Erasmusbericht

Internship from the 9th April until the 9th October in a scientific research group at Keele University in Stoke-on-Trent, England

1) Preparation

As the internship is obligatory for all students of neuroscience, it was obvious that I had to partake in it, but I decided by myself to go abroad. My main motivation was to improve my english skills, especially in the neuroscientific field of expertise. Furthermore, I think that living in another country is always an enrichment. To deal with another culture, getting to know different people, exploring the new country and speaking the language every day is a challenge, but a challenge you can enjoy. Finding a place for my internship was more difficult than expected. A lot of research groups do not have the space or the funding for an intern, especially for the duration of six months. I contacted the leaders of the research groups via e-mail and got to know their topics. Finally Professor David Furness from the Keele University offered me a place in his research group and the topic interested me, so we did an interview via Skype. We spoke about the details of my stay and my project, which should be about a protein in the stereocilia of the hair cells.

After finding my employment, I had to find accomodation. The nearest town to the university is Newcastle-under-Lyme, which is part of the city Stoke-on-Trent. Many students live there, that is the reason why there are a lot of rooms in shared houses or flats available. I realised quickly, that the rent is higher than in Germany. The prices are similar to those in Cologne, even if Newcastle is a much smaller, quieter town. In cities of comparable size to Cologne, rooms can be double the price or more. Another problem was that it is common to book a viewing for the house before moving in. Since I was still in Germany and did not want to go there without having a fixed accomodation, I had no opportunity to do that. I had to trust the description and photos which turned out to be a bad idea afterwards.

Further preparation was to apply for the Erasmus scholarship, find a tenant for my room in Cologne, book a flight and pack my bags. I had no problem with any of these things. The Erasmus documents were filled and signed quickly, enough international students are searching for rooms in Cologne and as the weather is not very different in England, packing was the easiest part.

Regarding language, I felt confident enough to go without any further studying.

2) Arriving

I arrived on the weekend before my internship so I had enough time to move in. Since I entered my new room for the first time, I knew that it had been a bad decision to sign a contract before having a viewing. It looked a lot different than on the pictures shown, it was not fully furnished and the housemates seemed to be very distant. All these first impressions were comfirmed during the following weeks.

My first week at work was not what I expected either, because Professor Furness was on a conference in the United States. However, he organised that his PhD Anya showed me around the Campus and I shadowed her for my first five days. This turned out to be a lucky coincidence, because she introduced me to the group of PhD, who ended up being my first contacts and finally friends. Depending on my future career, it was interesting to see how the PhD's are working. Furthermore I could observe how to do a dissection of a mouse and how to do a patch clamp with following electrophysical analysis. Anya did this with Fibrocytes which she dissected out of the cochlea's lateral wall.

3) Work

In my second week my own work started. Professor Furness entrusted me with a new research project about the protein CIB2. As there was not a lot of research about this before, we do not know a lot about this protein. I read the few papers I found online and determined that the protein is mostly known as a cause of the Usher's Syndrome. This genetically hereditary disease is caused by

a mutation in different genes. 3 of 6 of them result in an unfunctional CIB2 protein. Usher's Syndrome causes deafness and blindness. Due to the research group topic, I would concentrate on the mutation's impact on hair cells and especially the stereocilia of those. Stereocilia are hair like extensions, growing out of the hair cells connecting the cell to the tympanic membrane. The Stereocilia receive the mechanical stimulus of sound as the vibration of the mentioned membrane and transform it into a electrical stimulus for the downstream neurons. This occurs via ion currents through channels in the tips, which open as a result of the bending of the stereocilia caused by the tympanic membrane's vibration. It is already shown that these currents are absent in CIB2 Knockout mice (CIB2 KO; mice with unfunctional CIB2 protein). Since nobody found out why yet, my work should focus on the reason of the current- and the following hearing-loss. It is already shown that there are structural differences in the stereocilia of wildtype mice (WT) and CIB2 KO. Though there are no TEM (transmissional electron microscopy) pictures, measurements and analysis of this yet, so this would be my project during the next six months. Therefore I got (already in resin embedded) tissue, WT, CIB2 and additional tissue of heterozygote mice, which means that one allele of the chromosome has the CIB2 mutation and one does not (HET). I learned how to take semi and ultrathin sections of these tissues, using the microtome. The basics for doing that is learning how to make a glass knife, how to trim down the resin and how to operate the microtome. For making the glass knife there is a machine which breaks the glass in a controlled way. You still operate it manually, clamping, scratching and bending the glass with different handles and buttons. To the glass knife you add a little bag-like construction made out of tape. This gets filled up with water, so that the cut sections can float on the water surface. The most difficult part about the trimming is that the block of resin is very small and the tissue in it is even smaller (cochlae of mice= ??). If you think about trimming around this tiny piece of tissue with a very sharp razor blade and one wrong movement could destroy the whole block, this makes you sweat. And that is exactly how I felt. It was a challenge that is possible to overcome with a lot of training and patience. Operating the microtome was, compared to that, quite easy. Just some buttons to remember how to change the speed, the light and the thickness of your section.

Before taking any kind of section it is very important to align the blocks surface to the one of the knife. Doing this you have to be aware of getting the block as near as you can to the knife without touching and thereby damaging the knife. By changing angle and orientation of the block, it is possible to find special areas of interest, in my case the organ of corti with the hair cells and stereocilia.

A semi-thin section is 0,5 mm thick and its purpose is to get an overview about the tisues surface. The cut and floating section gets picked up with an eyelash, which is clamped in a retainer. It gets transferred on a slide, where it gets stained while heating it up over a flame. After this procedure it is possible to see the structure and the cells of the given tissue under a lightmicroscope. If needed, it is possible to connect the microscope to a camera and a laptop to take pictures of the section. Regarding the section, it is possible to searching for the area of interest. It is useful to make a quick sketch of the tissue with the localised area of use. Orientating on this, it is possible to trim away unecessary tissue around the main area of interest, because the smaller the area to cut, the slower the glass knife gets damaged what makes it easier to take nice and thin ultra-thin sections. Ultra-thin section can be between 50 and 90 micrometer thick. Important is, that the alignment is as correct as possible, that everything (block, chuck, knife) is clamped in tightly to avoid vibration and that the water surface is perfectly aligned with the knife edge. Triming away unnecessary tissue, especially bone or other hard substances, avoids damaging the knife and improves the results. If you finally get nice sections floating on the water, they get stretched out with vapourising chloroform by changing the water's surface tension. Finally small grids made of copper or nickel get tucked underneath the floating sections. By lifting them up, you pick up the sections, which now lay on the grids surface.

After drying the sections get stained. I used 2% uranyl acetate for 20 minutes and 2% lead citrate for 5 minutes. The grids just get laid into the chemicals for the mentioned amount of time and get washed inbetween and afterwards to rinse of surplus stain. Now the grids are ready to be observed

under the TEM. For taking good pictures I had to chenge magnification, beam size or intensity and contrasts. After doing several measurements to compare WT, KO and HET I identified a significant difference in the shape between KO and WT, but no difference between WT and HET. This shows that the one working allele in the heterozygote organism is able to compensate the lost of the other unfunctional allele. Furthermore the measurement give us more information about the effects of an unfunctional CIB2 protein. It let us suspect that CIB2 is an obligatory part of the structural building process or of the shape's maintenace. We found conspicuous differences in the actin structure between WT and KO, but could not proof or explain those differences yet.
Furthermore I tried to determine the distribution of the CIB2 protein via immunohistochemistry. First I tried immunofluorescence. For this I cut ultrathin sections, put them on grids and incubated them with a primary antibody which binds to the protein. Then I incubated it with a secondary antibody which is labeled with a fluorescend chemical. Using the Confocal microscope it was possible to see the distribution. We used a WT and a KO, so normally we should have seen the protein just in the WT and it should have been absent in the KO. Unfortunatly the results were not as aspected, as we could see labeling in the KO. Probably the antibody did not work good enough. We had similar results with immunogold labeling. For this I incubated the sections with the same primary antibody, but a different secondary antibody which is labeled with 10nm gold particles. Under the TEM the gold particles are visible as small black spots with a regular shape. After counting the goldlabels I could indetify an affinity to the tissue, but no significant affinity to the bundles. This supports the impression that the antibody is not working properly.

In addition to my own project I shadowed Professor Furness' PhD a bit more and learned the basics of cell cultures. I did medium changes for her growing fibrocytes and we made collagen gels for her patch clamps together. I learned that it is very important to avoid contamination of the cell cultures. That is the reason why every equipment you are using has to be sprayed with ethanol and it is not allowed to use the same equipment for different flasks or petri dishes.
Moreover I helped another intern, who worked in my lab, with her immunoblotting. We incubated already done Western Blotts with different stains, primary and secondary antibodies. Main part of this process was to improve the protocoll- focusing on incubation times, washing steps and staining chemicals. Unfortunatly it was not possible to determine the expression of the sought protein.

Summarizing I can say that my working experience was a big enrichment, even if I struggled with the needed patience sometimes. I learned many techniques, especially the sectioning and whole TEM procedure. I'm confident about finding areas in tissues via semi thins, sectioning them, using the microtome and the TEM and following several protocolls for immunochemistry. Furthermore I got an insight and cell culture laboratories and in the process of improving protocolls which I could transfer to different kind of procedures. In addition to this I got an insight into the daily work in the research group- about the thinking processes behind and the set up of experiments, about the way of making up, analysing and discussing data and about improving and changing ideas, protocolls and experiments. Moreover it was a nice experience to become part of this group, to have talks about work but also about other topics with colleagues. I experienced an unsuspected and surprisingly nice hospitality and helpfulness not just for work issues, but about freetime or travel activities to finding a new accomodation or sports classes.

4) Freetime and daily life

Even if I met the group of PhDs in my first week, I still had a lot of time for myself in the first months. During the week I used this time for reading books, cooking or going for a run in the nearest park. I stated going to the campus' gym at least twice a week with some of the PhDs. They invited me to birthdays and other events like festivals or concerts on the weekends which was really nice. On free weekends I tried to travel around the UK as much as I could. I spend whole weekends in Edinburgh, York, London, National Parks in Wales or England and smaller cities around Stoke-on-Trent. In Edinburgh I went on a free walking tour to see a look on the most important sights,

such as the Castle, Arthur's Seat and Calton Hill. I stayed over at a Couchsurfers place who I found on the 'couchsurfer' app, where people offer you a place to stay or to show you around the city. The main purpose of the app is the cultural interchange between travelers and locals. I used this app to find a place to sleep in York too and I met other travelers in the city. In Wales I hiked up the highest mountain, Mount Snowdon. Another hiking trip was to the Lake District, one of the most beautiful National Parks of England. The Peak District is a National Park near to Stoke and I did some shorter day trips there.

As I was very unhappy with my first accomodation, I spend a lot of time finding another one, writing emails to landlords and going on viewings. Finally I found a shared house with two housemates in Wolstanton. After three months, so half of my time, I moved to this new house and it was a really good decision. I got along much better with my new housemates. I went on weekend trips with my housemate and we spend the afternoons together after work.

5) Living costs and cultural differences

As already mentioned, the main price difference depends on rent- it is much higher in in England. But a big difference is, that students live in whole shared houses, not just in flats. So most of them have a quite big common area or living room, where you can spend time together. Most of the houses have two floors with stairs and corridors, so all in all there is more place than in most of the german student accomodation. However I reckon that these difference is not that big in the bigger cities like Manchester or London, as there is less living space. The price for food is just slightly higher, but british people eat a lot of processed or prepared food which is more expensive. Normally I mostly cook for myself, but it is tempting if everyone else is eating these kind of things and I realised that I changed my eating habits slowly but steady and not in a healthy way. Besides health and price, these kind of foods produce a lot of (plastic) waste and it seems like not many people care about this kind of topic, where germany is a bit more advanced or at least more aware of.
After some months I realised that my living costs were much higher than expected, even if the prices are not that much higher. I realised that the british people are more willed to spend there money. For example they go out for meals or drinks a lot more often, where people (especially students) in Germany cook or drink at home to save money. It is very normal in England to get a coffee or a sandwich to go instead of making it at home and take it with you. The pub-culture, which is more present than I originally thought, contributes to this expensive lifestyle too. The british spend time and money in these places with friends. I think it is a nice and socially connecting tradition, but not very good for my wallet. So summarizing my social interaction was one of the main reasons for my higher living costs.
Another main part were my expenses on the public transportation. Since the Keele University is outside of town and I did not have a car, I had to buy a bus pass. Furthermore I spend a lot of money on the train to travel around and explore the UK. Now I realise how lucky I am as a student to have the student ticket for public transportation in whole NRW, because it saves me much money and offers great opportunities to visit different cities.

6) Summary

All in all I enjoyed my stay very much and I will miss my friends, housemates and my work. I learned a lot in my research groups, especially the TEM preparation with sectioning and staining. What I learned in my freetime is the laid-back and very open way of the british and their hospitality. I like how they invite people to their events and how it is normal to pay for friends. Although I will keep these positive aspects, there are things I realised which are better in Germany and I started to appreciate those. For example the organised and productive way of working, the healthier lifestyle and the awareness about the environment. It was a great experience and the thought which motivated me in the beginning got all confirmed. It was an enrichment including new knowledge, laboratory skills, impressions, experiences and friendships. I even improved my english a bit, especially depending on informal or daily life expressions. I am very thankful that I had the opportunity to absolve my internship here and I am hoping to come back soon.