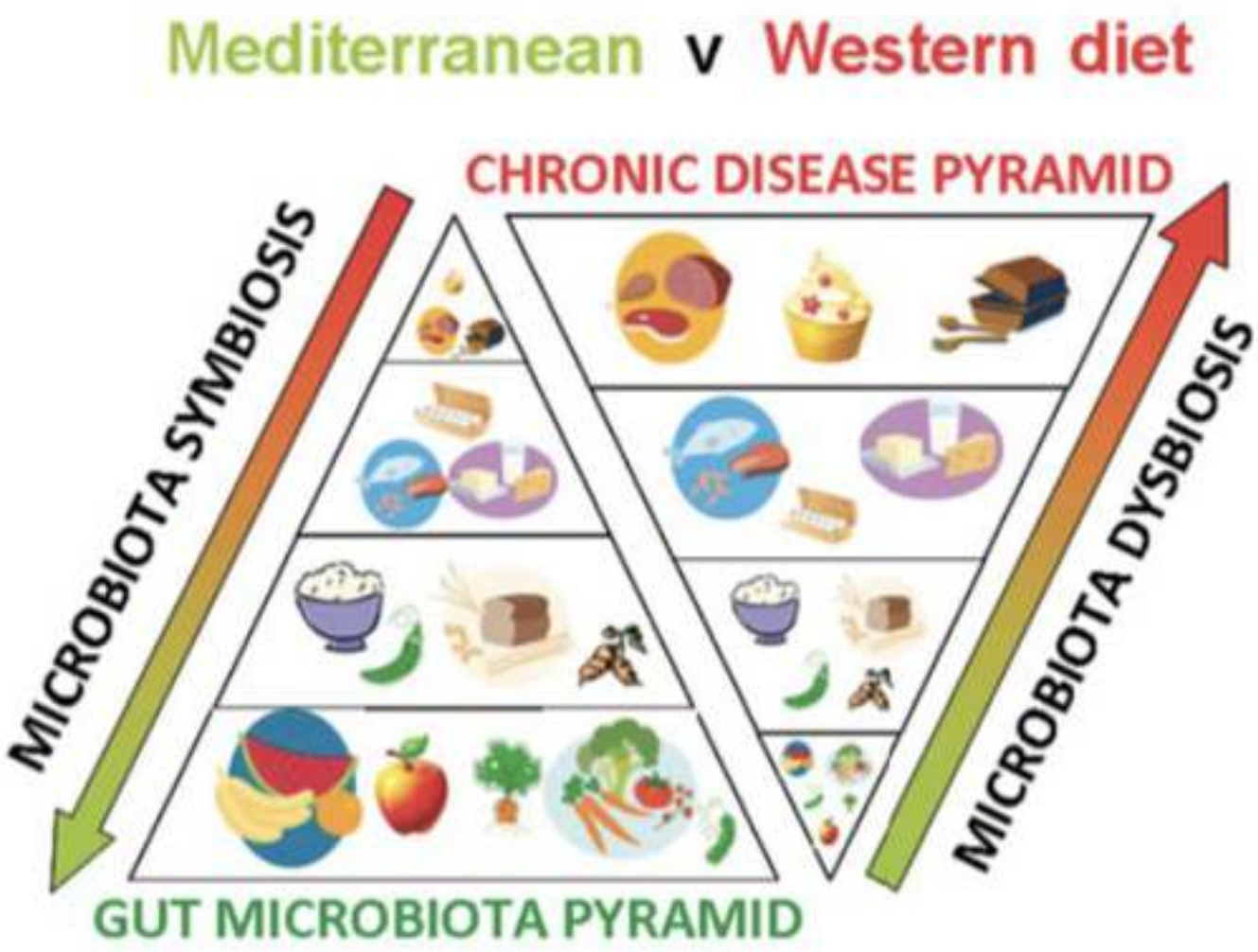
Mikrobiyota ve antimikrobiyaller

Long-term impacts of antibiotic exposure on the human intestinal microbiota

Cecilia Jernberg,[1] Sonja Löfmark,[2] Charlotta Edlund[3,4] and Janet K. Jansson[5,6]



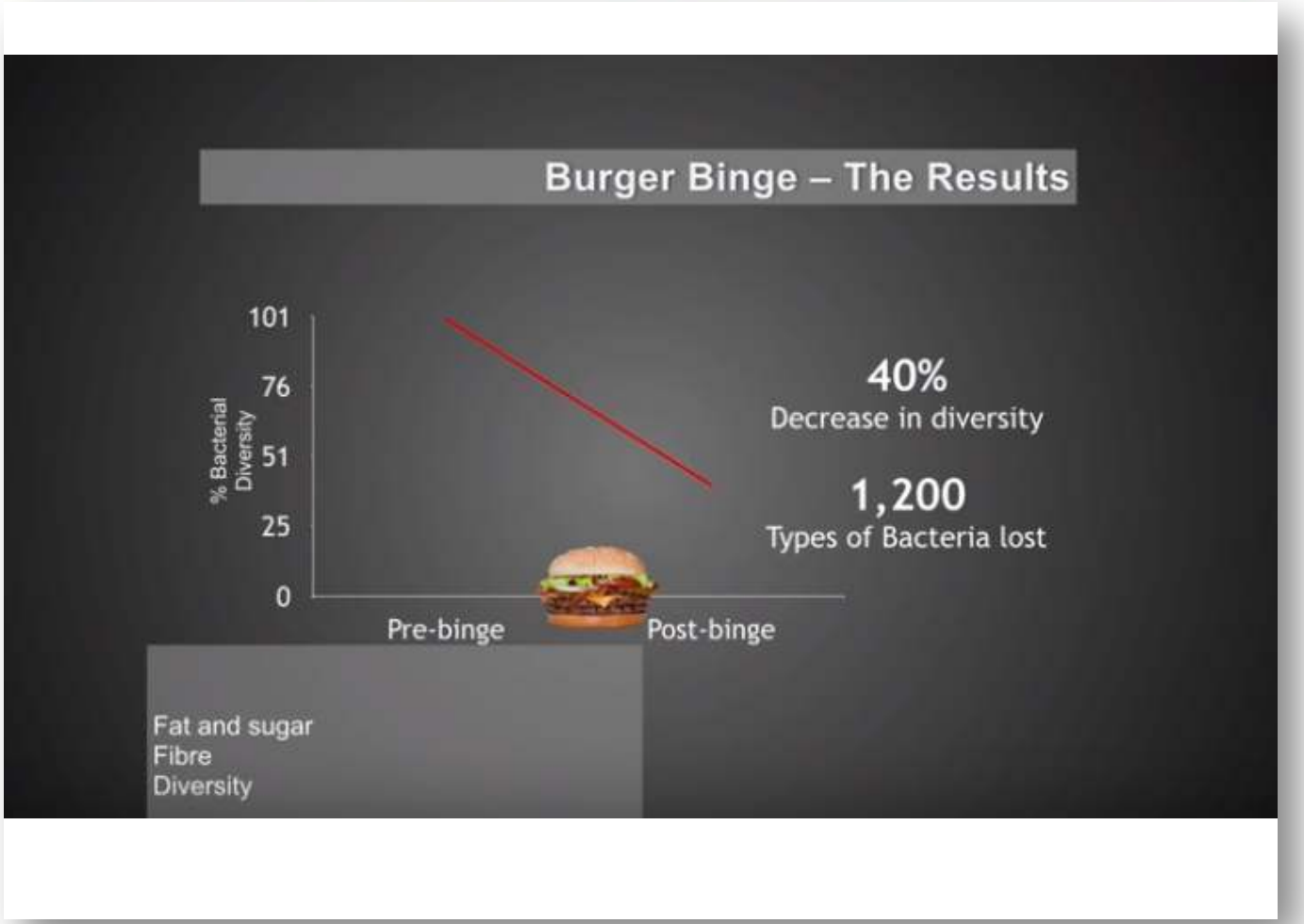
Mikrobiyota ve beslenme



Mikrobiyota ve Beslenme

- King's College'da genetik epidemiyoloji profesörü Tim Spector tarafından yapılan araştırma.

Mikrobiyota ve Beslenme

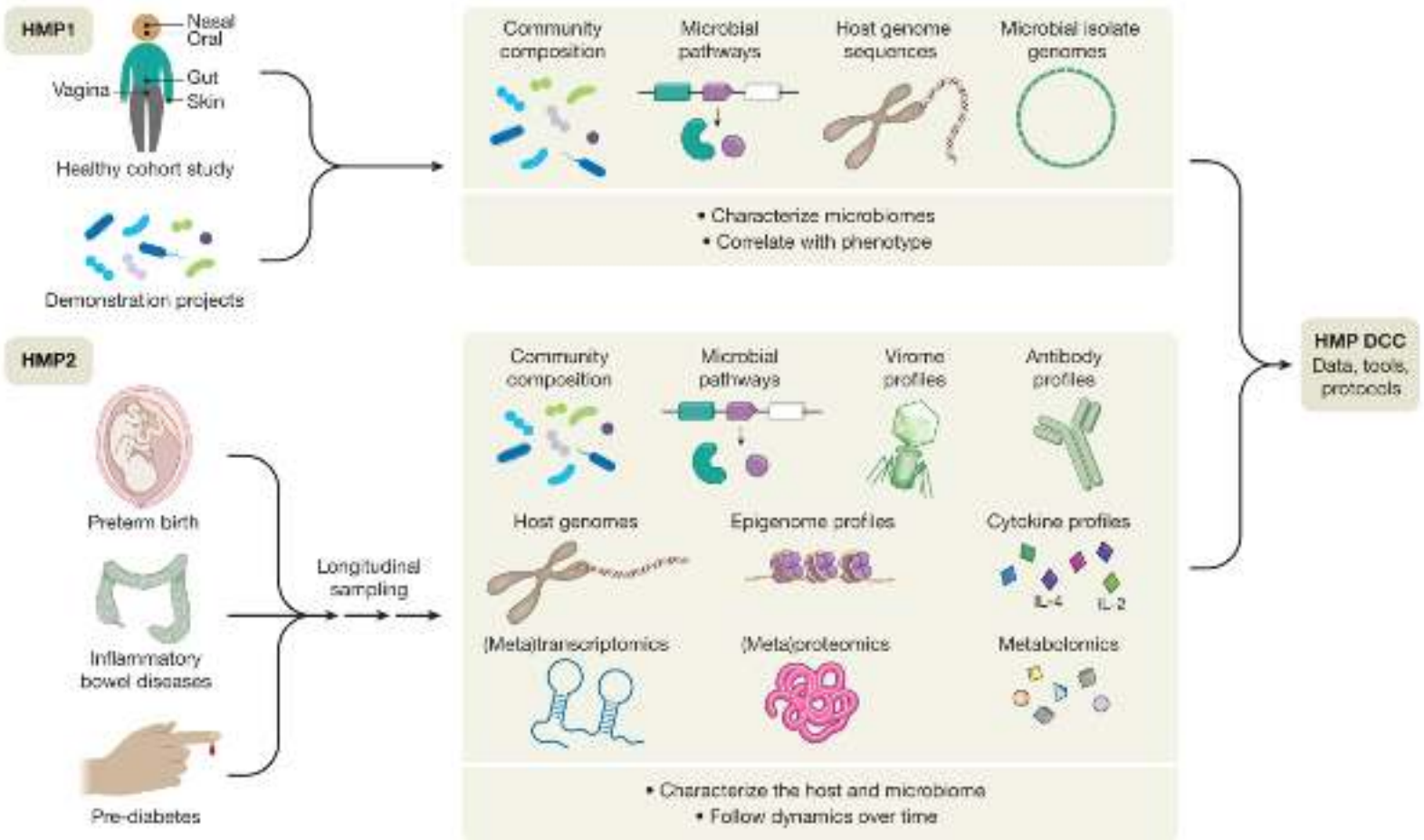


Mikrobiyota ve Evcil Hayvanlar

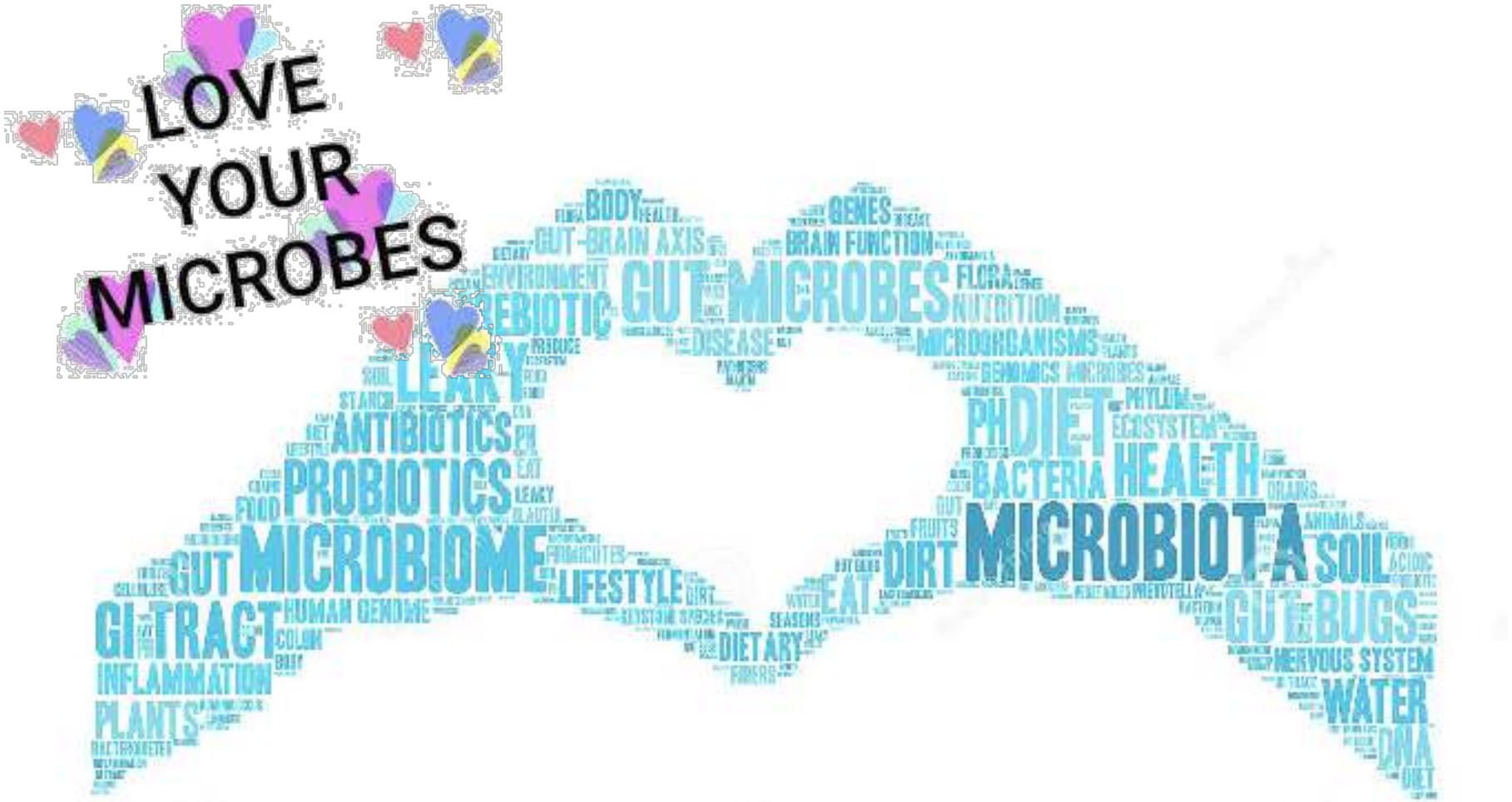
AnimalBiome

Mikrobiyota ve Evcil Hayvanlar

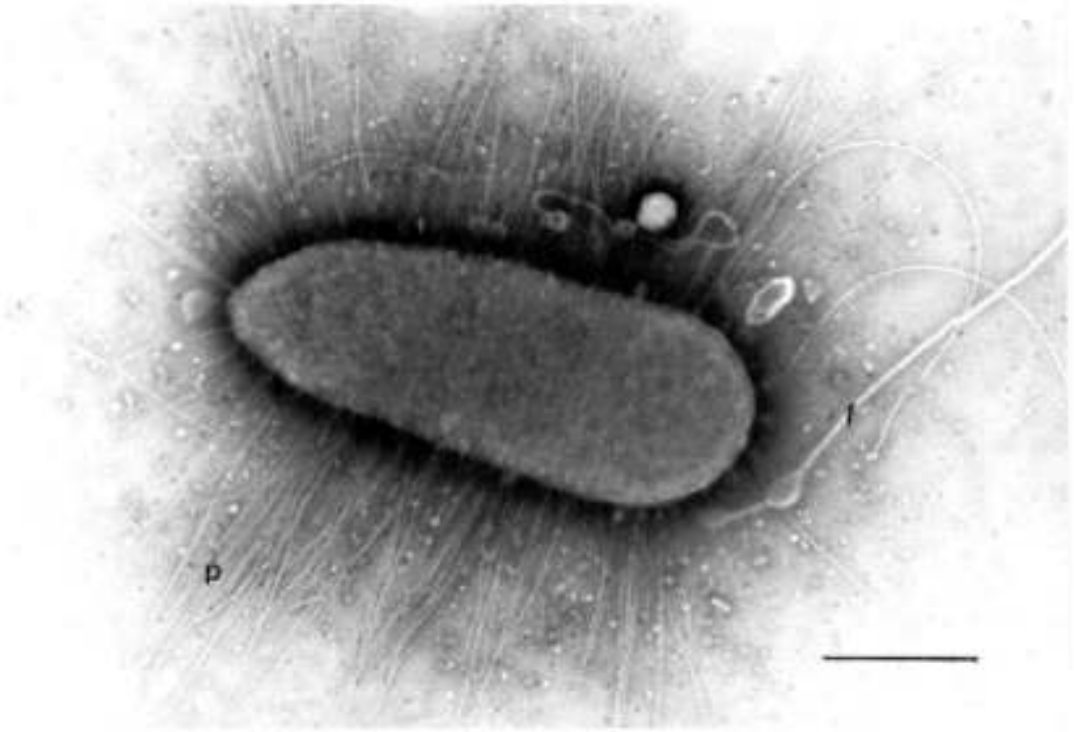
İnsan Mikrobiyom Projesi-iHMP



Mikroplarınızı Sevin



Ne zaman saldırgan hale geldiler ?



İlk Kanı Kim Akıttı!

Oysa her şey ne güzel başlamıştı

Milattan Önce 10.000

- Toplam insan nüfusu 10 milyon

How Hunter-Gatherers Obtained Food and Its Implications for Human Activity

by DAVID CSONKA on FEBRUARY 18, 2011 · 2 COMMENTS · in LIFESTYLE / WELLNESS

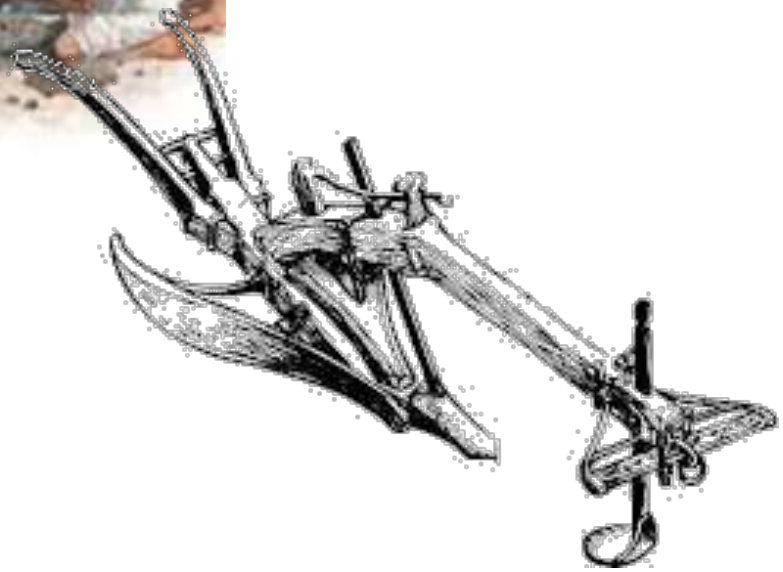
Biological anthropologists and the burgeoning community of paleo-minded people both have a desire to form a greater understanding of the lives and habits of early human hunter-gatherers.

Hunter-Gatherers

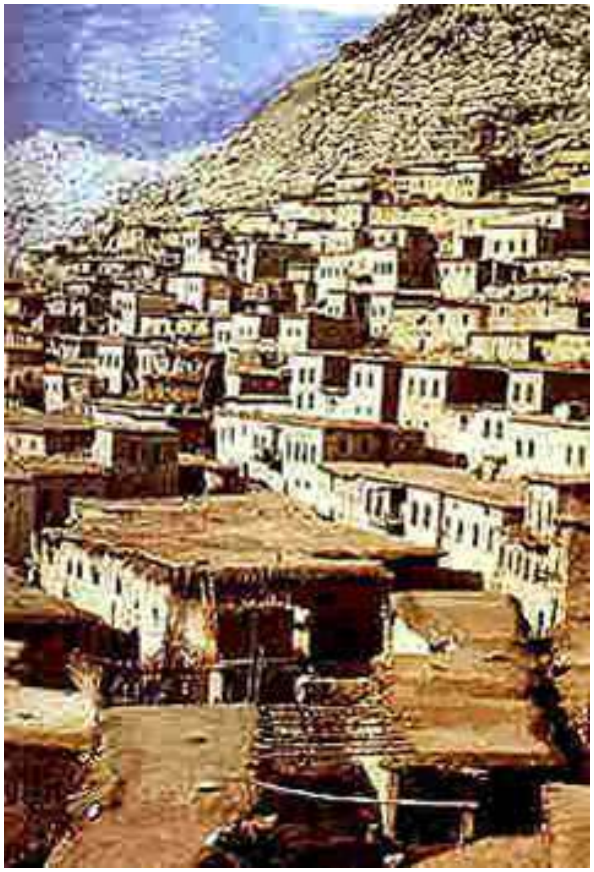
For those practitioners of the paleo diet and evolutionary fitness concepts, the goal is to apply knowledge of our biological ancestry towards living a more healthful life.

Because for obvious reasons directly observed evidence of paleolithic behaviors is impossible, we must rely extensively upon the few extant populations of hunter-gatherers, horticulturists, and tribal peoples still living in primitive environments. Often, these people have had exposure to modern technologies or cultures, but still retain some of their old traditions.

Tarım Devrimi ve Saban

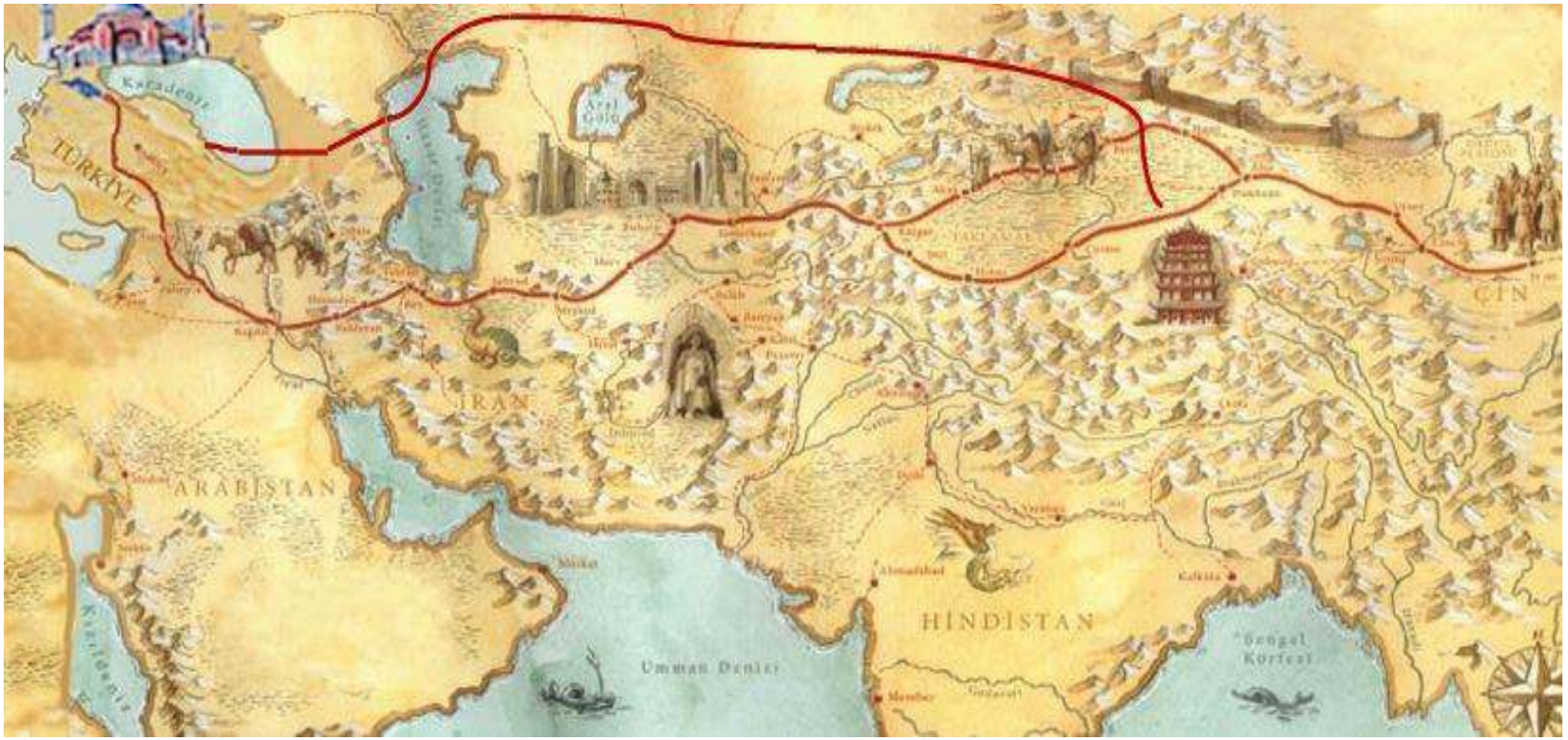


Tarım Devrimi ve Uygarlaşma

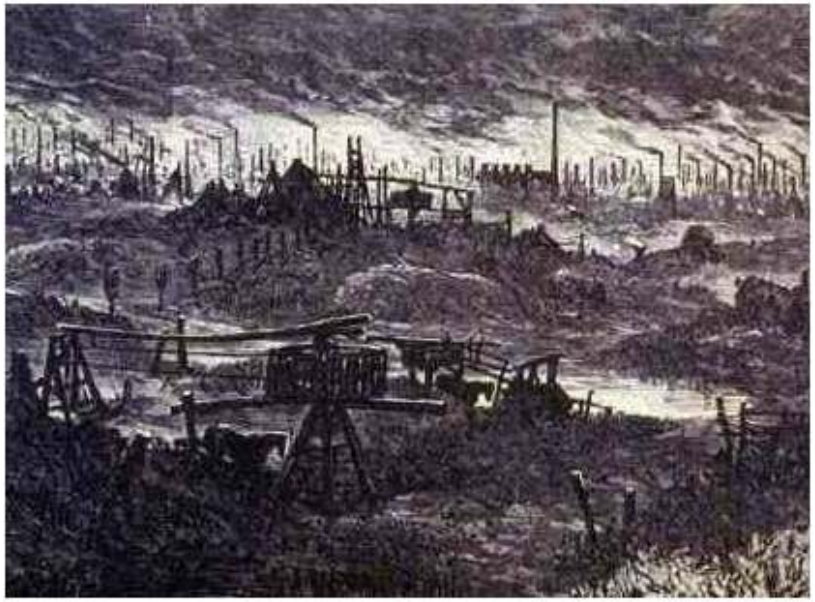


Ticaret

- İpek yolu



Endüstriel Devrim



Endüstriel Devrim

- Sanayi Devrimi - Tüberkülozun Altın Çağı

  “Verem epidemisi kapitalist toplumun insafsız emek sömürüsünü nedeniyle ödemek zorunda olduğu kefarettir” DuBois

Endüstriyel Devrim

Kalabalıklaşan dünya

Sosyal Adaletsizlik

Savaşlar

Cholera in Mariupol: Ruined city at risk of major cholera outbreak - UK

Dördüncü atlı ile tanışma

Dördüncü atlı ile tanışma

- Taliesin Kitabı 6.yy

Bil bakalım kim bu güçlü yaratık,

tufandan önce yaşamış,

etsiz ve kansız,

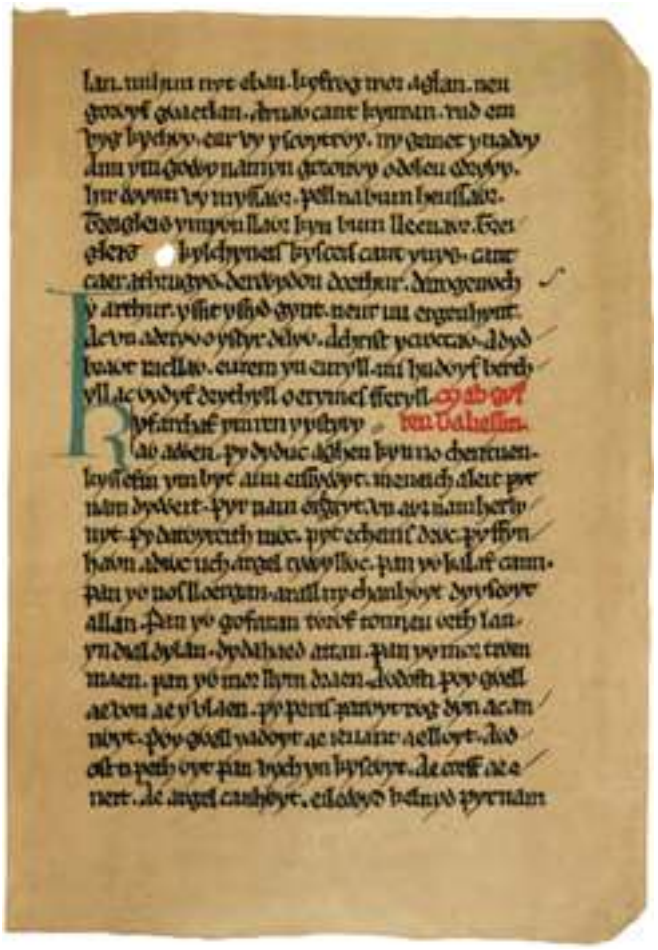
kemiksiz ve damarsız,

kafasız ve bacaksız

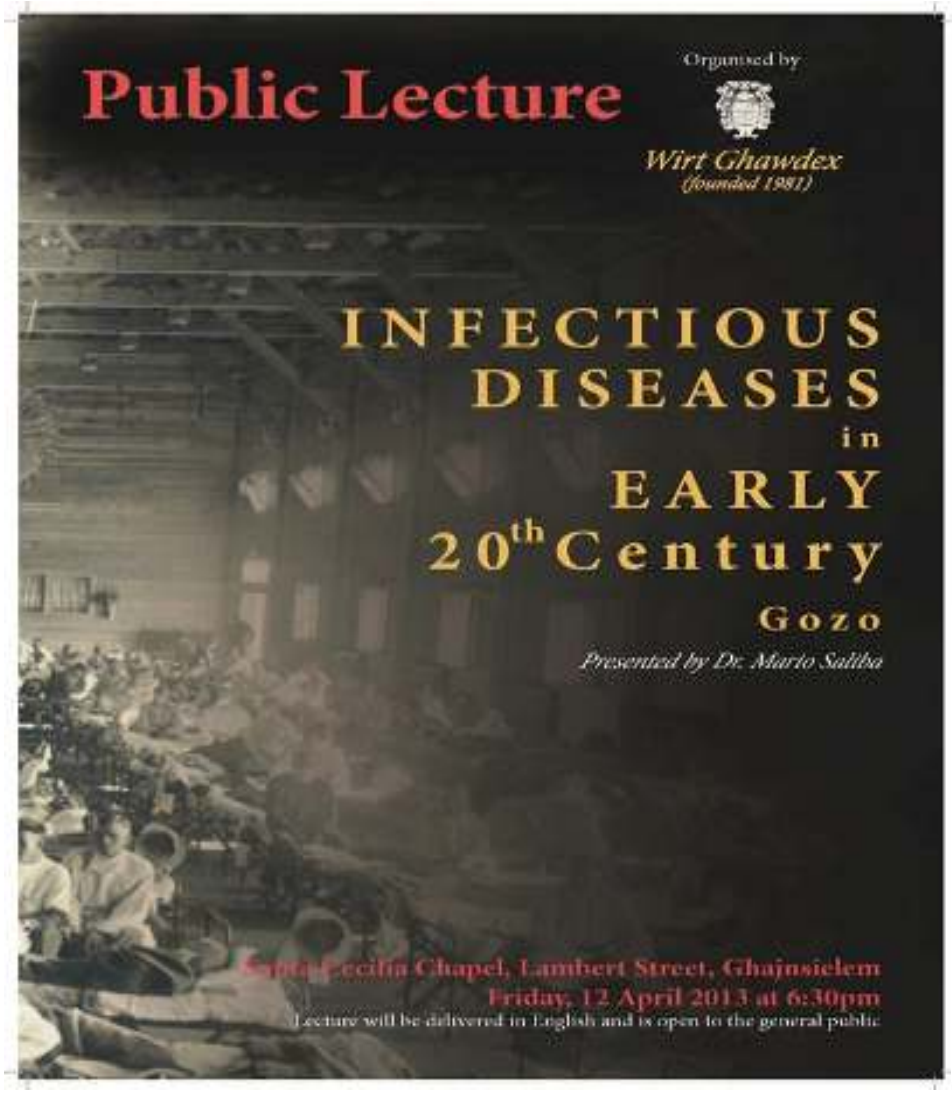
ne daha yaşlıdır ne de daha genç

başlangıçta olduğundan

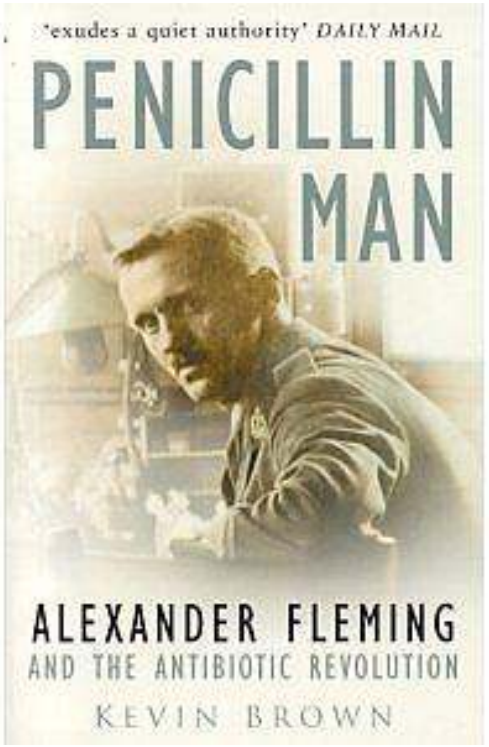
Taliesin



İnfeksiyon Hastalıklarından Ölüm



1929 - Antibiyotik çağının başlangıcı

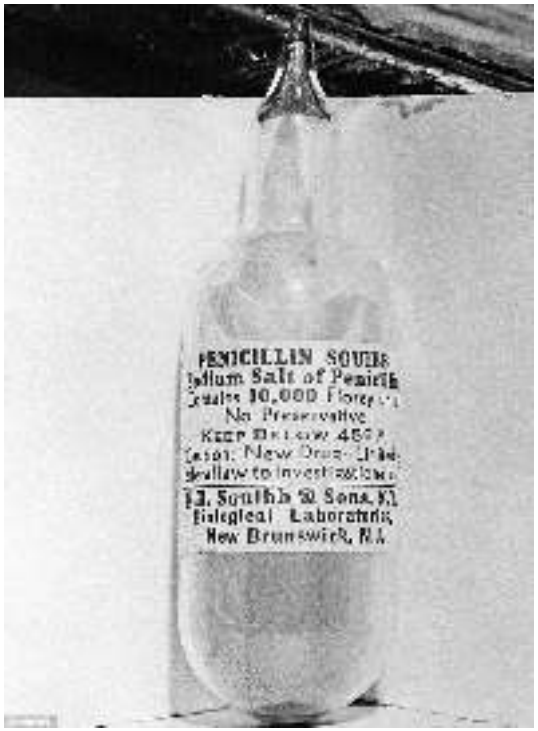


1941 - Penisilinin hazır hale gelmesi

Howard Florey Ernst Chain

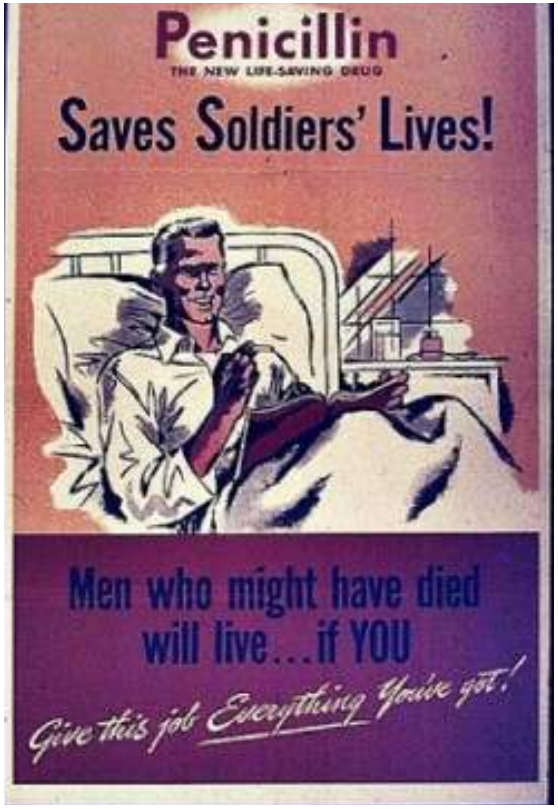
1942 - Penisilinin hazır hale gelmesi

The horror of diseases such as blood poisoning is easily forgotten. These pictures, taken in 1942 shortly after the introduction of penicillin, showthe improv-ment in a child with a bacterial infection four (photo 3) and nine (photo 4) days after treatment, and fully recovered (5&6)



1944 - Penisilinin tedavide kullanılmaya başlanması

- II. Dünya savaşı



1945 – Nobel Ödülü

- 1945 Nobel ödülü

Alexander Fleming receiving his Nobel Prize in

"It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body... ...and by exposing his microbes to non-lethal quantities of the drug make them resistant."

1947 - Penisiline karşı ilk klinik direnç

- Penisilin direnci ile ilgili ilk yayın

PENICILLIN-RESISTANT STAPHYLOCOCCI: MECHANISMS INVOLVED IN THE DEVELOPMENT OF RESISTANCE

By WESLEY W. SPINK and VIOLA FERRIS[1]

(From the Division of Internal Medicine, University of Minnesota Hospitals and Medical School)

(Received for publication September 9, 1946)

While staphylococci are among the species of gram-positive bacteria considered to be susceptible to the antibacterial action of penicillin, a number of investigators have reported that t
strains of coagulase-positive staph
are naturally resistant to penicillin (
added clinical importance is the fac
genic strains originally sensitive t
concentrations of penicillin may bec
to the antibiotic in patients who h
treatment with penicillin (7, 12 to
attempt to define the nature of the
staphylococci to penicillin, the resul
studies have appeared in which sen
have acquired a high degree of res
vitro methods (4, 11, 13, 18, 20 to
and Turner (25) succeeded in adapt
of staphylococcus resistant to penici
ing repeated subcultures of the coc
ing quantities of penicillin. Wher
had acquired resistance, they subcul
ganisms daily in broth without peni

the resistance displayed by staphylococci. Abraham and Chain (27) first showed that *E. coli* produced an enzyme, designated as penicillinase,

STAPHYLOCOCCAL INFECTION DUE TO PENICILLIN-RESISTANT STRAINS

BY

MARY BARBER, M.D.

(From the Department of Bacteriology, British Postgraduate Medical School, Hammersmith Hospital)

The incidence of strains of *Staphylococcus pyogenes* that are grossly resistant to penicillin is clearly increasing rapidly. The rate of increase in this hospital at present is so rapid as to be somewhat alarming. In a previous study (Barber, 1947) all cultures of *Staph. pyogenes* occurring in the routine bacteriological laboratory were tested for penicillin sensitivity; out of a series of 200 patients yielding cultures of *Staph. pyogenes* penicillin-resistant strains were isolated from 25 (12.5%). Since then cultures have been tested for their reaction to penicillin only if they came from an infected lesion. In analysing a series of 100 patients with staphylococcal infection between February and June, 1947, it was found that as many as 38 yielded penicillin-resistant strains. Table I gives a comparison of the two series. In

Analysis of Resistant Strains

The degree of resistance was in all 38 cases gross (see Fig. 1), and all, except one strain which was not tested, were shown to produce penicillinase; 36 of the strains were found to have a sensitivity to streptomycin approximately equal to that of the Oxford staphylococcus; one strain was not tested against streptomycin; and one strain, which came from a patient with tuberculous meningitis who was being treated with streptomycin was resistant to it.

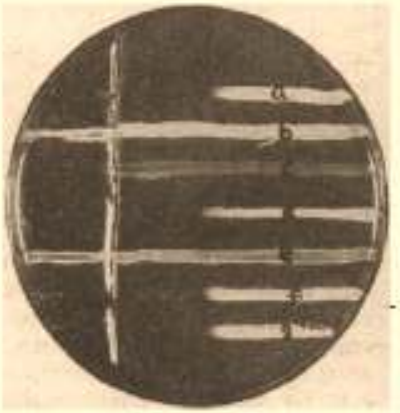
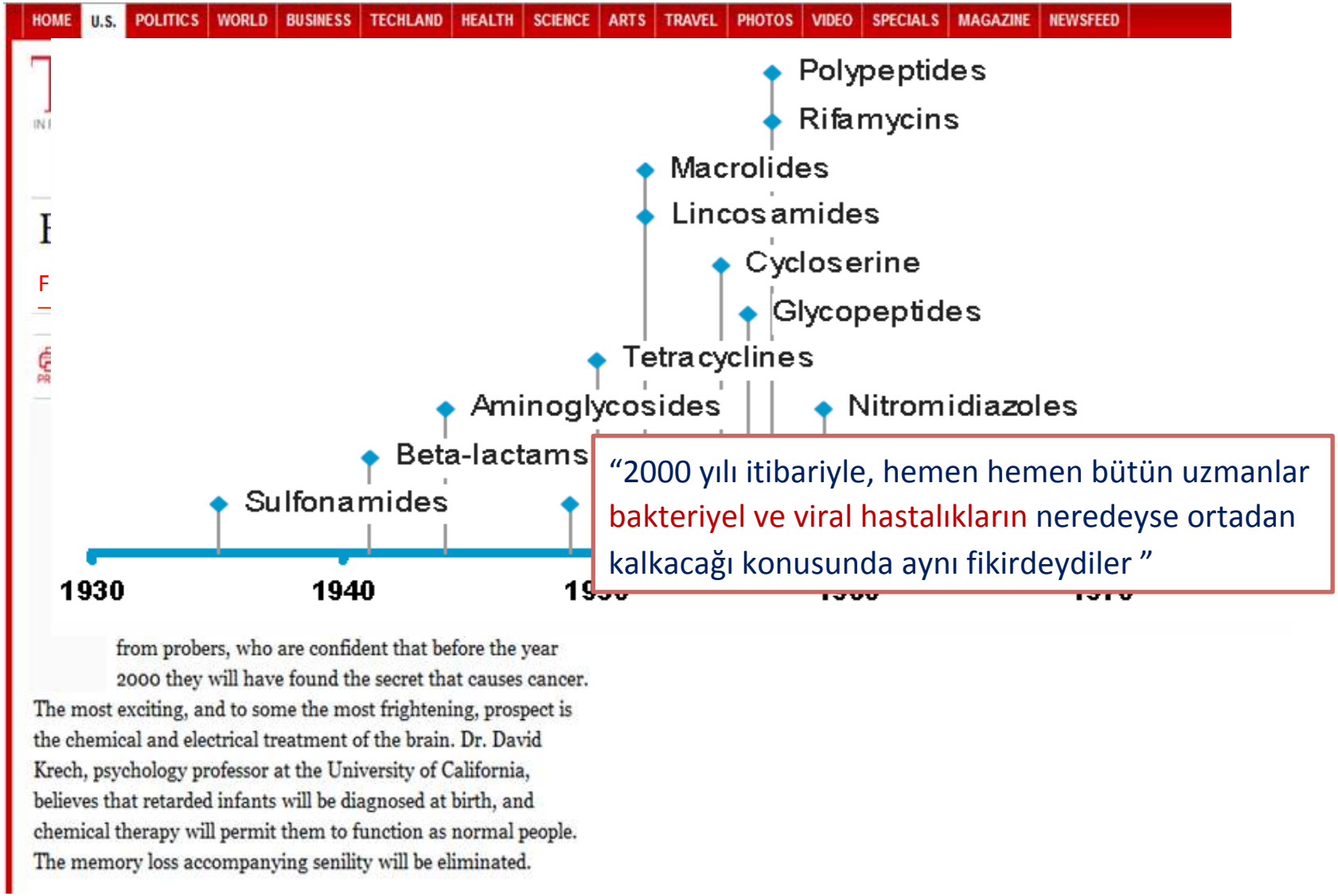


FIG. 1.—*a*, *d*, *f*, and *g* are penicillin-sensitive and *b* and *e* penicillin-resistant strains of *Staph. pyogenes*; *c* is a culture of *Salm. typhi*.

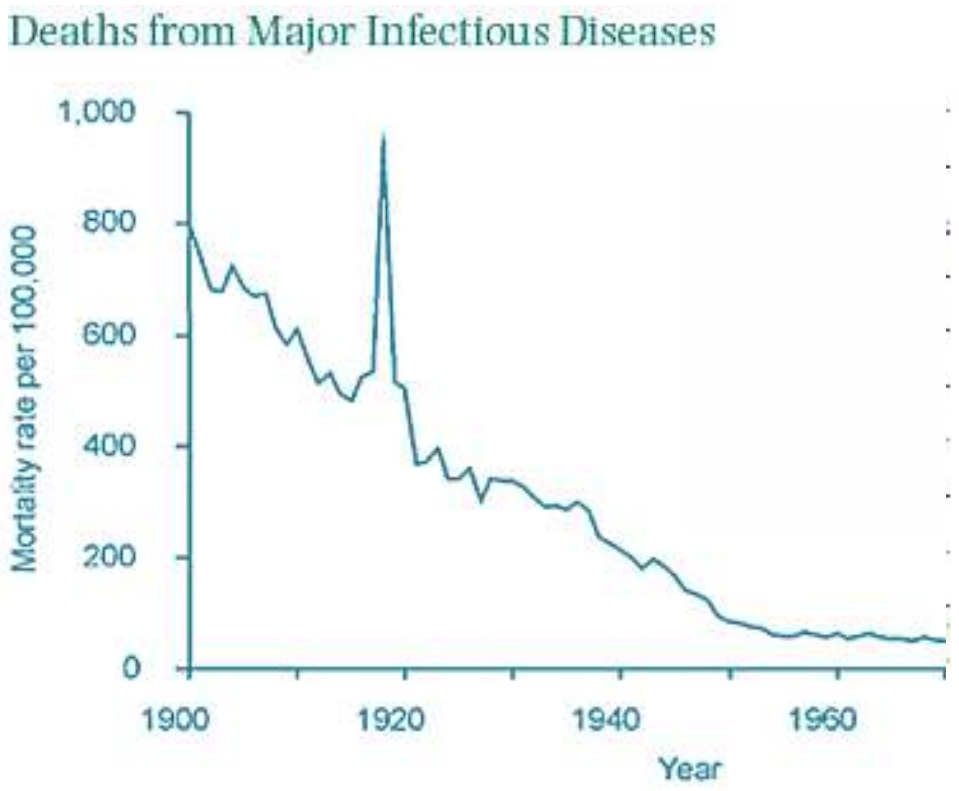
Antimikrobiyallerin yükselişi



"2000 yılı itibariyle, hemen hemen bütün uzmanlar bakteriyel ve viral hastalıkların neredeyse ortadan kalkacağı konusunda aynı fikirdeydiler "

Enfeksiyon hastalıklarına bağlı ölümler azalıyor

- İnfeksiyon hastalıkları kitabını kapatmanın zamanı geldi…

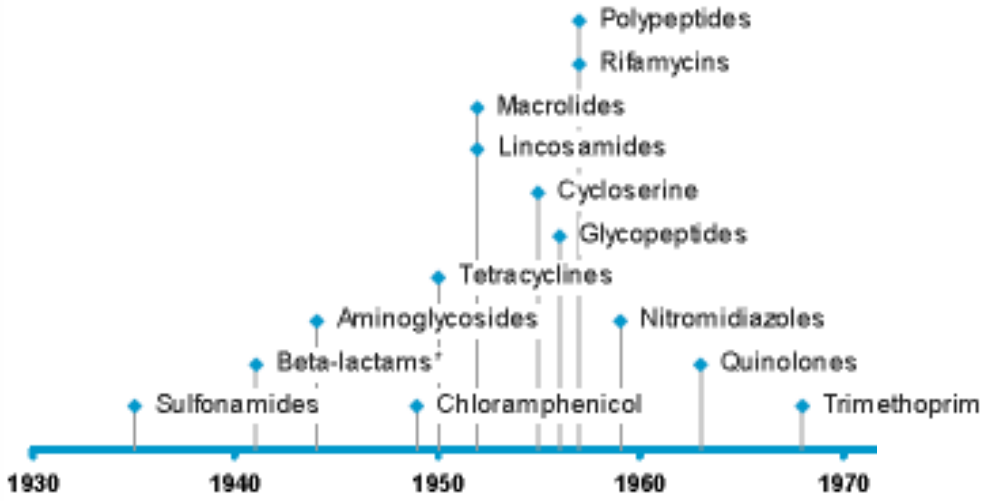


". . . It is time to close the book on infectious diseases. The war against pestilence is over."

William Stewart, Surgeon General
in a message to Congress, 1969

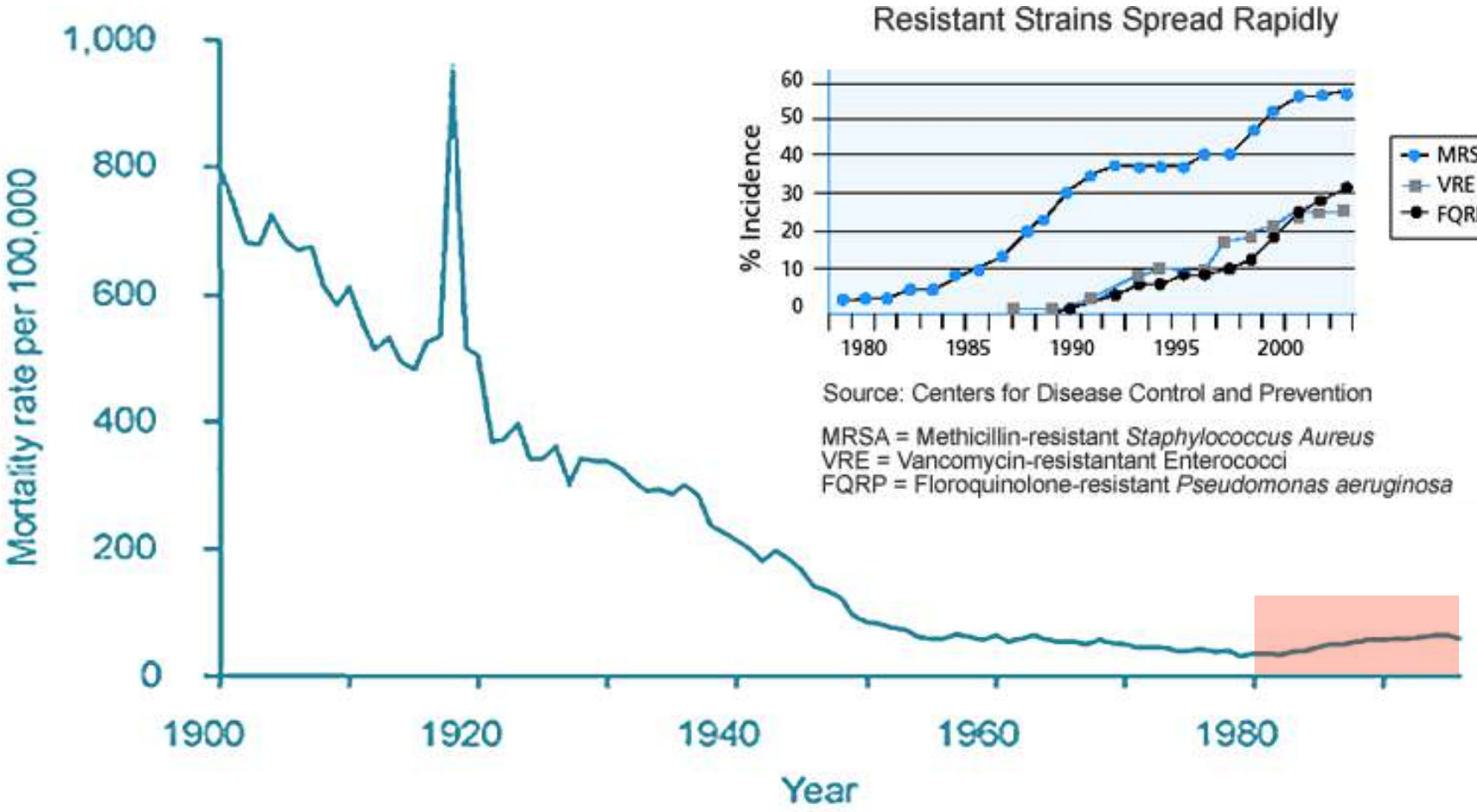
http://www.cdc.gov/ncidod/osr/site/about/graph.htm

Yeni antibiyotik sınıfları geliştirilemiyor



Yaklaşık 30 yıl yeni antibiyotik sınıfı keşfedilemedi.

Enfeksiyon hastalıklarına bağlı ölümler artıyor



http://www.cdc.gov/ncidod/osr/site/about/graph.htm

Antibiyotik Direnci

- Katil mikropların intikamı!

Research

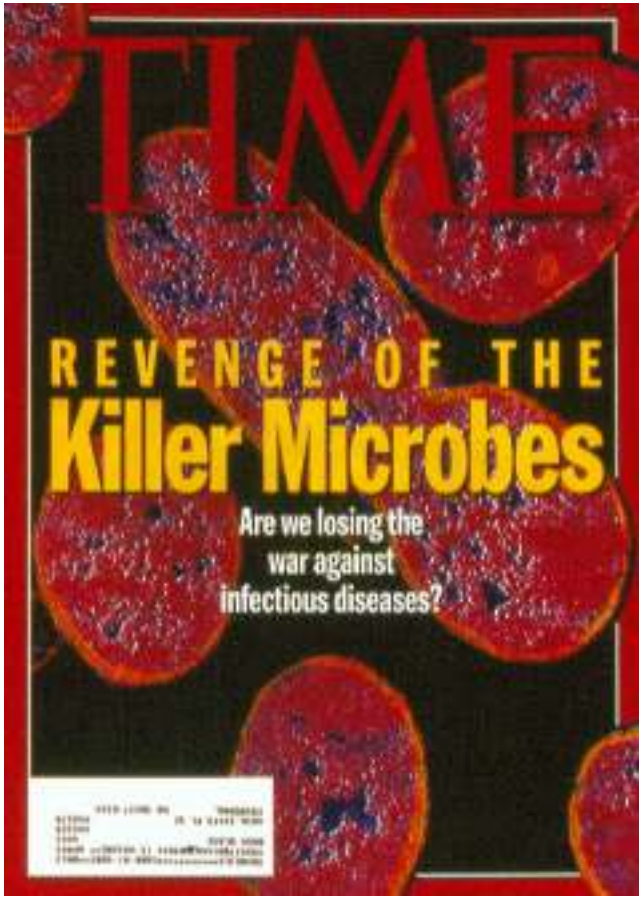
Revenge of the killer microbe

Sandra R. Arnold MD MSc

∞ See related article page 877

The cover of *Time Magazine* on Sept. 14, 1994, read "Revenge of the killer microbe" in reference to an article about emerging infections, including drug-resistant bacteria that are difficult to treat.[1] A lead article in *Science* just 2 years earlier cautioned readers about the possibility of a "post-antibiotic era" and stressed the importance of the discovery of new drugs and the prudent use of currently available antimicrobials.[2] The mantra of the ills of antibiotic overuse has been repeated in the medical and lay press over the past 10–15 years.

It is clear from ecologic studies that antibiotic use is a driving force in the emergence of antibiotic-resistant organisms in community and hospital settings. Both the inappropriate use of antibiotics for viral respiratory tract infections and the overuse of powerful, broad-spectrum antibiotics contribute substantially to this problem. Despite the long-term trend of decreasing rates of antibiotic use for common infections in outpatient settings, it remains imperative that we continue to reduce inappropriate antibiotic use if there is any possibility of slowing the further development of drug resistance in common pathogens.



Antibiyotik direnci – Mikropların intikamı

- 2007, infeksiyon kitaplarını açın!
- ….böyle bir şey söylemedim, William Stewart

William Stewart

nature medicine

The open book of infectious diseases

Christopher M Sassetti & Eric J Rubin

New classes of chemical compounds along with more efficient methods to identify drug targets have produced exciting developments in antituberculous antibiotics. Will the new drugs now entering clinical trials have an impact on treatment?

Poor William Stewart. This former US Surgeon General is unfairly credited with stating in 1967 that it was "time to close the book on infectious disease." Although it appears that he never said such a thing[1], the sentiment was certainly widely shared. For the past several decades, while microbial populations have been steadily accumulating drug resistance traits, there has been little interest in developing new antibacterial drugs. In fact, most 'new' antibiotics are merely derivatives of old compounds, and the technical innovations that have fueled drug development in other areas have been largely ignored in this arena. However, as reflected in three recent papers, many of these advancements are finally being harnessed to find more effective treatments for tuberculosis.

Why tuberculosis? Although current treatment can be effective if administered correctly, existing drugs must be taken for at least six months to prevent relapsing disease. Low treatment compliance contributes directly to the emergence of multidrug- and extensively drug-resistant (MDR and XDR) strains of *Mycobacterium tuberculosis*, which further limit the efficacy of standard therapy. To ensure compliance, the World Health Organization recommends that observers watch each dose be taken. The small cost of the medications themselves is dwarfed by the logistical expenses associated with maintaining clinics, drug supplies and observers. So treatments that are

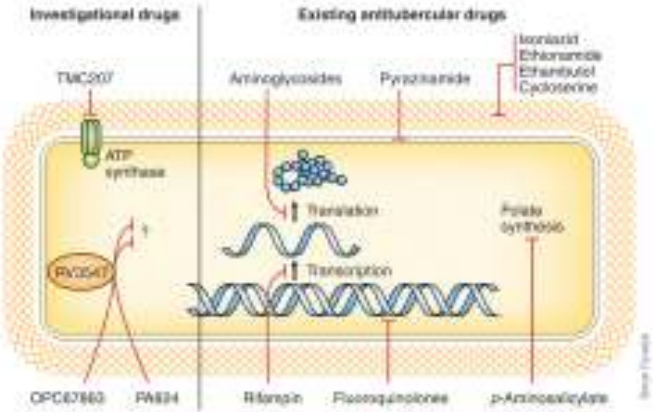


Figure 1 Mechanisms of action for current and investigational tuberculosis drugs. Targets of current drugs include cell wall synthesis (isoniazid, ethionamide, ethambutol and cycloserine), folate synthesis (p-aminosalicylate), transcription (rifampin), translation (aminoglycosides), DNA metabolism (fluoroquinolones) and the cell membrane (pyrazinamide). Three new compounds target other bacterial functions. TMC207 seems to inhibit the ATP synthase complex. OPC-67863 and PA-824 are prodrugs, the activation of which depends on the same cellular enzyme (Rv3547). The ultimate targets of these compounds remain unknown.

Mikroorganizma Sonrası; Bugün 346. yıl

- Salvarsandan bugünkü modern sefalosporinlere kadar geçen süreç göz önüne alındığında, "mikrobu bul, mikrobu yok et" felsefesinin çok da başarılı olmadığı ve yeni yaklaşımlara ihtiyaç olduğu bir gerçektir.

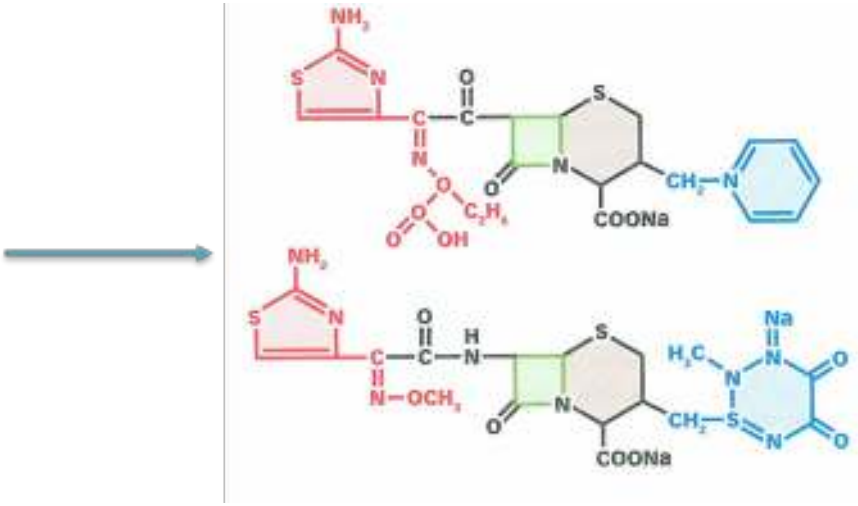

Das neue **Ehrlich**'sche
Syphilis-Heilmittel
bringen wir Mitte Dezember 1910 unter der geschützten Marke

„SALVARSAN"

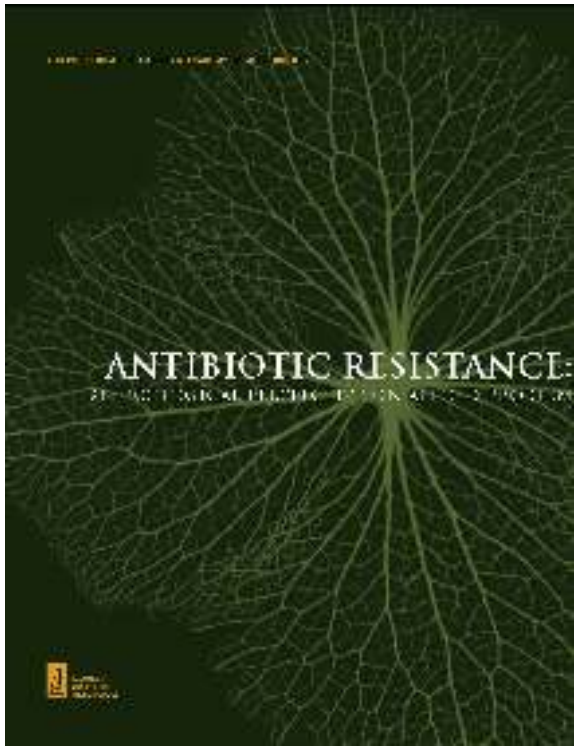
in den Handel.

Wegen Bezuges von „Salvarsan" bitten wir die Herren Apotheker, sich ausschliesslich an die Grossdrogen-Handlungen wenden zu wollen.

Farbwerke vorm. **Meister Lucius & Brüning,**
Hoechst a. M.



Mikroorganizma Sonrası; Bugün 346. yıl



« Antibiyotik direnci ile mücadele bir savaştır ve biz asla kazanamayacağız »

“ The strength of trillions upon trillions of microorganisms, combined with the ancient force of evolution by constant, unrelenting variation, will inevitably overpower our drugs”

- American Academy of Microbiology

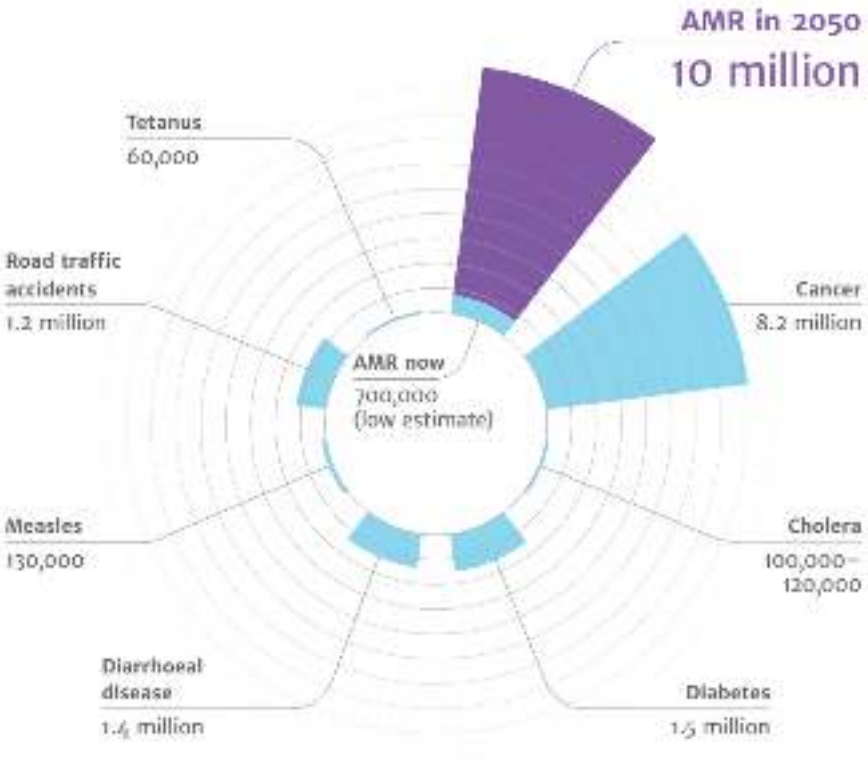
Bütüncül yaklaşım – tek sağlık

- Bu yeni yaklaşımların odağında,

  bir mikroorganizmanın hastalık yapması için konağın da ve hatta çevrenin de önemli olduğu bilgisi vardır.

Geliyorum diyen büyük tehlike!

- 2050 yılında beklenen ölüm yılda 10 milyon kişi.



Türkiye'de Antimikrobiyal Direnç ve Mikrobiyoloji Laboratuvarı

- Ülkemizde yüksek potensli antibiyotiklerin reçete edilebilmesi için gerekli olan kültür-antibiyogram zorunluluğu 2003'ten beri kaldırılmıştır.
- Ülkemizde reçete edilen antibiyotiklerin yaklaşık %40'ının birinci basamak sağlık hizmetlerine ait ve bu merkezlerin çoğunlukla herhangi bir mikrobiyoloji laboratuvarı imkanları bulunmamaktadır.

Türkiye'de Antimikrobiyal Direnç

- Günümüzde 3. basamak sağlık kuruluşlarında kültür isteme sıklığı bundan 10-15 yıl öncesine göre çok ciddi düzeyde artmıştır.
- Ancak bu artışın nedeni 20-25 farklı antibiyotikten sadece bir ikisine duyarlı kalmış etkenin hangi antibiyotikle tedavi edebileceğinin anlaşılması içindir.

Rudolf Virchow

« Tıbbın işi mikropları avlamak değil,

hastalıkları besleyen çevresel ve toplumsal etkileri ortaya çıkarmaktır »

1821-1902