

2013

Dear Duke of Arenberg,

Dear General Assembly,

Ladies and Gentlemen,

I'm honored to be present here at the University of Galway and to be nominated as the laureate of the Arenberg-Coimbra Group prize.

Europe is in a crisis, one hears every day. The same news was also true when I first went to Germany to study at the University of Heidelberg as well as the second time to do my Master's thesis in Darmstadt. Still despite the current unhappy news, it has never been easier to travel, to study and to work in another European country. This situation was great for me since even before I went to university I knew that I wanted to spend some time abroad, luckily European Union and groups like Coimbra Group had made my decision easy to fulfill.

To live is to learn! I can say that in this the Coimbra Group has succeeded. It has succeeded to enhance the integration of Europe and to make it easier for young, eager minds to deepen the European integration as well as open the minds of scholars willing to experience new. When it comes to fairly new subject, still constantly changing, like my favorite topic, biotechnology, working together and learning from different angles bring new insights and help to innovate new. This was especially true in my case. Without the exchange, my Thesis would had been completely different.

Dear Duke of Arenberg, dear Coimbra Group. I am honored that you chose me to be the Arenberg-Coimbra Group laureate this year.

Thank you.

Juho Terrijärvi – 2013 in Galway

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## Arenberg application

### My background

My name is Juho Terrijärvi and at the moment I am a Master of Science (tech.) graduated from the University of Turku Finland on March 2012. My major subject was biotechnology and as a minor subject I studied process engineering, commerce and German. I'm employed by my home university as a University Teacher and my duties include educational planning and research. I teach biotechnology laboratory exercise courses and manage project based learning courses with different universities and companies from the Turku area. My research focuses include novel luminescent materials and device development for the detection of them, the research has not yet provided published articles, but at the IFCC Euromedlab conference I will present a measurement device developed by me and a diagnostic company near Turku.

### Student exchange to Heidelberg

Prior to my exchange I had always wanted to stay some time abroad to learn the ways of another culture and take myself out of my own comfort zone. Thus I already at school learned multiple languages and one of them was German. I had always found the German culture and especially the language intriguing. When the opportunity presented itself at University to spend an exchange semester I immediately took it. So the winter semester of 2010 I spent at the University of Heidelberg in Germany.

My main motivation was to study the language and learn from another culture. I think that I succeeded in both of my goals. I had had troubles in learning German in Finland, since it is not one of the easiest languages to learn. But studying German in Germany was totally another matter, just to know that once you stepped out of the classroom you were filled with German and you were able to speak it all around. This totally reawaked my motivation towards the language. I became much more confident in speaking even though I knew that I still made mistakes, but the barrier to use the language was lowered. Culture wise I learned how to function in the German society, which helped me much in the future.

Besides the language skills I also studied lot of courses and laboratory exercises related to biotechnology and chemistry. I worked in a research project, the aim of which was to study the effect of glucose on wound healing. For his purpose I learned the principles of growing human cancer cell lines, Western blots and other cultivation techniques, I will return to this later in this essay. The platform we used to study wound healing was an impedometric cell sensor and using that platform awoke a novel concept of doing DNA analyses, which I'm about to try out at the University of Regensburg.

## Master's thesis

After the student exchange to Heidelberg my Master's thesis was the next thing to do. In Finland when one is doing a Master's thesis in the area of technology it is quite common to do it in a company. The Master's thesis in technology includes minimum of five months' work in a research project conducting hands on work. From this experience one writes the actual thesis.

When the departure back to Finland in the beginning of the year 2011 was imminent, I realized that I didn't want to go. I arrived to Finland, but I hadn't gotten enough of Germany after my student exchange. This is why I started to apply for Master's thesis positions in different German pharmaceutical companies. Well I didn't need to send many applications, since after sending the first it took 45 minutes when my boss to be called me and asked whether I was truly interested in the open position. We discussed a lot and he invited me to visit Merck Serono in Darmstadt. If you are not aware, Darmstadt is located somewhat 30 kilometers north from Heidelberg and thus I was truly enthusiastic.

During the interview it became apparent that the work to be sounded truly interesting. My future supervisors group was researching autophagy, a means for mammalian cells to eat themselves during times of starvation. His idea was to stop autophagy from functioning to cause cell deaths during starvation to cancer cells, since in cancer cells due to their increased metabolism autophagy often is activated. After the interview I knew that I was the one to take the place.

I started to work at Merck Serono in the beginning of May 2011 only 3 months after my departure from Heidelberg, all my dearest friends still being in Heidelberg. I worked for Merck Serono for six months 'till the beginning of November. During the work our group was able to prove that blocking autophagy cancer cells starved to death and normal cells in normal growth conditions survived. The impact was even greater with anticancer drugs and blockage of autophagy.

## Impact of Coimbra exchange to my Master's thesis

The previous chapters included a short explanation of what my exchange and my Master's thesis were all about. In this chapter I want to make clear how the two are related and why there couldn't have been the second if there wasn't the first.

Prior going to Heidelberg for my student exchange I had no experience in functioning in another culture. I had only lived in Finland and thus it was necessary for me to taste the German culture before I had the courage to actually work and live there. The student exchange is in some sense a safe way to get acquainted with another culture, since the receiving university provides housing and a welcoming atmosphere with lots of other people experiencing the same transition phase. Knowing myself it is safe to say that without the exchange I wouldn't have had the courage to work in Darmstadt at Merck Serono.

The second point is that I fear that Merck Serono wouldn't have had hired me without the laboratory experience from Heidelberg. At the University of Turku the emphasis on biotechnology is in diagnostics and in diagnostics one does not need to use mammalian cell lines to conduct research. It is all about lateral flow assays, like pregnancy tests, and immunoassays etc. Thus during my work at the laboratory for 2 months in Heidelberg I was taught how one cultivates mammalian cancer cell lines and all the necessary aspects one needs to consider. I had a lot of practical experience in growing cells and doing Western blots, which are used to quantitatively measure different protein amounts in cell samples. Without these abilities I would have been under qualified to do the research required for my thesis at Merck Serono.

Third issue to consider is the language capabilities. Granted, I had studied German since the fifth grade, but it is safe to say that at the age of 23 I was nowhere near enough qualified to work with the German language. I was afraid to use it and I did not have the necessary vocabulary to work with that language. I can safely say that all of this changed in Heidelberg. I had German classes worth 18 ECTS, which increased my vocabulary as well as my motivation towards learning the language. Prior I had always hated the German classes, but loved the language, after the exchange I loved them both. Still I can say that more than during the classes I learned German by interacting with German as well as non-German people. When I worked with my Master's thesis I did it in two different languages. All the written work, like in any other multinational corporation, was done in English, but all the actual interaction with my colleagues and laborants was in German. If I had been afraid to use the language I would had missed a lot of the conversation in the laboratory environment.

Fourth issue is the life after 4 o'clock and during the weekends. Every work needs a balancing factor. For me in Germany it was the friends in Heidelberg. Most of the exchange students stayed at Heidelberg for the whole academic year, as I departed after the winter semester. I made so many friends during my stay at Heidelberg and being able to visit them brought joy to my life after work.

### **Conclusions**

In this essay I hope I have assured the reader why my Coimbra exchange from the University of Turku to the University of Heidelberg was in so many ways crucial for my Master's thesis. I find it almost impossible that without the exchange there would not have been the Master's thesis I made.

### **Attachments**

Attachment 1: Master's thesis abstract

Attachment 2: Curriculum Vitae

Best regards,

In Turku 22<sup>nd</sup> of November 2012



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JUHO TERRIJÄRVI: Validating Uncoordinated 51-like kinase as an oncological target

Master's Thesis in Technology, 61 p.

Biotechnology

December 2011

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ULK1 (Uncoordinated 51-like kinase) is a key regulator of mammalian autophagy, which is an evolutionary conserved pathway to provide cells with nutrients through self-digestion in times of starvation and stress. Autophagy is also used for cell remodeling and as a means to degrade damaged proteins and organelles.

In this Master's thesis, the inhibition of autophagy through blockade of ULK1 kinase was investigated as a potential anticancer strategy at Merck-Serono.

For this purpose, knockdown by small interfering RNA (siRNA) of ULK1 was optimized: both ULK1 protein levels and the potential effect of ULK1 on LC3 (light chain 3 beta of rat microtubule-associated protein 1) lipidation dynamics in response to ULK1 siRNA were analyzed. The effect of ULK1 knockdown was also visualized on a phenotypical level with confocal microscopy by following autophagosomal formation. Then cancer cell proliferation and clonogenic survival was studied in the presence of the ULK1 alone or in combination with the therapeutic stress (anticancer drugs) or metabolic stress (starvation). The effect of ULK2 (ULK1 homolog) and ATG7 (important autophagy gene) knockdown on autophagy and cell proliferation were addressed to a lesser extent as well.

ULK1 knockdown was found to block autophagy: it decreased the number of autophagosomes and increased levels of ubiquitinated protein aggregates. Under normal cell culture conditions, the knockdown of ULK1 did not have a major effect on cancer cell proliferation or clonogenicity, nor did ULK2 or ATG7 knockdowns. However, under the conditions of therapeutic or metabolic stress, decreased cancer cell survival was observed, which was also the case for ULK2 and ATG7 but to a lesser extent. The results with ULK1 knockdown support the possibility to use it as a means in cancer therapy.

Keywords: Uncoordinated 51-like kinase; autophagy; cancer; oncological target; metabolic stress; therapeutic stress