Molecular Medicine – A journey into our body

An introduction to our course

Felix Graw

At the opening weekend in June we first met and got to know each other.

We – that are our course leaders Annette, Sabine, Elisabeth and Xin and ten members of the molecular medicine course who travelled to Adelsheim from all over Baden-Württemberg.

After a short introduction, we started off with a very funny, but also very difficult experiment. In groups of four we had the task to build a cover for an egg which had to be protected, because the egg should be thrown out of the window of the first floor.

The problem was that we only got a piece of paperboard, a balloon, a string and a pair of scissors.

Surprisingly, it was possible to build such a cover as two groups were successful and the egg didn't break. After this entertaining start, we began to plan the summer academy.

The course leaders informed us about the main topics, handed out some material and everybody chose a topic, which he/she was going to present in August.

Our course was held in English because four Chinese students were also taking part in the programme.

Of course, the Chinese members couldn't come to the opening weekend. So everybody was very curious at the beginning of our academy in August to finally meet them. They quickly integrated into the group and we soon became friends.

During the two weeks of the academy, our course examined a lot of topics concerning the human body.

We started with anatomy and had a closer look at different organ systems of our body, so the urinary system and the digestive system. We learned how the organs of these systems function, e.g. the kidneys, the liver and the pancreas. Furthermore, we talked about the vascular system with the heart and the blood and about the brain.

But we did not only work theoretically, we also had very interesting work experiences. So our course leaders organized pig organs and we dissected them.

For most of us this was a new but very interesting experience.

We analyzed histological slides of the discussed organs under the microscope and learned a lot about tissues and cell structures. So we had proceeded to the histological level of our body.

In the second week, we heard about the basics of the hormone system and its function in the human body.

Finally, we got onto the molecular level of our body and were introduced to the DNA, its replication, transcription and translation. We got to know the processes when a cell is dividing and what happens, if this is not properly regulated: cancer.

In order to see how research actually looks like, our course went to Heidelberg to the German Cancer Research Center (DKFZ). A scientist told us about her work, which deals with mechanisms of cancer formation resulting from a wrong hormone system, and showed us the laboratory.

As you can see from this report, we had two wonderful and interesting weeks at Adelsheim and we thank our course leaders very much for introducing us to this new world of molecular medicine...

In the back from left to right:

Hülya

- Always good-humored
- Turkey is her home
- Table tennis queen of Adelsheim

Dimi(tri)

- Speaks nonstop (even when nobody is listening to him)
- Black-haired half-Greek
- The table tennis king of Adelsheim

Yannik

- "The Clicker" during our PowerPoint presentations
- Got the gist immediately
- Paramedic in his school

Florian

- Guitarist with a fixed finger nail
- Some call him Flori, others Flo or Flocke
- Very nice curly hair

Felix

- Life-Science-Lab
- A passionate photographer
- Team worker

Elisabeth

- Camera-shy but nevertheless photogenic
- Our hormone expert
- Our tall student mentor

Paul

- Knows all Chinese table tennis players by heart
- Open-minded
- Liked German food and chocolate

In the front from left to right:

Xin

- Superb Power Point presentations
- Smiles all the time
- Speaks very good English

Sabine

- Always prepared to take risks. As a result she is often injured
- Huge amount of general knowledge

· Remains calm no matter how difficult the situation is

Natalie
- · Has a lovely voice
- · Plays tennis (very well!)
- · Our guide in Heidelberg

Ailís
- · Plays the piano very well
- · Native speaker
- · Her explanation of the heart made our hearts beat faster

Sandra
- · Loves playing tennis with Natalie
- · Smiles all the time
- · Drinks a whole Vittel bottle during each lesson

Sarah
- · Is very musical
- · Played "Fußbodenheizung" with Ailís
- · Got on very well with our Chinese friends

Janina
- · Stagestruck
- · Freezing all the time
- · Loves eating fruit and vegetables

Lily
- · Sang the DNA song ALL the time
- · Liked German dancing
- · A very outgoing person

Lily
- · Polite and friendly
- · A calm personality
- · Keeps contact with the German participants

Helen
- · Loves the DNA song
- · Stabbed Dimitri's finger 5 times
- · Played badminton very well

Annette
- · Laughs a lot
- · Studies Molecular Medicine in Erlangen
- · Makes a lot of jokes

Heart to Heart

Ailís Hunt-Haney

We have all watched a film or a series, during which at some point a person is brought to hospital, severely injured. Well known examples of series are "Emergency Room" and "Grey's Anatomy". The ambulance arrives at the hospital, the patient is quickly brought into the Intensive Care Unit and the surgeons start their work. But sometimes even they come too late. The heart monitor, also called electrocardiogram or ECG, shows a straight line, a long sound is to be heard. The person is dead.

Usually, however, the heart monitor shows a line resembling a row of mountains. It shows the electrical activity of the heart. This is one of the topics related to the heart I am going to explain to you in the following text. Enjoy yourselves!

Cross my heart and tell the truth

My heart is located in the thoracic cavity between the lungs.

This area is called the mediastinum. The tip of the heart, where the strongest sound may be heard, is just above the diaphragm and points left of the midline. Hence people have the impression that their heart is on the left side of their upper body.

Just as the whole body has an outer layer, which is the skin, the heart also possesses an outer membrane. This skin consists of three layers called the pericardial membranes (see Figure 1). Under these three layers you find the heart muscle which is called myocardium. The last layer of the heart wall is called endocardium. It is very smooth, which is a necessity for the heart – a rough surface would cause blood clotting.

My heart is my home

The heart can be compared to a house with four rooms, connecting doors, and doors exiting. The heart has four chambers and valves

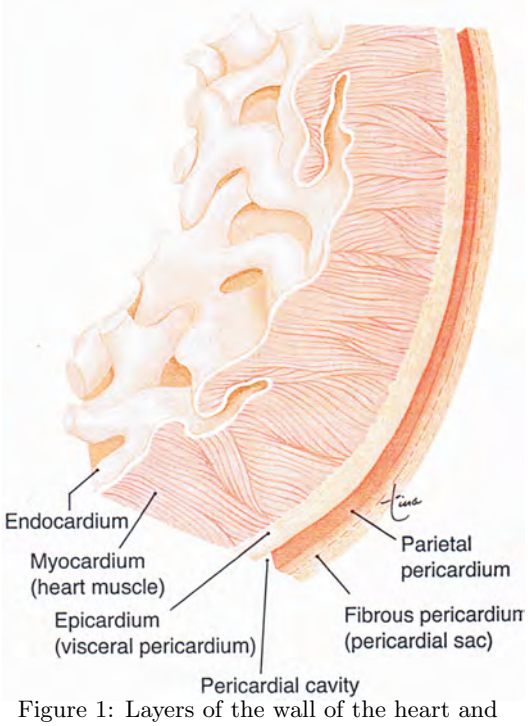


Figure 1: Layers of the wall of the heart and the pericardial membranes.

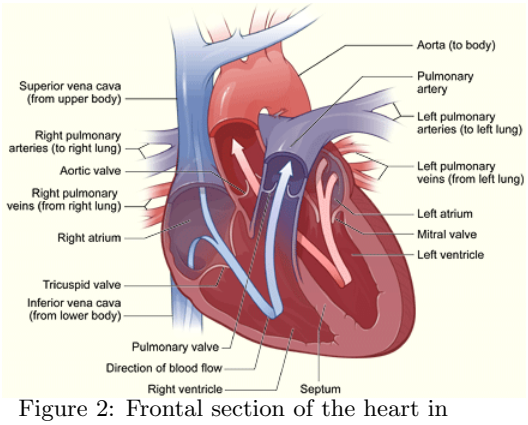


Figure 2: Frontal section of the heart in anterior view, showing internal structures and the blood flow through the heart.

connecting the chambers of the heart; other valves allow for blood to exit the heart.

However, not only does the heart have four different chambers, but it is also divided into two halves: into the right half and into the left half. The upper level of the heart gives the right and the left atria (singular: atrium) and the lower level represents the ventricles, as you can see in Figure 2.

I'm stirring up my blood!

Blood flows from the inferior and superior vena cava into the right atrium; when the pressure of the blood flowing from the veins into the atrium is high enough, the tricuspid valve is forced open. The tricuspid valve, which is also called the right atrioventricular valve (right AV valve), is found between the right atrium and the right ventricle, and prevents backflow of the blood. All this can be followed by looking at Figure 2.

Two thirds of the accumulated blood flows passively into the right ventricle; then the atrium contracts to pump the remaining blood into the ventricle. This contraction is called the systole. After the systole comes the diastole, i.e. the relaxation phase begins. At this time, when the atrium is relaxing, the ventricle begins to contract and starts its systole. The blood forces the tricuspid valve closed and opens the pulmonary semilunar valve. The pulmonary semilunar valve is found between the right ventricle and the pulmonary artery. The pulmonary semilunar valve then opens and blood flows into the pulmonary artery, exiting the heart.

The blood flow from the veins into the right half of the heart and out of the heart is shown as a blue arrow in the diagram. Blood then flows to the lungs to be oxygenated, flowing then back to the heart, entering it through the left and right pulmonary veins. The procedure which takes place in the right half of the heart is repeated in the left half of the heart; the blood flows into the atrium, then passively runs into the ventricle and the atrium contracts to pump the remaining blood into the atrium. Due to the pressure in the ventricle the mitral valve (the left AV valve) is forced closed and the aortic valve, leading to the aorta, is opened. This blood flow is also shown in Figure 2; the red arrow symbolises the oxygenated blood running through the heart. The blood now flows through the aorta into the rest of the body and supplies it with oxygen.

Follow your heart!

How is my heartbeat caused? We asked ourselves this question as part of our course. The answer is pretty simple: you might be able

to recall that your heartbeat consists of two beats, a first, strong one and a second, light one. The first beat, the longest one, is caused by ventricular systole closing the left and right AV valves. The second one is caused by the closure of the aortic and pulmonary semilunar valves.

You can define the cardiac cycle as the sequence of events occurring during one heartbeat.

Where does my heartbeat come from?

The cardiac cycle is the result of the cardiac conduction pathway. The cardiac conduction pathway is the electric activity of the heart, whereas the cardiac cycle is the mechanic activity of the heart. Electrical impulses flow through the myocardium of the heart and cause systole and diastole of the heart's chambers. If these electrical signals were not to happen, the heart would not function properly and would stop beating. So the electrical signals are essential for our survival. This electrical pathway can be observed in Figure 3, shown below.

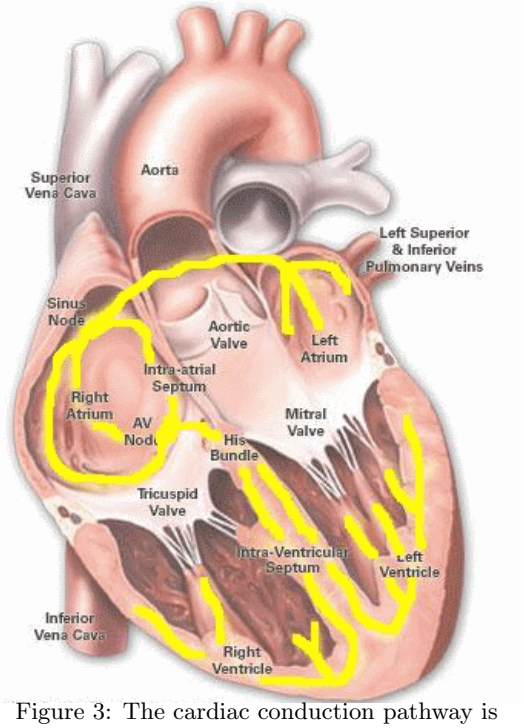


Figure 3: The cardiac conduction pathway is the electrical activity of the heart.

Our electrical signals travel a long way through our heart to facilitate the proper function thereof. The main pacemaker of the cardiac conduction pathway is the sinoatrial node (SA node), which is a group of muscle cells which are located in the right atrium. The SA node sends off an electrical signal which then travels through the right atrium to the atrioventricular node (AV node) which can be found between the right atrium and the right ventricle. The AV node is the only way for the electrical signals to travel from the atrium into the ventricle. This pathway from the SA node to the AV node brings about atrial systole. To make not only the right atrium, but also the left atrium contract, the electrical signals also travel into the left atrium through small fibres leading from the SA node into the left atrium. Now, the impulses are transmitted by the atrioventricular bundle (AV bundle), which is also called the bundle of His, to help cause ventricular contraction. The electrical signals, which are the main parts of this pathway, leave to the left and right bundle branches. And from the bottom of our hearts they lead into the Purkinje fibres, which then lead to ventricular systole.

The digestive system

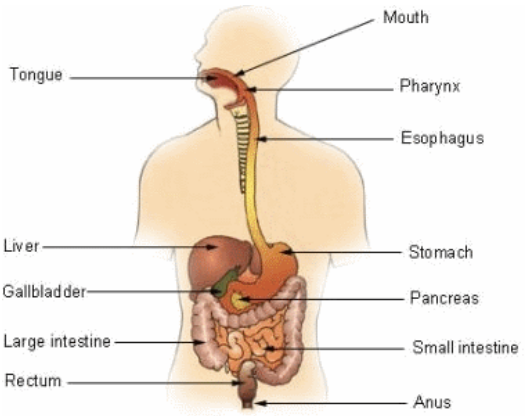
Janina Fausel

That is the major question I want to explain to you now. Please have a look. . . .

Here you have got a picture with all the important organs which are part of the digestive system.

What are the several functions of each organ and in which order do all actions take place?

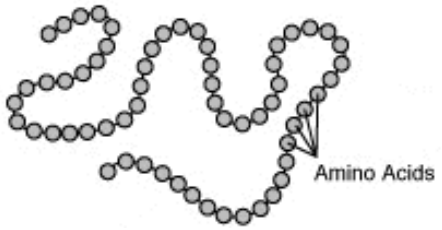
1. So first, you put something into your *mouth*. There you chew it into smaller pieces. Sugars in the food are already broken down (this is done by an enzyme called amylase).
2. Then you swallow and the journey goes on. The food moves through your *esophagus*



The digestive system

into your...

3. *Stomach.* There, all the proteins contained in the food lose their structure. You have to imagine that each protein is a long chain of amino acids. Normally this chain is folded quite complicatedly in a way, that the protein structure is compressed. In the stomach this structure is lost and the amino acid chains are unfolded.



Amino acid chain

4. After that, the food is transported into the *small intestine.* It is the main organ to digest food and absorb nutrients.

   It is also the largest part of the digestive system and is divided into 3 parts:

   - the duodenum

   - the jejunum

   - the ileum

   There the chains of amino acids are split up into the single amino acids.

5. The following *large intestine* is the last part of our digestive system and it is divided into five parts.

6. Finally, the food (or better the remainders) leaves your body through the *anus.*

This is the way our food moves through our body.

But two other important organs are also part of the digestive system.

One of them is the *liver.*

Its main function concerning digestion is the production of bile which breaks fat pieces into smaller ones.

The second is the *pancreas.*

It produces different enzymes which support e.g. the splitting of the protein chains into their components.

Histology

Now, after having explained to you the functions of the organs, we will just have a short closer look at the layer of our small intestine, which gets in contact with the food: the mucosa.

First, you can see a picture of it....

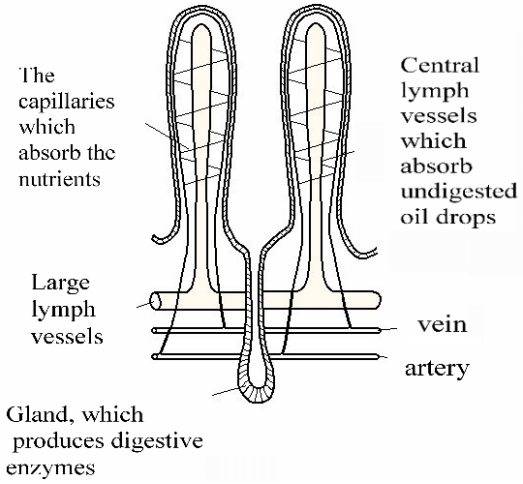


Diagram of the mucosa of the small intestine

In this picture you can see the structure of the mucosa of our small intestine.

The structures above the large lymph vessels are called villi.

And the glands, which are below the large lymph vessels, are called crypts.

The gland you can see at the bottom of the picture produces enzymes, which support the digestion of the food. These enzymes are given into the small intestine where they are needed. This action is called secretion.

The nutrients from the food are absorbed at the surface of the villi and get into the blood vessels of the mucosa.

This way we are provided with the energy without which we could not move or do anything, without which we can not survive.

After we had learned so much theory within our course, we also had the chance to prepare real pig organs:

- the small intestine

- the liver

First, we all were a little bit scared about it, because no one of us has ever seen a real organ before.

After we watched how Annette, our course teacher, cut it into pieces and explained us the several parts, we could make our own experience with the organs.

It was a very strange feeling, very much blood and at first we could not distinguish the different parts, everything looked the same, but then we learned it and it was a lot of fun!

Now we have talked about the digestive system, but you have already noticed, that this system just takes up nutrients and other substances from our food.

Maybe you are wondering what happens with fluids we drink, after they are absorbed, or what happens with metabolic end products our body can not use anymore.

You will learn something about this by Hülya in the next part.

The Urinary System

Hülya Erbil

As we learned, the digestive system is responsible for the food we eat. However, my topic, the urinary system, is very important for the process of transforming fluids we drink and substances in our blood into urine.

The urinary system consists of the two kidneys (left and right), two ureters, urinary bladder and the urethra (see Figure 1).You have to imagine that one part of the blood, that will later become urine, first travels through the blood vessels and then enters the kidneys (left or right); after that it goes into the ureters (left or right), then into the urinary bladder where it is stored and last but not least through the urethra out of the body. But now I will mainly focus on the kidney and first the most important things to know are the structure and the function of the kidneys.

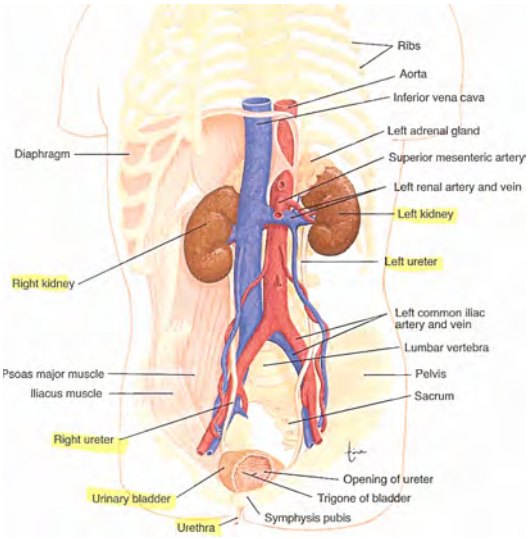


Figure 1: The urinary system

So let's begin with the structure: The kidney can be distinguished into 3 main areas:

First we have the renal cortex. It is a tissue layer lust like the second layer, which is called the renal medulla. The last area is a cavity formed by the expansion of the ureter and is called the renal pelvis (see Figure 2).

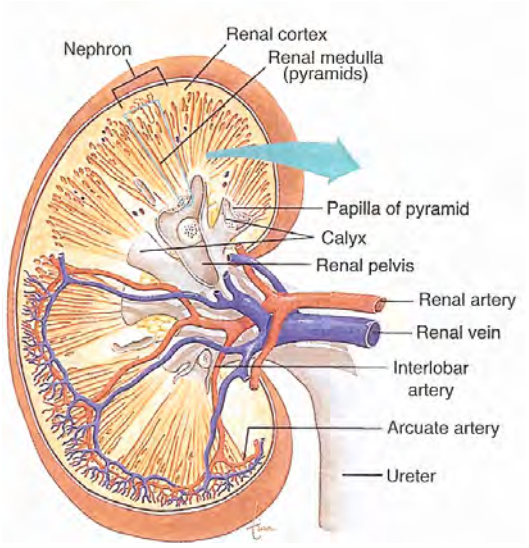


Figure 2: Structure of the kidneys

And of course the structure is strongly related

to the function. So the kidney is responsible for the production of urine, for the excretion of metabolic end products. Another function is the monitoring of our blood's pH, body's water and salt. Furthermore, it has to control our blood pressure. On top of that, hormones are produced and secreted here.

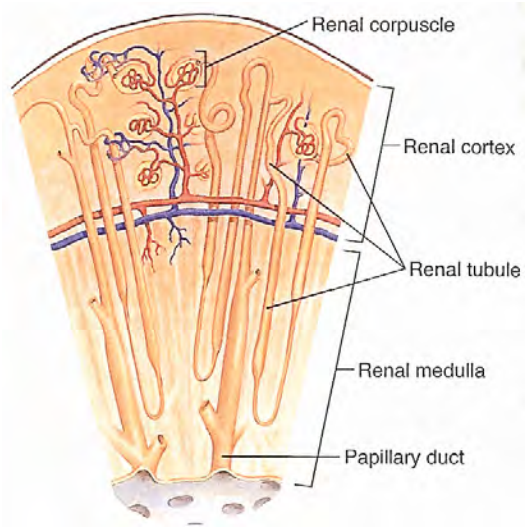
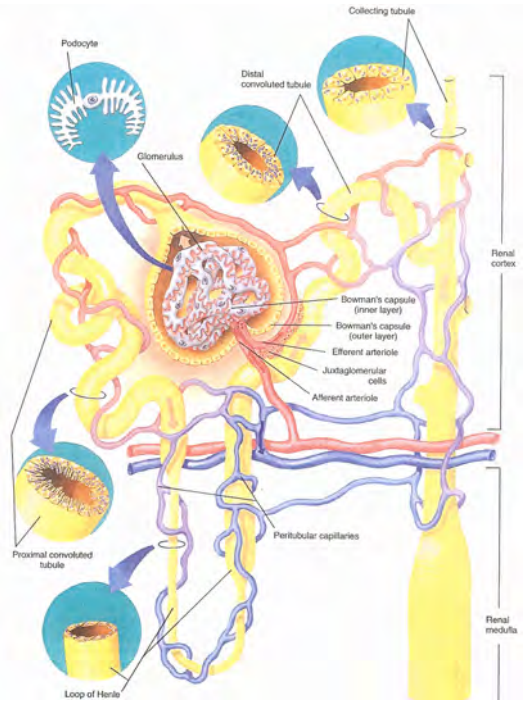


Figure 3: Structure of the nephron

Looking at Figure 3, you can see the structural and functional unit of the kidney: The nephron. Each kidney consists of about 1 million nephrons. Having a deeper look onto the picture we can see that a nephron consists of 2 main parts: Renal corpuscle and the renal tubules (Figure 3). The renal corpuscle itself consists of the glomerulus and the Bowman's capsule.

You have to imagine that the blood comes from the afferent arteriole (see Figure 4) and goes to the Bowman's capsule where it is filtered. The filtrate is no longer blood, but it is called renal filtrate and will later become urine. Then this renal filtrate goes out of the renal corpuscle and into the second part of the nephron, namely through different tubules.

The so called renal tubules continue from the Bowman's capsule and consist of: the proximal convoluted tubule, the loop of Henle, the distal convoluted tubule and the collecting tubule. Every tubule has very thin walls which provide an efficient exchange of materials and are surrounded by peritubular capillaries (tiny blood vessels). Their function is to receive the material that is reabsorbed into the blood.



The tubular system

But how is urine formed?

The answer to this is simple: There are three major actions happening in the kidney.

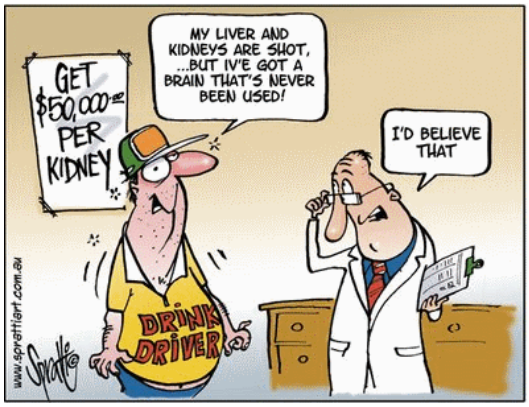
The first action is in the glomerulus. High blood pressure forces plasma, dissolved materials and small proteins into the Bowman's capsule and produces the renal filtrate.

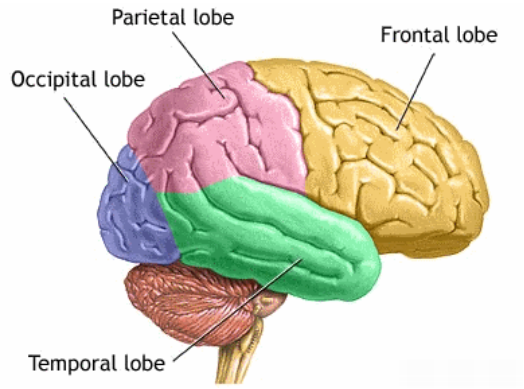
The second action, the tubular reabsorption, takes place from the renal tubules into the peritubular capillaries. In other words: In one day the kidneys form about 150-180 litres renal filtrate, but we only excrete 1-2 litres of urine, because 99% of the renal filtrate are given back to the peritubular capillaries.

The last action is the tubular secretion. It ensures that substances, e.g. substances that are toxic for our organism, are secreted from the peritubular capillaries into the renal filtrate and so it changes the composition of the urine.

So one could say that the tubular reabsorption and the tubular secretion act in opposite directions.

And in the end a funny picture!!





The Brain

Sarah Walther

Besides the heart, the digestive system and the urinary system, we also talked about the brain.

The brain is the control center of the central nervous system, responsible not just for behavior, but also for movement and muscle coordination. In mammals, the brain is located in the head, protected by the skull and also includes the primary sensory apparatus of vision, hearing, balance, the sense of taste and smell.

The human brain weighs about three pounds or 1.5 kg. In its natural state it is very soft, having approximately the consistency of pudding. When alive the brain is pinkish on the outside and mostly white on the inside.

Anatomy

The brain of the human body consists of five parts: The cerebrum and the cerebellum, the interbrain, the midbrain and the afterbrain.

The *cerebrum* is divided into the right and left hemisphere. Everything we feel, touch, see, hear, smell, taste, but also what we think is processed in the cerebral cortex. For the different perceptions, different regions in the cortex are responsible:

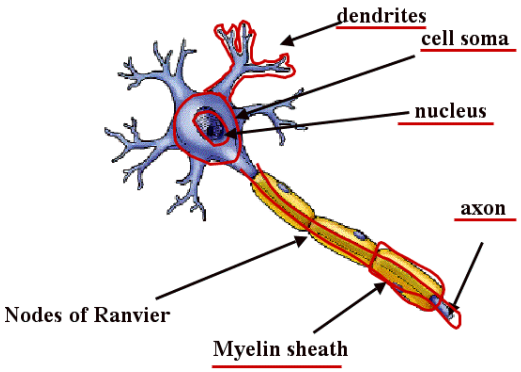
1. Frontal lobe: It is used for reasoning, emotions, judgment and voluntary movement.
2. Parietal lobe: It contains important sensory centers (only for the sense of touch).
3. Occipital lobe: It processes sensual information from the eyes.
4. Temporal lobe: It contains centers of hearing and memory.

The *cerebellum* also consists of two parts. It is responsible for the coordination of movements. If the cerebrum, for example, says: "Walk!" to the leg muscles, this command is first sent to the cerebellum, which then coordinates the performance of the movement. The function of the cerebellum will be reduced by the consumption of alcohol, so a drunken person is unable to walk straight along.

The midbrain, the interbrain and the afterbrain make up the *brain stem*. It has got a smooth surface and it is the connection to the spinal cord. Here, essential processes are steered, independently of our consciousness. The brain stem is the center for the rhythm of breathing and of our gut, for vomiting and it controls our heart beat.

Histology of the brain

The brain is composed of two classes of cells, neurons and glia. Neurons are cells in the nervous system that process and transmit information by chemical signals within the neuron. They are the core components of the brain. Glial cells actually outnumber the neurons by about 10 to 1. Glial cells provide support and protection for neurons. The four main functions of glial cells are to surround neurons and hold them in place, to supply neurons with nutrients and oxygen to insulate one neuron from another, and to destroy pathogens and remove dead neurons.



Neuron general structure

In our course we had a look at the brain cells under the microscope, which was very interesting. First it was very difficult to find everything, but after some time it became clearer. We saw the cortex with lots of cell bodies and also the pituitary gland. The pituitary gland is located at the base of the brain and secretes hormones regulating homeostasis of the body. We also had a look at the hypothalamus, which is located just above the brain stem. It is the control center of many autonomic regulatory activities of the body. In the hypothalamus we could see the axons of the neurons, which looked like long fibers.

Dissection of the brain

Like the heart, the liver and the kidneys, we dissected the brain of a pig, which is very similar to the human brain. Before dissection, I was very excited, because I had never done something like this before. I have never seen "real" organs in detail and so I did not know how my reactions would be. Fortunately, everything came up roses and my fear whether I would maybe topple down did not become reality.

In general, the pig brain was very interesting. You could see the interesting structure and even the brain skin. I mostly liked the cerebellum, which was bordered clearly of the rest of the cortex. The cerebellum looked like a leaf of a tree with all its grey nerves.

For me it is unbelievable that such a small organ is steering all the relevant functions and the behavior of the whole body. Furthermore the whole knowledge, memories and feelings are stored in it. Therefore it was very interesting for me to have a look at the brain and I still marvel lots of times about it.

Dissection

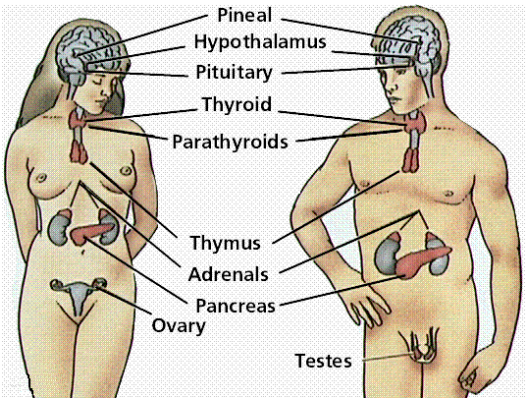
Above I have already talked about hormones, which can be produced by some parts of the brain, as for example the pituitary gland. But now Sandra will explain to you more in detail how hormones exactly work.

Hormones

Sandra Salvasohn

Hormones are chemical messenger substances in our body which transport signals from one cell to another. So they can influence growth, development, function of many organs, body temperature, salt and water balance, coordination of metabolism and so on...

The hormone system is also called endocrine system. It consists of glands located in the whole body that are able to secrete hormones.



Different glands of the hormone system

After the hormones are secreted, they are released directly into the bloodstream. They flow through it and when they reach a cell which has got a suitable receptor they bind to this receptor and cause an effect. A hormone is like a key that fits only into its proper keyhole. It depends on the target cell and its expression of receptors whether the cell reacts to a hormone.

In most cases these receptors are located on the cell membrane. But some hormones (e.g. the steroid hormones) are able to pass through the cell membrane and bind to a receptor, in the cytoplasm or the nucleus. When the hormone has bound to its receptor this activates biochemical reactions inside the cell (the so called primary response).

Hormones can cause one or more effects in the target cell. And in different cells, a certain type of hormone can also have different or even opposite effects. That means: in one muscle cell for example, the hormone can cause relaxation and in another cell the same hormone can cause contraction of blood vessels.

Already very little amounts of hormones can cause a big effect. And therefore it is important that hormone secretion is regulated. This is the task of so called control cycles. There are a lot of different control cycles. Via these control cycles the hormone production can be charged or reduced and so the amount of hormones can be influenced.

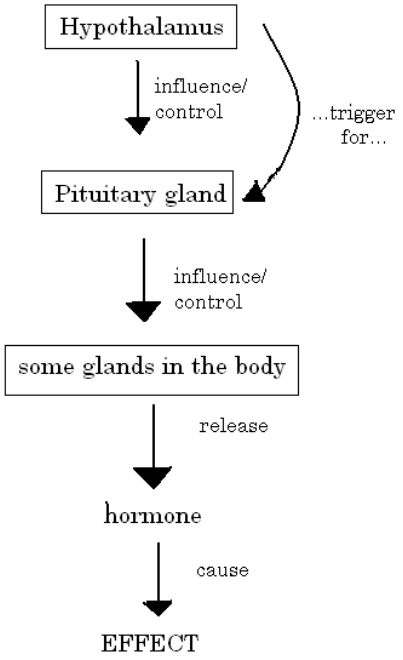
One important control cycle is the so-called hypothalamus-pituitary axis. This control cycle consists of more than only one step:

The hypothalamus is the superior inceptor. At first, it releases the so called releasing-hormone that causes the secretion of another hormone in the pituitary gland.

This hormone causes a peripheral endocrine gland to produce a third hormone. This third hormone generates the main effect.

The concentration of this hormone in the blood is permanently controlled. The hypothalamus and pituitary gland get a feedback and so they can increase or reduce the hormone secretion (positive/negative feedback).

Now to the pancreas:



Hypothalamus-pituitary axis

The two hormones insulin and glucagon produced by the pancreas both regulate the blood glucose level, just with opposite effects. They are antagonists. Insulin is responsible to keep up the nominal value during the day. For example when we eat something and our blood glucose increases, insulin is released into the blood. The effect: The glucose is absorbed by the tissue cells, the blood glucose level decreases. Later, when the glucose level reached the nominal value, the insulin production is reduced, too and so the balance can be kept up.

Diabetes

If this system does not work well, one will develop diabetes.

Diabetes is a metabolic disease. The main symptom is the increased concentration of glucose in the blood. The reason for this is either absence of insulin or insensitivity to insulin. Depending on the cause there are two different types of diabetes (Type I and Type II). The frequency in Germany is about 550.000 cases of type I and about 5 millions of type II. Type I has its onset especially among children and teenagers, but there is no age limit. Type II affects adults from about 40 years on.

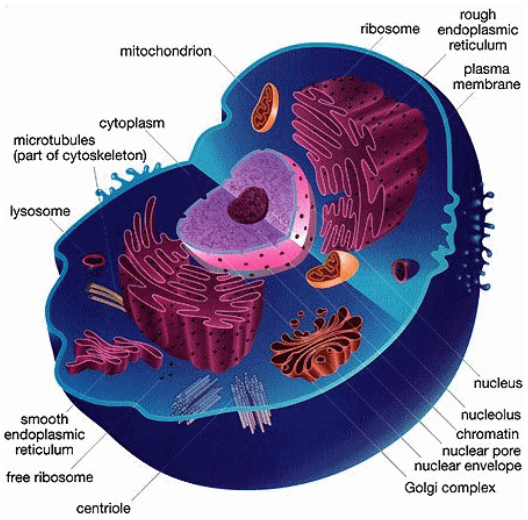
In general: Transport of information by the hormone system is not as fast as by the nervous system. That means: When the hormones are released from a gland, it can take a few seconds (e.g. adrenalin) up to hours or even days to cause an effect.

After we had looked at many different systems in our body so far, for example the hormone system, we went on to the molecular level, to the DNA and its elements.

DNA – The Genetic Information

Florian Göser

The DNA (deoxyribonucleic acid) is a molecule which is located in the nucleus of every single cell. This molecule contains the genetic information to make all the proteins of our human body.



A eukaryotic cell

The structure of the DNA

The DNA has a double helix structure and is made up of 2 single-strands.

A DNA strand consists of nucleotides. They are composed of a base, a sugar and a phosphate.

In the DNA we can find four different types of bases: Adenine (A), Thymine (T), Guanine (G) and Cytosine (C).

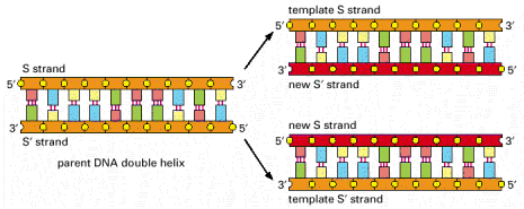
Hydrogen bonds between the bases of the two DNA strands make the DNA strands stick together.

Adenine always binds to Thymine and Guanine always binds to Cytosine.

The duplication of the DNA

If a cell divides, the DNA also has to be copied. Therefore the two strands first separate from each other and are then used as templates for new DNA strands. That means that to each base of the two original strands binds a nucleotide with the correct "partner-base".

So to every nucleotide with an A base will bind a T base and to every nucleotide with a C base will bind a G base. The bound nucleotides form the new DNA strands.



DNA replication

The messenger RNA (m-RNA)

If a cell has to build a protein, the genetic information of the DNA in the nucleus is needed.

BUT that is a big problem, because the proteins are built in the ribosome, which is located in the cytoplasm, and the DNA with the needed genetic information is in the nucleus and cannot leave it. So there has to be a link between the DNA in the nucleus and the ribosome. This link is called the messenger RNA. The messenger RNA is a copy of the DNA, which can be carried out of the nucleus to the ribosomes. The difference between the DNA and the messenger RNA is that the messenger RNA is single stranded and has uracil bases instead of thymine bases.

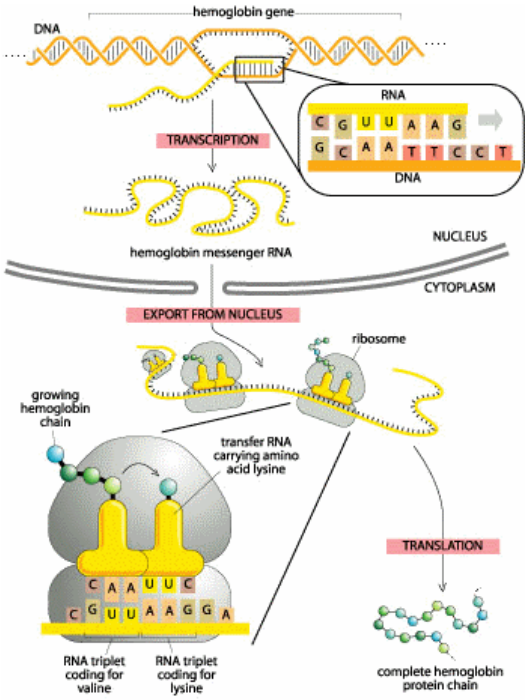
mRNA, transcription and translation

How is a protein actually built?

In a process known as transcription a molecular machine first unwinds a section of the DNA helix to expose the genetic instructions needed to assemble a specific protein molecule. Then these instructions are copied and a molecule known as messenger RNA is formed. When the transcription is complete the slender RNA strand carries the genetic information through the nucleus pore complex into the cytoplasm.

The messenger RNA strand is directed to a two part molecular factory called a ribosome. In the ribosome the process of translation begins: inside the ribosome the messenger RNA gets translated into many amino acids which will make up the protein. The sequential arrangement of amino acids determines the type of the protein.

When the chain of amino acids is finished, it is moved from the ribosome to a machine which folds this chain properly. Then the protein is complete and ready for usage.



mRNA, transcription and translation

DNA in bacteria

One difference between the DNA in an animal cell and in a bacterium is that the genetic information in a bacterium just lies loose in the cytoplasm. This ring of DNA in a bacterium is called a plasmid.

The plasmid lies in the cytoplasm of the cell, in contrast to an animal cell, there is no nuclear membrane in a bacterium, and the plasmid is easy to manipulate. That is why it is often used for genetic engineering.

The manipulation of the plasmid in a bacterium can for example be used to produce proteins, e.g. insulin. Therefore, scientists remove a piece of the plasmid DNA strand and put the genetic information for insulin production into the plasmid.

The DNA system looks quite safe, but sometimes there are also exceptions to that.

If the so called cell cycle does not work correctly there is a potential of getting one of the worst diseases known in our world – cancer.

Cell Cycle and cancer

Dimitri Nothdurft

To understand how cancer really works, you first have to know what the cell cycle exactly is:

The cell cycle is the cell's daily schedule, that means every cell goes through this schedule once a day.

During the 4 phases of this schedule, namely the Gap phase 1 (=G1), the Synthesis phase (=S), the Gap phase 2 (=G2) and the Mitosis phase (=M), the cell is divided.

In each of the phases mentioned above something happens:

During G1 the cell organelles and proteins are doubled, so that they can be transferred to the 2 daughter cells later.

During S Phase the DNA is doubled.

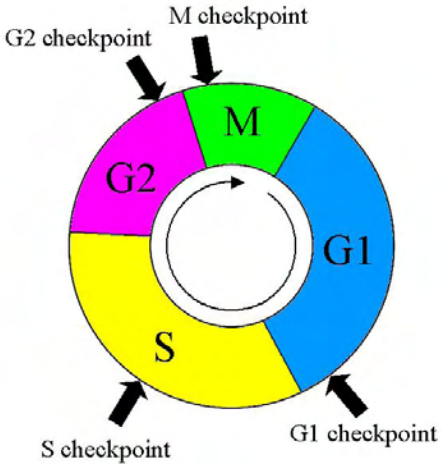
During G2 the cell is prepared for the M Phase, during which the cell is finally divided into two daughter cells.

In order to avoid unwanted mutations in the cells' genomes, the cell cycle has several checkpoints at which the result of each phase is checked.

The 3 main checkpoints are the G1, the G2 and the metaphase checkpoints.

The G1 checkpoint controls, whether doubling of organelles and proteins has taken place properly.

At G2 checkpoint the replicated DNA is controlled for mutations.



The cell cycle

Then in the middle of the Mitosis Phase the complete cell division is controlled. To continue with the next phase after a checkpoint, there has to be a special signal. This signal is only sent if the product of the phase does not have any mistakes. If there are mistakes like for example mutations in the DNA, the cell tries to solve the problem via its cell repair mechanisms.

If it is not possible the cell kills itself (Apoptosis).

But how is this complex cycle controlled? Interestingly it is controlled by two types of proteins: the CDKs (cyclin dependent kinases) and the cyclin proteins.

Cdks are enzymes which control cell activity by adding phosphate groups to certain proteins. But they can only work if they are directly bound to cyclins. So the time when the CDKs are active can be controlled.

After we had learned all this, we thought the cell cycle was a quite safe way of doubling cells.

But despite this save system there can be irregularities in the cell cycle. These can cause problems like disease cancer, a highly dreaded disease which was our next topic.

Cancer cells are cells which have unlimited potential regarding growth and reproduction. This means they can double as often as they want. Together they make up a tumor, a large accumulation of cancer cells. Such tumors can be built up nearly everywhere in the human body.

But how exactly is cancer caused?

Normal cells are influenced by factors in the environment, called carcinogens. Carcinogens can be, for example, UV radiation, different chemicals in food or polluted air. These carcinogens work as so called mutagens. Because they can change the cell's DNA so that essential cell functions can be affected.

For example, a mutagen can change the gene for encoding a certain hormone receptor so that this receptor binds to other hormones.

Through this change the production of cell growth factors can be increased.

That could lead to cancer formation.

These mutated genes which can trigger uncontrolled cell growth are called oncogenes.

Surprisingly that is not the only way of inducing cancer cells:

There are also some viruses which have oncogenes integrated into their genome.

When docking onto a host cell, the RNA of the virus modifies the normal cell's DNA and adds these oncogenes. As a result of that the host cell eventually grows uncontrolled.

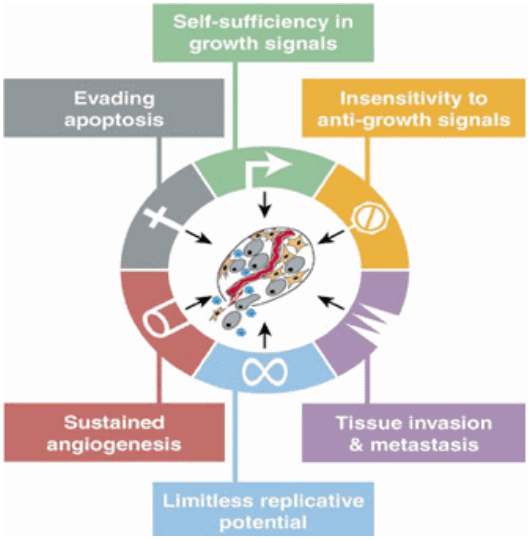
After we had studied the development of the cancer cells we went over to their abilities.

We talked about the scientific publication "Hallmarks of Cancer", by Robert Weinberg, which describes six acquired abilities of cancer cells by which you can characterize and recognize them. (The single hallmarks are shown in the picture below.)

As we first heard these complicated names we were unable to deal with them, but their meaning was explained to us shortly afterwards:

Self-sufficiency in growth signals

The cell is able to produce its own growth signals and does not depend on signals from the



Cancer hallmarks

outside. Therefore it grows limitless.

Insensitivity to antigrowth signals

The cell does not react to signals from the outside which make a normal cell stop growing.

Limitless replicative potential

The cell can divide as often as it wants (normal cells have a limitation).

Evading apoptosis

The cells are able to inactivate their apoptosis function, which means that the cell cannot kill itself when it detects a mutation in the DNA.

Sustained angiogenesis

The cancer cells can induce connections from normal blood vessels to a tumor. Through this ability the tumor never has any problems with getting nutrients.

Tissue invasion and metastasis

At a certain stage the cells of a tumor can travel to another part of the body via the blood vessels and build up a tumor there. So if a tumor is removed from your body, there is still a chance of getting cancer a second time.

Finally I can say that the high amount of new information has helped us moving on to a totally new perspective on cancer and the cell cycle.

After all the theory on the molecular level in the last lessons, it was our turn again to do also some practical things.

Another Way of Blood Donation

Yannik Laich

This lesson we wanted to make an experiment with our blood. At first, we got the description of the experiment which was called the blood smear experiment. After reading and posing some questions, we started with cleaning the microscope slides with water and after that with alcohol. Then, we took our gloves and we discussed who should be stabbed into the fingertip. The stabbing was a little bit painful (especially for Dimitri who was stabbed a lot of times). After several trials, we succeeded to smear the blood drops onto the microscope slides. So we had to make two microscope slides with a blood smear.

The Staining of our slides

But the two smeared blood drops had no real colour so that we still had to do the Pappen-

heim staining. This staining gives the blood cells some colour so that we can distinguish them under the microscope. When the two preparations had been air-dried, we covered them with some May-Grünwald solution and waited for 3 minutes. After that, we had to add some drops of distilled water and 1 minute later we poured of the May-Grünwald solution. After cleaning the slides carefully with distilled water, we had to cover the preparation with another toxic solution: The Giemsa solution. After that, we waited for fifteen minutes, which was a good possibility to talk to each other. Then we had to clean the preparations again with distilled water and the glass undersides with alcohol.

There were lots of stairs to the castle

As the preparations were dried, we put a drop of oil on them because we used a special microscope which only worked with oil. Under the microscope we were able to see our blood cells, especially the erythrocytes and the leucocytes, which had different colours and forms. It was very interesting to have a look on your own blood with the blood cells, but the experience how to make a microscope slide was also very good. So all in all it was a very interesting lesson.

The excursion

Yannik Laich

On Monday, we had our excursion to the German Cancer Research Center in Heidelberg so that we were able to get an insight into real research. We had to get up early in the morning and after a short breakfast we went to the train station by car. The ride on the train was a good possibility for sleeping and relaxing some time.

One and a half hour later, we arrived at the main station in Heidelberg. We went by bus through Heidelberg to Heidelberg's Old Town where we saw the church, the Neckar Bridge and some famous shops like the chocolaterie YilliY. But of course we also visited Heidelberg's most famous sight: Heidelberg Castle. We had to climb 330 steps, which was very exhausting. But as we arrived in the palace garden, we forgot the stress because of the great view.

Cleaning of our slides

From the castle's balcony, we were able to see nearly entire Heidelberg for example the Neckar with the great promenade, the impressive church, the mountains... After some time of relaxing and eating our lunch packets, we had a look on the huge wine barrel and made a short tour through the German Pharmacy Museum. Then, we had to go back to a bus station in the city center. Our next destination was the Café Frisch where we had lunch which tasted very good.

First thing after lunch, we went by bus to the German Cancer Research Center (DKFZ), which was actually the main target of our ex-

cursion.

There, at 2 pm, we met Professor Doris Mayer, a scientist who researches in the DKFZ. At the beginning of her presentation, she wanted to check our knowledge on hormones. Then, she talked about the basics of the endocrine system and how insulin and estrogen are able to influence cancer: These two hormones can stimulate the cell growth or even cause cancer. After a short break, she talked about her own research, which deals among others with a vicious cycle with insulin and estrogen in cancer development. In the end, we had the possibility to look into a real laboratory, where she showed us the most important equipment which is used by her students and her researchers.

Doris Mayer explained how to use a pipette

After this very interesting visit and a short travel through Heidelberg, we arrived in a Chinese restaurant where we had made a reservation for dinner. The buffet was very rich and delicious and we had a lot of fun during the dinner.

The return journey in the train was also amusing. But unfortunately we did not have enough space in the cars to transport all people and so some people had to walk from the train station back to the LSZU. The walk was a little bit exhausting after a day like that and so we arrived totally tired at 10 pm.

All in all, the excursion was very good for the atmosphere in our course and we got to know each other much better.

An essay on our course atmosphere

Natalie Plewig

Nobody in our course had a real idea of what the work in the course would look like. It could be like in school, with a formal atmosphere, a defined structure and where the single individual is not that important. Or it might be a group, which can be compared to a workshop, where you achieve not a feeling of hierarchy, so see the group as a whole and where you reach something through teamwork. So there were some conceptions, but nobody really knew.

But what we then experienced during the opening weekend surprised the majority. Our teachers often changed their presentations and used a variety of media. This factor and the illustration with pictures, videos and everyday life examples, made it easier for us to understand. That is why we got a good impression of molecular medicine, about which we would learn in detail during the academy. Experiments that were conducted right at the beginning made us think that practical work would make up an important part of our work, what was different to school lessons. One was able to do something and reason by oneself. Because this aspect was pushed strongly by the course teachers, they clarified, that we should ask questions to show them that we understood the topic and that we dealt with the subject. Nevertheless, at the beginning, nobody was brave enough to do this. We wanted to leave a good first impression.

At the end of the opening weekend we were told the topics of our presentations. We had to choose between topics that dealt with the brain and the nervous system, the digestive system, the urinary system and the heart. After we had decided, we got the corresponding information material. Then we were told to amplify the contact with the German partici-

pants and to get in touch with the Chinese participants for the first time, by reporting about how the work for the presentations went on. The anticipation for the academy grew with the contact with the course participants, with the preparation of our presentations and with receiving the script that contained the basic principles of molecular medicine. And meanwhile the time until the academy passed by...

There we were then: the beginning of the academy. Now everything would really start, although we had experienced a lot and collected different impressions so far. In that situation, it was comforting to spend some time in the common environment of the course. It was now, that we met the Chinese participants for the first time and before we started with Molecular Medicine, we got an interesting insight to Chinese culture. That delivered new topics of conversation with the Chinese participants.

The following days our course teachers and we, the course participants, changed into presenting and working on the course topics. With that we talked through all the topics bit by bit. Here, the practical part was not neglected. We had a closer look at pig organs and investigated histological slides through the microscope. During our work in the course we grew together more and more and the special feeling of us as a whole group rose increasingly. Everyone got in contact with everyone and step by step friendships were built – not only on one nation – level. Of course, the course teachers were included in our group, too. There was no teacher-pupil-connection between us, but a peer-to-peer-relationship, where everyone faced the other one with respect.

This especially became obvious during the rotation. In small groups of three, we worked out self-chosen topics, whereat we were supported optimally by the course teachers. Material, for example, that they had used in their presentations so far, could be used by us without any exception, what made it ways easier for us to prepare. But the time to finish was quite short and that is why some of us were a bit stressed. But also in this situation, the course teachers acted understandingly, which calmed us down. Eased and satisfied, as everybody was after the rotation, personal conversations were conducted, that dealt with the own presentation or the rotation on the one hand and with our own person on the other hand. That enforced the feeling as a unity, because the single person felt understood and encouraged to open up a bit more.

Our course in the Chinese restaurant

With this knowledge, our behaviour changed. We finally asked more and more, and even wanted to know things that transferred what we discussed to other topics, for example. We always admitted that we sometimes did not understand. In fact, some days before, our course teachers had recognised a certain disquiet, after that, they discussed the reason for this with us and started to change their way of presenting immediately. Fortunately, everything got resolved fast and improved very much.

Now everyone was looking forward to our excursion to Heidelberg which was an unique highlight. Not only because of the informative content, but also because we grew together again. After the effective trip, the final spurt started: We all aimed for the comprehensive closing presentations that contained a lot of work. Luckily, in this phase, we were supported by our course teachers again. This rich processing step represented the perfect forerun to the ending, because during the last moments and the farewell, we were extremely happy with what we achieved since our arrival in Adelsheim. On our way home we looked back onto the experiences we collected and swore to never forget the great time we spent in our course at Science Academy 2008.