Astronaut microbiome

Daddy: we know that microbes live in our body, but how do they like to travel in space with us?

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Storyline

The microbiome is called the new organ of the human body. It influences substantially the health of the human host, and its microbial composition is an indicator of the health state of human body. Different stress factors can change the microbiome and thereby its influence on us. In space travel such stress factors include microgravity, radiation, the closed space and crowdedness of the station, and the constant contacts with crew members. Moreover, we do not yet know how microbes in our body themselves react to long-distance space travel. Information on the microbiomes of astronauts and their specific changes related to space environment is very important in order to make proper prognosis on the health of astronauts during their long-time stay at the orbital stations, as well as on space missions to other planets. Knowledge about the human microbiome in space can also give scientists clues to causes of various human disorders on Earth.

The Microbiology and Societal Context

The microbiology: microbiome changes and immune system responses; adaptation to extreme factors; sterilization of premises; microbial corrosion; space nutrition. *Sustainability issues:* health; social behavior; partnership for the goals; sanitation; disaster risk reduction; science for future.

Astronaut Microbiome: the Microbiology

1. The microbiome is an association of all microorganisms that live inside and outside the human body, from intestinal bacteria to microorganisms on the skin. In total, over 10 thousand species of various microbes live in the human body. These include primarily bacteria, but also viruses, protozoa and fungi. Scientists estimate that more than half of the cells in our body are microbial, not human. The human microbiota can weigh two to three kilograms and has a huge impact on us. Scientists call the microbiota "the new human organ."

The most representative human microbiota in terms of the number of microorganisms is in the intestine: the number of bacterial cells in it is 100 times greater than that of human cells.

Most of the microbes of the human microbiome are very important to us. They are involved in the digestion of food, in protection from foreign and harmful microorganisms, in maintaining our immune defences, and so on. Interestingly, about 70% of the resources of the immune system depend on the condition of the intestines. It is in the intestines that most of the immune cells are found that fight against viruses and disease-causing bacteria.

The microbiota interacts with almost all of our organs – even with the brain – and provides vital amino acids, vitamins, converts polysaccharides into glucose, and can even synthesize the necessary active substances to relieve stress in a person. Each person has his own unique microbiome that interacts with the microbiomes of the environment and other people with which they have contact.

The main microbial taxa and their subgroups of the microbiome of the human gastrointestinal tract and skin and of the International Space Station (ISS), in the order of their predominance.

2. The concept of the microbiome has now expanded thanks to the latest methods of gene sequencing (decoding the sequence of genes in DNA). All bacteria of the human microbiome belong to several large taxonomic or phylogenetic groups (groups of microbes that are related to one another). Different phyla of microorganisms dominate in different parts of the human body. In total, the largest number of cells belongs to two groups: the *Firmicutes* and the *Bacteroidetes*, which account for about 90% of all our microbes. In addition, *Actinobacteria*, *Proteobacteria*, and a number of other microbial groups are found in the human microbiome. In addition, a large number of fungal genera are present on healthy human skin, among which *Rhodotorula* and *Penicillum* predominate.

It is the ratio of different groups of microorganisms in the microbiome that largely determines the state of human health. This ratio changes with age, disease, and even on psychological state. Depending on the microbiome composition of a person, it is sometimes possible to make a prognosis in relation to an existing health disorder.

We can get harmful bacteria from food or from infection. The more diverse the composition of the microbiome, the higher our resistance to disease. Microbial diversity decreases with age.

3. Space flight involves exposure to various stresses that cause changes in the microbiome. A long stay on the International Space Station (ISS; [https://www.youtube.com/watch?v=IagxIpCvMl4\)](https://www.youtube.com/watch?v=IagxIpCvMl4) leaves a special "microbial imprint" on the cosmonauts. Astronauts are people in excellent health, but they spend weeks or even months exposed to microgravity (a more accurate definition of what we usually call weightlessness in space stations), and cosmic radiation, as well as to extreme confinement during takeoff and return. Traveling at speeds of about 17,000 miles per hour and 300 miles above the Earth, astronauts see 16 sunrises and sunsets every 24h "day", which impacts their biological clock. This is further exacerbated by other stressors, such as social separation, restricted movement in a confined cabin, altered sleep-wake cycles, noises, breathing pure oxygen, and the need to be alert.

In the future, a large number of tourists may go into space, whose health will not necessarily correspond to the health of astronauts. Therefore, it is very important to know how changing the microbiome in space can affect the human health condition.

An unexpected *increase* in the diversity of the gut microbiome has been found in ISS crew members who have been in space for six to twelve months, despite the relatively sterile space environment and food that is undergoing rigorous bacterial control. An increase in the diversity of intestinal microbes is considered a positive finding, because the more diverse the species composition of intestinal bacteria, the more chances the body has to resist diseases. It was suggested that such a finding could be the result of a more diverse diet of people on board the ISS than on Earth, since the astronauts have more than 200 dishes and drinks at their disposal. However, after further research, this conclusion turned out to be not entirely accurate as is mentioned below.

Unlike the gut microbiome, the microbial community of the skin did not show any definite tendencies to change - in some astronauts it became more diverse, in others less diverse. However, a decrease in the number of *Proteobacteria*, a group of soil microorganisms, that is an indicator of the cleanliness of the room was found in all cosmonauts.

4. Space flight increases the secretion of stress hormones such as cortisol and adrenaline, which are known to suppress the immune system. Inside our bodies there may be viruses that are in a latent (inactive, "dormant") state, for example, some of us carry the herpes simplex virus (HSV-1) which causes cold sores. Such latent viruses can reactivate and start multiplying when immune cells are no longer able to suppress and destroy them, in the same way that stress or infections can activate HSV-1 to give us cold sores. If there is a person with an infection in the closed space of a spacecraft, then the disease can easily spread. All this could jeopardize the health of immunodeficient people and newborns on long space flights in the future.

Thus, an important research area is the development of strategies and microbial resources to influence microbiome compositions that can mitigate the stress of the space environment for future astronauts to stay healthy on extended space missions. These strategies can also help ordinary people on Earth maintain healthy microbiomes in the face of various stressors throughout their lives.

5. The microbiomes of the two twin astronauts began to differ greatly when one of them flew into space. In November 2012, NASA selected astronaut Scott Kelly for its first year-long mission to the ISS. His twin brother Mark, who is also an astronaut and is therefore identical with Scott not only in terms of genetics, but also social lifestyle, remained on Earth. The microbiomes of both twins were analysed by microbiologists.

The results of the study showed that Scott's gut microbiome changed significantly, and in addition, the activity of various genes changed, which collectively affected his immunity. Scott's body perceived being in space as a challenge and changed the way its systems work at the cellular level. The same indicators for Mark did not change over the same period of time. The scientists involved in the study concluded that the distinct changes in Scott's microbiome caused by space flight were most likely caused by microgravity, rather than radiation, diet, or other factors.

During his time on the ISS, Scott received a relatively small dose of radiation. Scientists have estimated that astronauts could be exposed to 8 times more radiation on a space mission to Mars. It is not yet known how the body and its microbiome will react to this amount of radiation.

6. The microbiomes of mice on the ISS were also studied. Mice are the best studied model vertebrate animal and proxy of humans. Mice were also transported to the ISS and studied, and compared with identical mice on Earth maintained under identical conditions of temperature, humidity, etc., with the exception of cosmic factors. In space flight, mice were exposed to gravity overload and vibration during the launch, as well as microgravity and cosmic radiation at the station.

Comparisons of the microbiome compositions of mice with that of Scott Kelly during his stay on the ISS revealed similar trends, namely changes in microbiome composition and increases in microbial diversity, which suggests that such changes are indeed caused by space flight. The scientists concluded that microgravity was the main cosmic factor affecting the microbiome.

7. Astronauts on the ISS influence its microbiome. The microbiome of the ISS itself, i.e. the microbial composition of its internal surfaces and air, which has been in operation for a long time, was found to be similar in composition to that of rooms of typical terrestrial buildings. Approximately 68% of the species of microorganisms identified on the ISS are also members of the human microbiome, and only 32% were typical of environmental habitats such as soil or water. Moreover, according to the results of the analysis of the ISS microbiome, it is possible to tell which astronauts were on board because each member has an own specific microbial signature that leaves traces in the ISS microbiome. However, the proportions of the main groups of microorganisms in the microbiomes of the astronauts and the ISS are different (see image), and these diverge if the station is mothballed for a long time, without contact with astronauts (see below).

Microorganisms that live on the skin feel great on the ISS, since human skin is warm and contains organic and chemical substances that bacteria can use as food to grow. However, astronauts do exercises, comb their hair, eat, and during these processes constantly shed skin cells, and the microorganisms living on these skin cells. After being transferred from the skin to various surfaces of the ISS, microorganisms enter a different environment that is cold and lacking food. In such conditions, microorganisms turn on "dormant genes" that allow them to survive and even promote mutations.

The proportions of the main microbial groups of the microbiomes of astronauts and the ISS.

8. A complete catalog of bacteria and fungi found inside the ISS (NASA) has now been created. Knowledge of the composition of microbial communities can be used to develop safety measures during long space travel or life in space. It is important to identify the types of microorganisms that can accumulate in confined environments associated with space travel and to understand their impact on human health and spacecraft infrastructure.

9. The microbiome of the ISS adapts to cosmic factors and conditions. After 12 years of operation, the Russian orbital station Mir began to experience power outages, its computers failed, and leaks in the climate control system occurred. All the problems were caused by microorganisms that multiplied in the station. The astronauts discovered that droplets of water formed at zero gravity, which were cloudy from various microorganisms developing in them.

Many bacteria and fungi – about 100 species – have adapted to attack plastic and metal in the harsh conditions of space. The astronauts noted that the station smelled of rotten apples. The reason for this was mold fungi, which released certain enzymes that gradually destroyed the plastic parts and produced the rotten apple smell.

Colonies of fungi obtained from the ISS samples and grown on a Petri dish (photo by NASA). The plate also contains many bacterial colonies.

Since the assembly of the station modules was carried out under sterile conditions, it is obvious that the microorganisms were brought to it by the crew members arriving at the station where they subsequently adapted to the conditions of the ISS.

On the ISS, scientists have discovered a stable population of about 55 different types of microorganisms that have adapted to life on metal surfaces. In the long term, these micropassengers can be a threat to the normal operation of the station. To maintain cleanliness, astronauts must regularly wipe down the surfaces of the station with antimicrobial wipes and use vacuum cleaners and filters that purify the air and trap moisture. Currently, in the ISS air is treated with weak pulses of electric current that puncture holes in the cell walls of microbes, thereby killing them.

A spacecraft is a sealed system, and any kind of microorganism that enters it can remain there forever. On Earth, rooms that need to be near-sterile, such as operating theatres in hospitals, are sanitized with highly effective chlorine-based disinfectants. But such powerful disinfectants cannot be used on the ISS because, in closed systems, chlorine-containing compounds are dangerous to people. This is the reason why developing strict microbiological protection standards in the ISS is very important. It is also quite important to prevent occupation of the station by microorganisms that have adapted to the conditions of space flight, if the astronauts leave it for a long time.

10. Microgravity conditions may induce increases in bacterial antibiotic resistance and expression of genes specifying functions involved in bacterial pathogenesis. During experiments on the ISS, researchers found that strains of the common gut microbe *Escherichia coli* (*E. coli*) became more resistant to the antibiotic gentamicin. There were several reasons for this:

a. the cell wall and cell membrane became thicker under microgravity conditions,

b. bacteria began to clump together and the antibiotic failed to penetrate the centre of the clump – the outer cells sacrificed themselves, dying from the antibiotic, thereby helping those in the "center" to survive, and

c. some bacterial cells began to produce specific molecules that allow them to "communicate" with each other, a process involved in multicellular activities including infection.

These findings raise the possibility that pathogenic strains of bacteria (including some strains of *E. coli*) may be more dangerous in space, and more difficult to treat.

11. When flying to other planets, the human microbiome can change even more. The experience of astronauts aboard the ISS shows that humans can coexist with their microbiome in low-Earth orbit without any serious negative consequences. The radiation on the ISS is relatively low due to the protective effect of the Earth's radiation belt (Van Allen belt). However, it is not yet known how the microbiome will react during flight outside of the Van Allen belt, when the impact of the space environment, primarily radiation, on a cosmonaut will increase significantly. Perhaps the evolution of microorganisms by mutation will accelerate? Such issues will arise when creating, for example, a permanent lunar orbital station or during space travel to Mars, lasting a year or longer.

12. When landing on other planets, it is important not to infect them with terrestrial microorganisms. Microbes inside our body travel with us everywhere. Whatever we touch, we leave behind a microbial trail. On Earth, other microorganisms compete with and prevent the uncontrolled multiplication of these bacteria. However, when bacteria do not have competitors, as in sterile conditions on other planets, if they are able to multiply, they might multiply uncontrollably: they may become invasive species. It is therefore extremely important not to bring

terrestrial microorganisms to Mars when delivering rovers there, for example, as part of the ExoMars mission, which should look for signatures of life on this planet. The assembly of the ESA (European Space Association) rover was carried out in the UK in a clean room, the engineers were dressed in special suits, special underwear, masks and gloves. And of course future astronauts on Mars must strictly ensure that terrestrial microorganisms do not fall on the Martian surface, for example, from the outer surface of spacesuits.

In laboratory experiments, it has already been shown that a number of terrestrial microorganisms not only survive in the conditions of Mars, but also multiply. These microorganisms, in particular, include archaea that form methane. A large number of these microorganisms live in the rumen of ruminants, but small numbers of them are also found in the human intestine. It is quite likely that other microorganisms of the human microbiome are also able to adapt to Martian conditions.

A situation may arise that the microorganisms that scientists may one day find on Mars will be of terrestrial origin. We still do not know if life exists on Mars and other planets, and therefore it is important not to infect them with a terrestrial life form at the very beginning.

Some of the terrestrial microbes can survive and multiply on Mars, competing with putative native microorganisms for areas of existence.

13. An even more serious issue is the possible transport of alien microorganisms to Earth. In the programs of various astrobiology missions, procedures are developed to obtain and transport back to Earth extraterrestrial surface samples to gain insight into their compositions and origins, including Martian soil. The focus thus far has been the minerology and chemistry of the samples, but in future the biology will be in the spotlight.

Science fiction has long warned us about the dangers of such contamination through films such as The Andromeda Strain or The Thing. If astronauts return, for example, from Mars, then we need to be absolutely sure that their microbiome has changed under the influence of space flight factors, and not due to potential Martian biology.

Alien microorganisms can theoretically become enemies of native organisms on Earth. In the science fiction novel by H.G. Wells, *War of the Worlds*, the Martians who arrived on Earth were defeated, namely, by terrestrial microorganisms.

14. Scientists believe that it is possible to manage human health through the microbiome. In 2017, a large Human Microbiome Project was launched by IBM in cooperation with the Broad Institute at Massachusetts Institute of Technology (MIT) and Harvard University, whose goal is to find out how the human microbiome affects the development of various diseases. In modern science, the prevailing point of view is that many diseases really depend on the state of our microbiome. The latest developments within the Human Microbiome Project confirm the concept of maintaining health through the equilibrium state of our microbiome. This can be especially important for long-term space flights.

15. Creation of an artificial microbiome by genetic engineering may improve the living conditions of astronauts. The American biologist Craig Venter, author of the world's first artificial genome of a living organism, states that this goal can be realized by manipulating the genes of microorganisms in the direction of creating organisms with useful properties. Such properties can be more efficient in assimilating nutrients, fighting against pathogens, making more pleasant the smell that human bodies periodically exude, which is especially important for people who spend a long time with each other in an enclosed space, and so on. In addition, there is bacterium *Deinococcus radiodurans*, which withstands radiation levels 7,000 times higher than that which can kill a human. Moreover, microbes produce compounds that protect against radiation. One of these is melanin. Currently, there are experiments in the ISS testing whether melanin-coated space suits and ISS surfaces can reduce radiation exposure (https://magazine.publichealth.jhu.edu/2019/melanin-space#:~:text=Melanin the%20pigment%20that%20produces%20hair%2C%20skin%2C%20and%20eye,use%20mel anin%20to%20capture%20heat%20from%20the%20environment). The possibility of changing the genome of the astronauts themselves with the help of special genes of microorganisms to simplify their life during long space flights is a more distant prospect.

Relevance for Sustainable Development Goals and Grand Challenges

The microbial dimension of acquisition of a companion dog relates to several SDGs (*microbial aspects in italics*), including

• **Goal 2. End hunger, achieve food security and improved nutrition and promote sustainable agriculture** (*end hunger and malnutrition, increase agricultural productivity)*. The crew of the space station is conducting experiments on board to grow plants in conditions of space factors. This is a very promising direction, which may lead in the future to the creation of agricultural greenhouses and the provision of food for both astronauts and future space settlers.

• **Goal 3. Ensure healthy lives and promote well-being for all at all ages** (i*mprove health, reduce preventable disease and premature deaths).* The microbiome provides humans with useful substances and protects them from pathogens. To be able to perform these functions, microorganisms in the human body must maintain a proper stable and diverse composition. Gaining an understanding of what constitutes a good composition and how it can be stably maintained will aid efforts to increase human wellbeing. The topic gives understanding the importance of proper balanced nutrition. It directly influences the composition and activity of human microbiome and therefore human health. The topic also contributes to the problem of stress in social life. Since stress factors like space flights affect the microbiome, there is a necessity to monitor your psycho-neurological health. This is another confirmation of the direct connection between the state of mind and the development of diseases.

• **Goal 7. Ensure access to affordable, reliable, sustainable and modern energy for all** (e*nsure access to clean, renewable and sustainable energy, and increase energy use efficiency)*. In airless

outer space, the role of solar batteries as the most important source of energy is significantly increasing. This type of energy allows the operation of many segments of the station and the life support of astronauts.

• **Goal 8. Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all** (p*romote economic growth, productivity and innovation, enterprise and employment creation)*. The constant development of the space industry and the increase in the number of space programs will in the future increase employment both in space and on earth when organizing various experiments on board the space station in the field of medicine, biotechnology, chemistry, physics, etc.

• **Goal 12. Ensure sustainable consumption and production patterns** *(achieve sustainable production and use/consumption practices, reduce waste production/pollutant release into the environment, attain zero waste lifecycles, inform people about sustainable development practices)*. This problem is related to the closed space of the space station, where all the waste products of the astronauts must be carefully isolated. Liquid waste goes through the stage of complete purification and is reused.

Relevance of the Astronaut Microbiome to other Challenges

1. **Enhancing systems thinking.** Most people most of the time tend to consider issues in isolation, rather than in the context of related issues to which they are connected and dependent upon. There is a serious need to promote *systems thinking*. Studying the astronaut microbiome helps us to understand the close relationships between human physiology and health and the microbiome and its composition and activities, on one hand, and the importance of interactions between human organs and microbial cells, and interactions between the microbiome and the external environment, on the other. This in turn encourages systems thinking and its extension to other issues that confront us.

2. **Preservation of cleanliness in the ISS is an important challenge for space exploration.** Understanding how human microorganisms can adapt to the space environment and become more dangerous for astronauts in the closed environment of the ISS is key to sustainable space flights and time spent on space stations and, ultimately, for maintaining the safety of near-sterile environments, like hospital operating theatres, on Earth.

3. **The ethical and scientific issues of contamination of other worlds with terrestrial microorganisms.** The need to avoid contamination of other cosmic bodies with microbes from Earth emphasizes the importance of strict sterility requirements for all space vehicles used for planetary exploration and for adequate procedures for in-space decontamination.

4. **Understanding true dangers of contaminating Earth with alien microbes from other space bodies.** Studying the astronaut microbiome allows us to understand how terrestrial microbes can change their properties under new environmental conditions. We do not yet know how much they can change during extended periods of space conditions. This emphasizes our lack of appreciation of what and how alien microbes might be, and the need for proper isolation of all extraterrestrial material when delivered on Earth for study, and future strict quarantine of astronauts returning from other planets.

Pupil Participation

1. Class discussions

a. of the issues associated with space microbiology

b. about good and bad microorganisms in relation to human health. Can good microbes change their properties so that they become dangerous? If so, which factors can initiate such changes?

c. space microbiology has positive and negative consequences for the SDGs. Which of these are most important to you personally/as a class?

2. Pupil stakeholder awareness

a. why is sterility of rooms is especially important for astronauts working at ISS and how the astronauts maintain sterile conditions?

b. what dangers might astronauts face during flights to other planets and can their microbiome help to cope with them?

c. is contamination with alien microbes dangerous and why?

d. would you like to acquire new properties from microorganisms that would help you cope with the difficulties in life?

3. Exercises

a. Consider and propose requirements for the crew and the handling of their wastes during long-time flights to other planets, and how to organize safe and effective closed matter cycling. What role do microorganisms play in your proposals?

b. Consider and propose measures to maintain healthy astronaut microbiomes during long-time autonomous space travel?

c. As a consequence of (a) and (b), can you suggest basic principles of space microbiology for astronauts on space missions?

The Evidence Base, Further Reading and Teaching Aids

The invisible universe of the human microbiome. <https://www.youtube.com/watch?v=5DTrENdWvvM> Human Microbiome Project https://www.youtube.com/watch?time_continue=197&v=OLH4Av6YU8A&feature=emb_logo

Tomlin E. These Tiny Organisms are a Big Deal. <https://www.issnationallab.org/blog/microbiome-research-microgravity/>

Bacteria found to thrive better in space than on Earth. <https://www.youtube.com/watch?v=3kpcPAa8Z7E>

The ISS

<https://www.youtube.com/watch?v=IagxIpCvMl4> <https://www.youtube.com/watch?v=-Y04Zic1-r4> <https://www.youtube.com/watch?v=B9EKx5l9Pv8> <https://pubmed.ncbi.nlm.nih.gov/24695826/>

Scott and Mark Kelly <https://www.youtube.com/watch?v=Bo2igadkAHU> <https://www.youtube.com/watch?v=Taz8XVk15Nk>

https://www.youtube.com/watch?v=0WgqebLbfPw&feature=emb_logo [https://news.feinberg.northwestern.edu/2019/04/nasa-twins-study-gut-microbiome-shifts](https://news.feinberg.northwestern.edu/2019/04/nasa-twins-study-gut-microbiome-shifts-during-spaceflight/)[during-spaceflight/](https://news.feinberg.northwestern.edu/2019/04/nasa-twins-study-gut-microbiome-shifts-during-spaceflight/)

Nasa says the ISS is covered in metal eating bacteria. BBC. <https://www.bbc.co.uk/newsround/47854828>

Microbes and fungi on the ISS and beyond. NASA. <https://www.txstate-epdc.net/microbes-and-fungi-on-the-iss-and-beyond/>

Glossary

Protozoa - are single celled organisms of different shapes and sizes. They can be both free living in a wide variety of moist habitats (fresh water, marine environments, soils) and host-dependent (parasitic or symbiotic). Their presence in ruminants results in a higher and more stable ruminal digestion of organic matter.

Fungi - are the group of organisms that includes microorganisms such as yeasts and molds, as well as mushrooms. In ruminants they may play a significant role in the assimilation of fibrous feeds by ruminants.

Microbiota - is a vast and complex collection of all living members in multicellular organisms such as bacteria, archaea, fungi, algae, protozoa and viruses. They play a very important role for metabolic homeostasis of their host.

Gene sequencing - is the process of determining the order of nucleotides in the sections of DNA that contain genes.

Taxon (plural **Taxa**) - is a group of one or more populations of an organism or organisms forming a particular unit.

Microgravity - refers to the condition where gravity seems to be very small. Many people mistakenly think that gravity does not exist in space. In microgravity, astronauts can float in their spacecraft - or outside, on a spacewalk. Heavy objects move around easily.

Latent – is existing or present but concealed or inactive until circumstances are suitable for development or manifestation.

Petri dish - (Petri plate or cell-culture dish) is a shallow transparent lidded dish that biologists use to hold growth medium in which cells can be cultured.

Earth radiation belt (Van Allen belt) - is a zone of energetic charged particles, most of which originate from the solar wind, that are captured by and held around a planet by that planet's magnetosphere. The belt is named after James Van Allen, who discovered it.

ExoMars mission (Exobiology on Mars) - is an astrobiology programme of the European Space Agency. The goals of ExoMars are to search for signs of past life on Mars. It includes a rover equipped with a scientific laboratory.

ESA (European Space Agency) - is an intergovernmental organisation of 22 member states dedicated to the exploration of space.

Human Microbiome Project (HMP) - was aimed at characterizing the microbiota of healthy human subjects using gene sequencing in order to further our understanding of how it impacts human health and disease. The HMP was supported by the National Institutes of Health (NIH) Common Fund from 2007 through 2016.

Genetic engineering - (genetic modification) is a process that uses laboratory-based technologies to alter the DNA makeup of an organism. This may involve changing a single base pair, deleting a region of DNA or adding a new segment of DNA. The techniques employed in genetic engineering have led to the production of medically important products, including human insulin, and hepatitis B vaccine, as well as to the development of genetically modified organisms such as disease-resistant plants.