Fat at the cellular level

Membranes are fatty, fluid barriers

In 1972, Seymour Singer and Garth Nicolson proposed the 'fluid mosaic model' of the cell membrane: a matrix made up of a fluid lipid bilayer containing membrane proteins and glycoproteins. The cell membrane is a partially permeable barrier that lets some molecules in while stopping others, and it's the lipid composition of the cell membrane that determines how it behaves.

In animal cells, the phospholipid molecules create a watertight bilayer. Cholesterol molecules change the fluidity of the membrane, stopping it from crystallising but also allowing certain small molecules to pass through it.

Each phospholipid in the lipid bilayer is composed of two hydrophobic, non-polar fatty-acid tails attached to a hydrophilic, polar head made of a glycerol molecule and phosphate group. On each side of the membrane, the heads face outwards, while the tails pack tightly together on the inside to escape their watery surroundings. The polar heads may have carbohydrate chains attached, forming glycolipids, which are involved in cell signalling and direct cell-to-cell interactions – the sugar components are exposed on the surface of the cell where they can be recognised by other molecules.

Pathogens can also use these glycolipids. The bacterial toxin that causes diarrhoea in cholera, for example, binds to a particular glycolipid receptor displayed on gut cells, and uses it to get inside the host cells.

Fatty membranes separate inside from out

Lipid membranes are found in living things from bacteria to blue whales. Biological membranes contain a double layer of phospholipid molecules, as well as cholesterol (in some mammalian membranes and Mycoplasma bacteria) and glycolipids (see 'Go with the flow'). In eukaryotic cells, membranes are important for compartmentalisation – many of the organelles are bounded by lipid membranes, although not always in a double layer.

In adipocytes (fat cells), fats are stored for energy (see 'Fat and obesity'), while in nerve tissue they act as electrical insulators (see 'Fat on the brain'). The myelin sheath of a nerve cell is actually formed from the lipid membranes of other cells called Schwann cells, which grow to be much larger than other cells, meaning they can wrap themselves around the nerve axons. These particular membranes are also unusually rich in glycolipids. It's thought that the glycolipids may help stick the myelin sheath and axon together.

Lipids also carry messages between cells. Prostaglandins, derived from fatty acid structures, are hormone-like molecules first discovered in sperm, but they have functions all over the body including in triggering inflammation and pain, clotting blood, and even inducing labour.

We need fats for our nervous system

Your brain is 60 per cent fat.

As the human brain develops in the womb and in childhood, it needs a constant fatty acid supply to support the growth of nerve cells (neurons). Even the adult brain needs fat to maintain the membranes and myelin sheaths surrounding these cells – all 86 billion of them – and in comparison to the protein components of neurons, the fatty components need to be replaced more regularly.

The myelin sheath is a fatty insulating layer that speeds transmission of nerve impulses along neurons. It is produced by oligodendrocytes in the central nervous system and Schwann cells elsewhere.

Without myelin, our nervous systems couldn't function properly. In multiple sclerosis, people gradually lose the myelin in parts of their brain, which causes problems with movement, sight and thinking. In the 1990s, scientists found that people with multiple sclerosis had very low levels of certain fatty acids in their red blood cells and plasma.

We think of fish as brain food, partly because the omega-3 oils found in oily fish are key to a healthy brain. Studies have linked mental health conditions such as depression and hyperactivity to low or altered levels of essential fatty acids. Beware bogus claims, however.

It's not clear whether we get the benefits of omega-3 when it is taken in fish oil supplements. For example, some recent studies suggest the supplements do little to prevent the decline of brain function in older people. There is a billion-dollar industry built on fish oil supplements, but the evidence for beneficial effects for a range of conditions is mixed.

Plants use lipids for a variety of functions

We get a lot of our lipids from plants: sunflower oil, olive oil, nuts and seeds are all good sources of fats. But why do plants need fats? They don't have nerve cells, they can't feel the cold and they make their own food (glucose) by photosynthesis.

Well, they need phospholipids to make up their cell membranes, as animals do. Another important function of lipids in plants is as the energy store in seeds. Germinating seedlings cannot make their own sugars through photosynthesis, so they rely on stored lipid droplets to fuel their growth.

Other functions of lipids include making hormones and the formation of the cuticle (the waxy, waterproof coating for leaves and stems) and the exine (a tough, stiff coating for pollen grains).

Some genes involved in fat storage in plants have equivalents in yeast and mammals. In humans, mutations in the gene that controls synthesis of the molecule seipin can cause a disorder where fat is stored around the muscles instead of in adipose tissues. The flowering plant *Arabidopsis* has versions of this gene, suggesting that plants could help us to understand more about human disease.

Fats can be used as fuel in our bodies

When we burn fat, we must first convert it from stored fat sitting in our adipose tissues into a form that can be respired. How do we do that? In adipocytes, the fat is stored as chemically unreactive triglycerides, each composed of three fatty acid chains bonded to a glycerol molecule (see 'Storing fat' for how they form).

The first step is the hydrolysis (breaking) of the bonds between the fatty acids and glycerol, which is carried out by hydrolytic enzymes called lipases. The free glycerol and fatty acid molecules are then transported to other tissues and incorporated into the process of cellular respiration. Glycerol is converted to triose phosphate and enters the glycolysis pathway. Fatty acids undergo beta-oxidation and are split by enzymes into (2-carbon) acetyl CoA molecules, which enter the Krebs cycle.

At this point lipids, like sugars, become fuel for aerobic respiration in the mitochondria. Respiring a gram of fat releases more energy than a gram of carbohydrate. This is because fatty acids are oxidised completely. The hydrogen ions are picked up by NAD and FAD and fed into the electron transport chain.

While respiring fat releases a lot of energy (see our 'Fat by numbers' infographic), it also produces chemicals called ketones, which can be dangerous at high levels. This can happen in people with diabetes who are short of insulin. A lack of insulin means that they can't get enough sugar into their cells, so they break down fat instead. The build-up of ketones can lead to vomiting, hyperventilation and one rather strange symptom: breath that smells like pear drops. People suffering from starvation or on low-carb diets may also taste pear drops, because ketones are sweet-smelling, sweet-tasting molecules.

Brown, white and beige fat?

There are two main types of adipose tissue, or fat, found in mammals: white adipose tissue (WAT), or white fat, and brown adipose tissue (BAT), or brown fat. White fat serves three functions: as heat insulation, as mechanical cushioning and, most importantly, as an energy source. Brown fat is important for thermogenesis (making heat) in newborns, but precisely what purpose the cells serve in adults is still unclear.

Very young babies don't shiver to keep warm; they burn brown fat instead. In newborn infants, brown fat makes up about 25 per cent of the body mass and is located on the back, along the upper half of the spine and toward the shoulders.

In adult mammals, the presence, amount and distribution of each type of fat depends upon the species, but there is much more white fat than brown. Adults carry many kilograms of white fat but just a few grams of brown fat, concentrated in the front part of the neck and the upper chest.

In 2012, scientists discovered a third type of fat, something called beige fat. Beige fat cells are brown fat cells that occur in white fat tissue in response to certain triggers, like extreme cold.

What do we know about brown fat?

Brown fat is made up of heat-producing cells full of mitochondria (energy-generating structures), and it is metabolically active, unlike white fat. The brown colour comes from iron that is attached to proteins in these mitochondria.

Its high number of mitochondria means that brown adipose tissue is very efficient at respiring and therefore considered healthier than WAT.

Researchers investigating a protein called PRDM16 (PR domain containing 16) found that this protein could trigger cells that usually make white fat cells to make brown fat cells instead. Kahn and colleagues extended this work, and they found that a protein called BMP7 (bone morphogenic protein 7) is vital for the generation of brown fat cells. The researchers artificially increased the amount of BMP7 made in some mice and used untreated mice as a control. After five days, treated mice had more brown fat, lower weight gain and a higher body temperature than the untreated animals.

Could brown or beige fat be used in weight loss?

Currently, anti-obesity measures focus on a reduction in energy or food intake. Could targeting brown or beige fat lead to new treatments for obesity?

Perhaps. Researchers are exploring the differences between brown fat and beige fat, and are working to understand what they do in the body. A 2013 review paper reports: "Regardless of its natural role, increasing the activity of brown fat, beige fat or both through drugs or other methods holds tremendous promise for the treatment of metabolic disease."

What are the potential implications of these treatments?

Although addressing the growing problem of obesity is crucial, the obvious problem with seemingly ‘quick fix’ treatments like this is that they do not tackle the root causes of the condition.

Having such treatments available could well encourage more people to eat unhealthily and/or lead more sedentary lives with little or no exercise. Similarly, people who are obese may simply decide they are going to eat more and end up lessening the effects of the treatment or cancelling it out entirely.