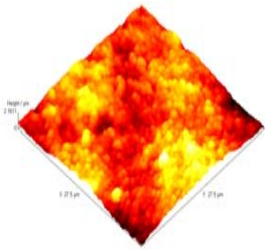

Figure 3: topography of biofilm in *Salmonella* bacteria

★ Bacteria may produce a protective layer (biofilm) and hide inside it. The biofilm prevents entry of the antibiotic agents into the bacteria. The formation of the biofilm can increase bacterial resistance up to 1000 fold.

★ Bacteria can activate intracellular mechanisms (called pumps) that throw the antibiotics out of the bacterial cell or seal the bacterial envelop to prevent penetration of antibacterial agents

In a recent study, knowledge about the way aminoglycosides (family of antibiotics) kill bacteria was utilized in parallel to knowledge about how resistant bacteria break down this antibiotic to develop an innovative product that also affects resistant bacteria.

One of the greatest challenges for medical science in this century is the quest for new materials that inhibit or kill bacteria.

The research will focus on:

★ Discovery of new antibiotics

★ Intelligent design of new derivatives of existing antibiotics that will operate better on the target site and will be less sensitive to bacterial resistance mechanisms

★ Discovery of new materials such as peptides (short proteins) with antimicrobial activity

ERA-NET PathoGenoMics

The brochures are published by the ERA-NET PathoGenoMics. Trans-European cooperation and coordination of **geno**me sequencing and functional genomics of human-**patho**genic **mic**roorganisms.

For more information on ERA-NET PathoGenoMics:

www.pathogenomics-era.net

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ERA-NET PathoGenoMics

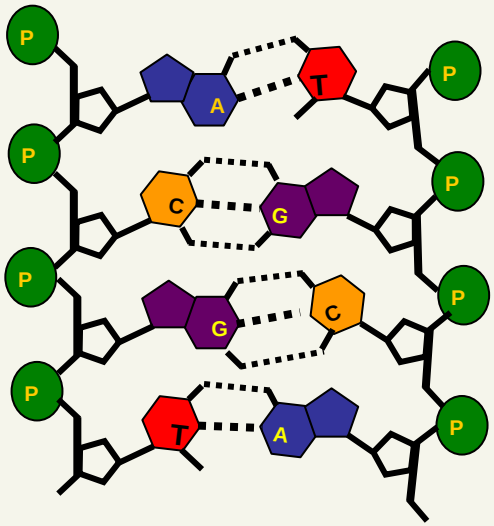
The World of Bacteria

Experts claim that in each gram of soil there are 1 billion bacteria. To date only 2 percent of bacterial species have been discovered.

Only 100 strains of bacteria are known to be direct pathogens (cause diseases).

Genes are working subunits of DNA. The DNA is a vast chemical information database that carries the complete set of instructions for making all the proteins a cell will ever need. Each gene contains a particular set of instructions, usually coding for a particular protein.

The DNA is a double-stranded molecule twisted into a helix (think of a spiral staircase). Each spiralling strand, is comprised of a sugar-phosphate backbone and attached bases. The bases are adenine (A), thymine (T), cytosine (C) and guanine (G).



Genome- The name for the entire genetic information encoded by the DNA

Pathogenomics - The science that deals with the genomes of all pathogenic bacteria.

Epidemiology -The study of how diseases spread

Virulence - the degree of ability of an organism to cause disease

Why is it important to investigate causes of diseases?

Develop vaccines for diseases

Fight diseases better

Find new treatments

Identification

Epidemiology

In the past, epidemics caused the death of millions of people. Examples include an outbreak of deadly bubonic plague (the black death) caused by *Yersinia pestis*, the cholera epidemic caused by *Cholera* bacteria and the typhus epidemic caused by *Rickettsiae* bacteria.

Epidemics today?

The world's ecology and technology is changing and so human behaviour . The changes are causing the appearance of new bacteria and viruses. Examples include HIV and the outbreaks of SARS and avian 'flu'.

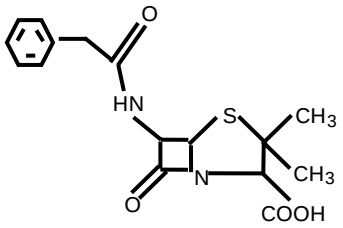
Is there a difference between bacteria from the same family?

Bacteria from the same family with high similarity in their genomic sequences can strike different species with different severity. In the *Salmonella* bacteria, a mere 10% difference in the genome can cause significant changes in virulence. This is the reason why there are virulent and non virulent bacteria in the same strain. In *Vibrio* bacteria the addition of few genes can determine whether the bacteria will be virulent or not.

Are there new bacteria?

* Today we are able to identify some bacteria that we could not identify in the past
* With time, non virulent bacteria became virulent
* We now know that some bacteria cause diseases that were not familiar in the past or caused diseases that were not defined as infectious diseases, (e.g. *Helicobacter pylori* which is known to cause ulcer or various viruses that cause cancer)
* Bacteria may be modified for biological terrorism

Antibiotics - **A class of natural and synthetic compounds that kill or inhibit the growth of microorganisms**



The chemical structure of penicillin

Penicillin was the first antibiotic agent to be discovered and is still widely used. It is derived from the Penicillium mold.

Since 1940 antibiotics have been used:

as therapeutic agents in humans

in therapy, preventive treatment and supplements to promote faster growth of animals

as disease control in plants

The wide range of antibiotics that have been used, has enabled the bacterial pathogen populations to develop mechanisms that led to their resistance to antibiotics

How bacteria acquire resistance to antibiotics?

Many bacteria are naturally resistant to antibiotic drugs that are in common use but even sensitive bacteria are able to develop resistance. This has a number of causes:

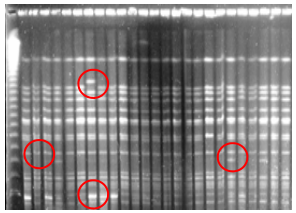


Figure 1: the complete genome of *Salmonella virchow*. In circles, examples of changes in the bacteria genome sequence, shown by with different banding patterns

★ Bacteria may acquire fragments of genetic material from the environment, which make them resistant to antibiotics. There are long fragments known to encode resistance to 7-8 different antibiotic drugs. They pass between bacteria and turn sensitive bacteria into resistant strains.

Today it is possible to analyze and compare the complete bacteria genome and to detect the omission or addition of genetic material (Figure 1).

★ Bacterial genetic material (DNA) is changing with time. The changes may cause bacteria to become resistant.

Today it is possible to isolate a specific gene and examine differences in the DNA sequence (Figure 2) . Sometimes only a minor change is enough to transform sensitive bacteria into resistant ones.

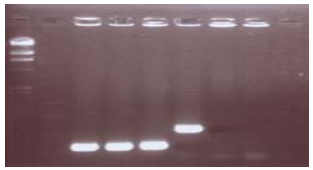


Figure 2: amplification of specific gene in *Salmonella* bacteria