SCoPE

Scientists' Collaborative Project with Educators

The Cell Explorer:
Research Summaries for Students

These summaries include some terms and concepts that will go beyond the A-level curriculum. These summaries have been created to encourage students who are interested to investigate and further develop their biology knowledge.

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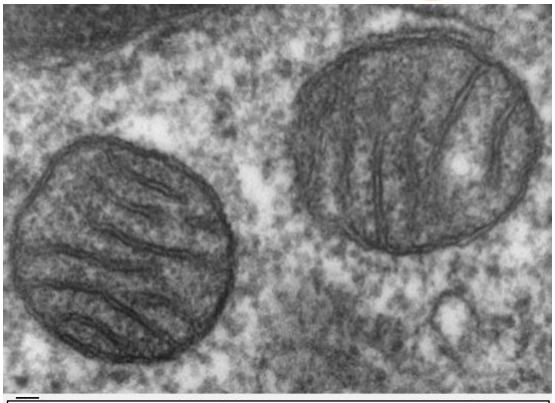
Mitochondria

Primer on Mitochondrial disease
https://www.nature.com/articles/nrdp201680



Two mitochondria from mammalian lung tissue imaged with an electron microscope. More details available here.

Mitochondria are organelles that are the sites of cellular respiration (the breakdown of nutrients to produce energy). Mitochondrial disease results from mutations of either nuclear or mitochondrial DNA (nDNA and mtDNA respectively). There is much variation, which makes both diagnosis and treatment of the disease difficult. Often the oxidative phosphorylation stage of respiration (in which ATP is produced) is affected by faulty protein synthesis machinery, which can be deadly.
More recently, newer sequencing techniques have i
donation for women has shown promise in preventing

How Mitochondrial mutations are transmitted
http://europepmc.org/articles/PMC4091738

Mitochondria contain their own DNA called mtDNA. This mtDNA is inherited only from the mother. As we age, mutations in mtDNA lead to a variety of diseases. In this research article, the transmission of artificially mixed mitochondrial genomes (both mutant and functional) was tracked over several generations. The host has a safety mechanism that can limit the transmission of disease-causing mutations and favor functional genomes (i.e. purifying selection). However, some mutant genomes may overcome this mechanism and allow themselves transmission. Even then, the 'battle' is not over, as the nuclear genome can evolve other defenses to suppress the mutant mitochondrial DNA.

Cell Membrane

Lipid Membrane and Lipid Rafts, a primer
https://www.nature.com/articles/nrm.2017.16

Cell membranes are laterally heterogeneous, i.e. they contain distinct subcompartments. These domains (also called lipid rafts) are generated by interactions between lipids such as cholesterol. Lipid rafts serve to regulate the activity of their components. For instance, they can increase the concentration of molecules for catalytic activity and play a role in immune signaling. Lipid rafts continue to be difficult to visualize experimentally or observe directly with a microscope, although recent advances suggest this may soon change.

Function of lipid rafts with respect to blood clotting
https://www.nature.com/articles/s41598-018-28363-4

Platelets are blood cells that protect the vascular system from damage, for instance by forming a plug at the site of bleeding. However, excessive production may cause blood clots (thrombosis). This is dangerous, since thrombosis in a coronary artery may lead to angina or myocardial infarction. In particular, platelets shed extracellular vesicles (EV) that expose a substance called phosphatidylserine (PS), which encourages thrombosis. Lipid rafts coordinate cell signaling and were shown to be important for the release of such vesicles, although the exact interaction is unclear.

Ribosomes

Review on Ribosome profiling and translation
https://www.nature.com/articles/nrm4069

Ribosomes are organelles that serve as the site of protein synthesis by translating an mRNA strand. Ribosome profiling is a sequencing technique (the process by which a nucleic acid sequence is determined) that helps monitor translation. Central to the technique is the idea that a ribosome will protect about 30 nucleotides from enzyme activity, which gives an indication of the ribosome's position along an mRNA strand. Thus, snapshots of the cell state can be generated. Profiling sheds light on potential mechanisms for translation, and an estimate of the quantity of translated protein. Profiling has also helped in the discovery of new proteins.

Discovery of viral ribosome proteins (another way to hijack the host)
https://www.nature.com/articles/s41467-019-08672-6

Viruses take control of the biochemical machinery of a host cell to ensure their survival and propagation. Moreover, they resist host defensive systems and can control transcription and translation of proteins. Viral genomes encode some ribosomal proteins that can replace native cellular versions. These proteins may ensure the translation of virus transcripts, provide interfaces for virus-specific translation factors, and keep an optimal metabolic cell state for the virus.

Lysosomes

Primer
https://www.nature.com/articles/nrm2217

Lysosomes are organelles that receive input from the secretory, endocytic, autophagic and phagocytic pathways. They can also fuse with the plasma membrane and provide the additional membrane required for plasma-membrane wound repair. Lysosomes interact with late endosomes by 'kiss-and-run' events and by direct fusion. Fusion results in the formation of hybrid organelles, in which the degradation of endocytosed macromolecules occurs and from which lysosomes are re-formed. Lysosomes may also fuse with phagosomes and autophagosomes. Upregulating autophagic pathways could help with Huntington's and Parkinson's disease.

Reversible storage of drugs in lysosomes
https://www.nature.com/articles/s41388-019-0695-8

Palbociclib is a kinase inhibitor drug that treats cancers by halting the cell cycle and promoting senescence. It is reversibly trapped and concentrated in vesicles in the cell - a process called lysosomal trapping. This process helps explain the long-term effects of Palbociclib even when the treated cells are washed and immersed in drug-free medium. In addition, treated cells may release Palbociclib into the extracellular medium, causing paracrine senescence.

Vacuoles

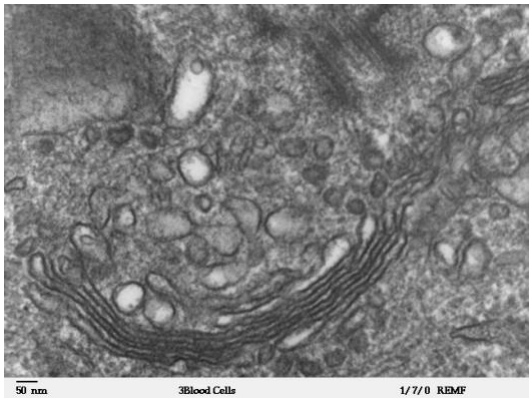
Vacuoles are storage compartments found in cells. Animal cell vacuoles tend to be smaller, numerous and temporary. Some vacuoles (called phagosomes) form as part of phagocytosis, the process by which the cell engulfs a foreign particle such as a bacterium. Plant cell vacuoles are larger, fewer and permanent. A plant cell usually has one large vacuole that can take up to half its volume. The vacuole contains water, food and waste products. In doing so, it maintains the cell's osmotic pressure and provides support.

Powerful pumps in fruit and flower vacuoles are responsible for whether citrus fruit tastes sour or sweet and whether petunias are red or blue
https://www.nature.com/articles/s41467-019-08516-3

Golgi Body

The Golgi body is a stack of flattened sacs. It is continuously formed from one end by vesicles from the endoplasmic reticulum. It processes and sorts molecules. For instance, some proteins are modified to form glycoproteins, or sugars to cell wall components in plants. The Golgi body forms vesicles of its own – called Golgi vesicles – that transport molecules to different parts of the cell or secrete them via exocytosis.

Investigating how the Golgi sorts proteins
https://www.sciencedirect.com/science/article/pii/S1534580718308785?via%3Dihub
This paper investigates the biochemical mechanisms by which some proteins are sorted in the Golgi body.



This is a high magnification transmission electron microscope image of the Golgi body, visible here as a stack of semi-circular black rings near the bottom of the image. Circular vesicles can be seen in close proximity to the organelle. More details available here.

Centrioles

Two centrioles are found close to the cell nucleus in a region known as the centrosome. Each centriole is made of microtubules, which are arranged in a ring to form a cylinder. The centrosome acts as a microtubule-organising centre for assembling microtubules that make up spindle fibres during nuclear division (for example, microtubules can do other things too). Although the centrioles are found in the centrosome, it is uncertain whether they are also crucial to the formation of the spindle apparatus.

The de novo centriole assembly pathway in HeLa cells
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2171814/

The structure of centrioles in human sperm may provide clues about male fertility and early embryonic development
https://www.nature.com/articles/s41467-018-04678-8

Flagellum

The flagellum is a tail-like structure that protrudes from some bacteria and eukaryotic cells. The number and function of flagella varies based on the cell. The primary function is locomotion. Bacterial flagella are often helical and provide a rotary movement, whereas eukaryotic flagella have a wave-like motion. Some flagella are also used in sensation. Flagella are related to cilia in structure, but the latter are usually smaller and move differently.

Bacteria eject their flagella to save energy
https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3000165

Nanorobots are designed to mimic bacterial flagella in their abilities to swim and sense the environment
https://www.nature.com/articles/s41598-017-14457-y

Rough and smooth endoplasmic reticulum

The endoplasmic reticulum (ER) is a complex system of membranes in the cytoplasm. The membranes form interconnected sac-like cisternae. The cisternae are the site of processes separate from the cytoplasm. The ER is divided into rough and smooth, although the quantities can interchange based on the cell's metabolic requirements. The rough ER is dotted with ribosomes, which are responsible for translating proteins. The smooth ER produces lipids, steroids and hormones. Produced molecules are modified and transported in the ER. Some sacs break off to form the Golgi body, another organelle important for processing molecules.

The ER is a crucial organelle in successful cellular reprogramming* (turning somatic cells into induced pluripotent stem cells (iPSCs) - adult cells that have been genetically manipulated into an embryonic stem cell-like state).
https://advances.sciencemag.org/content/5/4/eaaw0025

If unfolded proteins accumulate in the ER and the 'unfolded protein response' (or UPR) is not triggered appropriately, disease can result. A mitochondrial protein plays a role in regulating this response in the ER.
https://www.nature.com/articles/s41467-019-12816-z

*see Stem Cells section below for more information on reprogramming

Cytoplasm

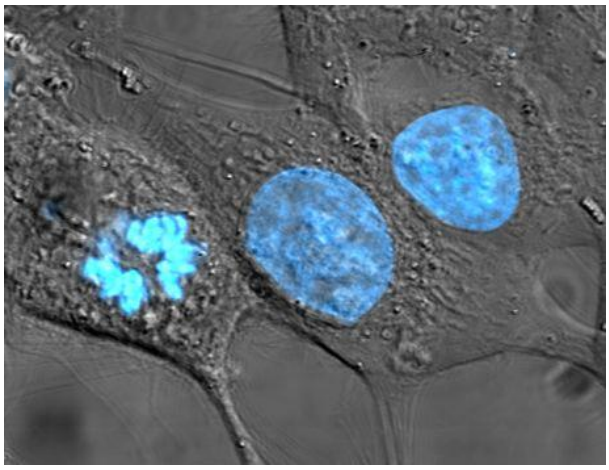
The cytoplasm is a thick fluid-like substance present between the cell membrane and nucleus. It is mainly composed of water as well as some organic and inorganic substances. It contains a network of actin filaments and microtubules that help the cell to maintain its shape and form. This network is called the cytoskeleton. The cytoplasm also contains the organelles.

The cytoplasm can be a busy place, full of many structures and molecules rapidly moving around. Scientists have developed a way to control this traffic by using lasers and are using this method to understand the effects and causes of intracellular transport.
https://www.nature.com/articles/nmeth.4656
https://www.nature.com/articles/s41556-017-0032-9

Nucleoplasm

The nucleoplasm is the substance that fills the nucleus of eukaryotic cells. It is a highly viscous liquid contained by the nuclear membrane. The nucleoplasm acts as a suspension medium for components of the nucleus including the nucleolus, and chromatin. It consists mainly of water, dissolved ions, and a complex mixture of other molecules. Thirty-two percent of all human proteins are experimentally shown to be present within the nucleoplasm.

Genetic information flows through eukaryotic cells from DNA in the nucleus to the production of proteins in the cytoplasm.
Researchers propose that mRNAs move through channelled pathways in the nucleoplasm to ensure a steady and continuous wave of travel towards the nuclear pore complex.
https://www.nature.com/articles/ncb2056



HeLa cells stained for nuclear DNA in blue dye. The cell on the left is undergoing mitosis and its DNA has been condensed. The central and right cells are in interphase, so the entire nucleus is visible. Imaged with an electron microscope. Image available here.

Nuclear envelope

The nuclear envelope is the double-layered membrane surrounding the nucleus in eukaryotic cells. The nuclear envelope contains nuclear pores that allow and regulate the transport of materials such as RNA between the nucleus and the cytoplasm.

The shape and structure of the nuclear envelope is important for health and function of cells and organisms. Defects in the architecture of the nuclear envelope are associated with human diseases such as cancer. Researchers investigate how defects, such as micronuclei, occur.
https://www.nature.com/articles/s41586-018-0534-z

Nucleolus

The nucleolus is a small, spherical structure found in the cell nucleus, made of RNA and proteins and it is responsible for making ribosomes. The ribosomes are exported via the nuclear envelope to the cytoplasm, where they are responsible for translating proteins. Nucleoli also serve other functions such as stress response and the production of particles that recognise and direct proteins.

Research suggests that small nucleoli are a visible marker of longevity and metabolic health.
https://www.nature.com/articles/ncomms16083

This paper suggests that the nucleolus may play a role in quality-control of proteins, which can help reverse the mis-folding of proteins due to prolonged stress. When the nucleolus doesn't perform this function properly, misfolded proteins can accumulate and become toxic.
https://science.sciencemag.org/content/365/6451/342

DNA/RNA

Histone modifications primer:
https://www.nature.com/articles/cr201122

Chromatin is the loosely coiled form of DNA found in the cell nucleus. The DNA wraps around histone proteins to give a beaded appearance. Histone modification is a way for chromatin to respond to external cues. This may form the basis for epigenetic inheritance, although the entire process is not well-known. The modifications affect chromatin structure and may change nucleosome ordering and affect DNA repair and replication.

Hachimoji DNA - Challenging the 4 ntd model
https://science.sciencemag.org/content/363/6429/884/tab-pdf?fbclid=IwAR2jtWINJ9zszQD1_OOeJHY5kDMFbKYw_7HJXAE3Es9gURPbqfAlRASwN14

DNA and RNA contain our genetic code. They consist of four nucleotide bases. For instance, DNA consists of adenine, thymine, guanine and cytosine. It is possible to engineer synthetic forms by replacing or adding nucleotides. Hachimoji DNA consists of eight nucleotide bases instead of four. It is stable and can increase information density of DNA by 'expanding the alphabet'. It can also be transcribed to RNA, which could potentially be translated into some novel protein. Lastly, it gives an indication of the variety of molecular structures that could support life, even outside Earth.

RNA modifications - a new frontier
https://www.ncbi.nlm.nih.gov/pubmed/29186125

Acute myeloid leukaemia (AML) is an aggressive blood cancer. Treatments have changed little for decades and outcomes remain poor. Research with the CRISPR-Cas9 technology has found that AML cannot survive without the METTL3 gene. The METTL3 protein helps in the translation of several other proteins the leukemia needs. It does this by adding methyl groups to several transcripts (RNA) of AML cells. When METTL3 was inhibited, the production of these proteins was stymied too, and the cancer cells started undergoing cell cycle arrest and apoptosis (dying). Therefore, a drug that inhibits RNA methylation could be effective against AML without affecting normal cells.

DNA Damage and repair
DOI:https://10.1038/s41556-018-0140-1.

In humans, the mutated BRCA1 gene increases the risk of developing cancer. Some BRCA1 cancer cells may not respond to promising therapies that use PARP inhibitors (targeted cancer drugs). The resistance may be attributable to low levels of certain factors. One of them is Shieldin, a protein complex that protects the ends of DNA from damage and regulates repair. Reduced Shieldin expression was shown to increase cancer resistance to drugs. Monitoring Shieldin in patients could be a useful indicator that the PARP inhibitor therapy will work, and potentially prevent wasted time.

Stem Cells

How Reprogramming occurs
https://www.sciencedirect.com/science/article/pii/S1097276514005334

The transfer of nuclei from a cell to another and back is a way to reprogram the cell with a different transcription pattern. In the experiment, somatic (non-reproductive) cell nuclei were transplanted into oocytes (female reproductive cells). Sequencing of produced RNA showed a marked genome-wide change towards the oocyte type rather than the pluripotent type. The reprogramming is rapid and comprises a hierarchical sequence of events.

FOXO3, stem cells and anti-aging
DOI:https://doi.org/10.1016/j.stem.2019.02.008

The FOXO3 protein is associated with longevity. It is a transcription factor that regulates genes responsible for cell death (apoptosis) in the nucleus. In this paper, stem cells with a modified version of FOXO3 in mice helped with blood-flow recovery and reduced necrosis in mice with ischemic injury. Its action was not just therapeutic but also reversed senescence. Humans suffering from Werner Syndrome also showed reduced expression of biomarkers for senescence when treated with FOXO3-enhanced bone marrow cells.