ADVance Laboratory Course Zurich, March 11-22, 2013

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Summary:

PREFACE

Here we report on the *ADVance* workshop which was held in Zurich from 11th to 22nd March 2013 at the Irchel University Campus of Zurich, Switzerland.

The organizers put together an exciting schedule of training activities on scientific concepts and complementary skills, laboratory experiments and social events. It featured a symposium of renowned speakers in the field of adenovirology and cell systems biology, seminars fostering the competences on research management, career development and scientific writing and a practical lab course on liquid handling and fluorescence imaging of adenovirus infections. The overall objectives of the workshop were learning to formulate and test scientific hypotheses, handling advanced approaches in dissecting adenovirus infection, acquiring skills to be able to perform high quality research and to develop a successful career. Several social events in the evenings of week days, and a trip to the mountains at the weekend helped to increase interaction among the participants.

I. INTERNATIONAL SYMPOSIUM: *VIRUS INFECTION BIOLOGY & ADENOVIROLOGY*

The programme started with an **International Workshop on Virus Infection Biology & Adenovirology**. A wide variety of renowned national and international speakers, invited by Urs Greber and Andrew Baker, presented their research. The morning session was dedicated to

Virus Infection Biology, and the afternoon session to Adenoviruses, with presentations from the *ADVance* group leaders.

Short report on the presentations

Ari HELENIUS (*Institute of Biochemistry*, *ETH*, **Zurich,** Switzerland) kicked off with a general introduction to virus entry and uncoating. He pointed out that there are multiple pathways possible for virus entry and that different viruses make use of different pathways. He spoke about vaccinia virus (a pox virus), which uses three distinct ways into cells: apoptotic mimicry, macropinocytosis and membrane fusion. Evidence for these pathways is based on light microscopy assays, interference with dominant negative constructs or small RNAs, and automated high-throughput imaging of siRNA knockdown screens of host factors. Having elucidated viral entry mechanism for vaccinia virus, his team is also interested in virus uncoating. For this purpose they study Influenza A virus when travelling from the cellular membrane towards the nucleus. Similar to vaccinia virus research methods comprise mainly siRNA based knockdown screens of host factors. By these means it was possible to assign 23 host genes to specific steps of the entry process, including virus genome import in the nucleus.

Lucas PELKMANS' group (*Institute of Molecular Life Sciences*, *UZH,* **Zurich,** Switzerland) studies the correlation of cell phenotypes with respect to physiological or pathological features, such as virus infections. For this, his lab carries out single cell analysis on a very large scale ($1x10^6$ single cells) by means of high-throughput microscopy and machine learning algorithms, so called support vector machines. Their first study showed that one needs to analyze approximately $2x10^5$ single cells to obtain data that can be readily used to fit into a reliable model. Considering the cell population context, the interpretation of siRNA screens increases reliability, precision and statistical power. For example, masked phenotypes can be identified that would otherwise be hidden within the overall population averages. Combining these screens with analyses of infection patterns, the Pelkmans group aims to annotate the impact of certain genes in a cell population context. Deducing context-dependent gene functions harbors the opportunity to a better understanding of the influence of certain genes on viral spread and cellular behavior in a given microenvironment.

In line with the previously presented work, **Christian VON MERING** (*Institute of Molecular Life Sciences*, *UZH***, Zurich,** Switzerland), is interested in high-level bioinformatics analysis of RNAi pathogen entry screens. Although these screens are standarized laboratoy practice, it was stressed that siRNAs often have manifold off-target effects. Increasing the amount of tested siRNAs for one gene allows for some correction of the off-target effects, but in general they dominate at a single siRNA level over the on-target effects. He proposed to interpret the data in a wider perspective, so that the bias in results can be more strongly reduced. Additionally Christian von Mering introduced the established freeware STRING that was developed in his lab to represent protein interaction networks. It is an elegant tool to visualize interactions of proteins based on published data and inferred putative and experimental interactions where data are gathered from data mining in publically accessible databases.

Glen NEMEROW (*Department of Immunology and Microbial Science*, *The Scripps Research Institute,* **La Jolla**, California, USA) presented his latest research on structural and biophysical analyses of Adenovirus. He uses an integrative structural biology approach where X-Ray diffraction, Atomic Force Microscopy (AFM) and cryo-Electron Microscopy methods were employed. After an initial struggle with the crystal structure formation – adenoviruses with long fibers do not form crystals – his team succeeded in the characterization of an Adenovirus structure with short fibers. This study revealed new interactions between capsid cement proteins and hexon, important to hold the capsid together. Physical features of Adenovirus were also assessed by AFM experiments in collaboration with Wouter Roos from VU Amsterdam, where they studied the flexibility of Ad on its different axes. It was found that the 5-fold axis is more elastic and flexible than the 2- and 3-fold axis. Investigating this same setting in the presence of human defensins, which bind to the virus capsid, they found that defensins stabilized the capsid at the vertex and this is thought to block structural changes in the virus during entry into cells. Contrary effects were seen with integrins, which destabilized the particle and made it easier for the virus to disassemble and possibly expose the inner-capsid protein VI. Following the lively talks and discussions, the audience was reminded of the upcoming 11th International Adenovirus meeting in San Diego 2014.

The afternoon session featured presentations of the ADVance group leaders. **Niklas ARNBERG** (*Division of Virology, Department of Clinical Microbiology*, **Umeå,** Sweden) presented his work on sialic acid containing compounds to treat ocular infections caused by Adenovirus. It was described in previous work that Adenovirus D serotypes that cause epidemic kerato-conjunctivitis (e.g. Ad37) bind to glycan moieties of glycoproteins. These resemble the di-sialylated glycan that is present in the GD1a ganglioside. In line with these findings they produced different sialic acid containing compounds and showed that these compounds were effective *in vitro* against HAdV-D infection.

Urs GREBER (*Institute of Molecular Life Sciences*, *UZH*, **Zurich,** Switzerland) discussed the Adenovirus entry and uncoating program. In particular, he explained the stepwise uncoating program of Adenovirus species C into epithelial cells which leads to productive infection. The infection process starts with viral fiber binding to Coxsackie-Adenovirus-Receptor (CAR), and alpha v/ beta 3/5 integrin binding to the penton base of the virus. Acto-myosin dependent drifting motions of the fiber and the confinement from the integrins exert a physical force that leads to fiber shedding allowing for exposure of protein VI and subsequent escape of virus from endosomes.

Balázs HARRACH and **Maria BENKÖ**'s groups (*Department of Virology*, *VMRI*, **Budapest**, Hungary) work on the identification of novel adenoviruses in a variety of animals. In a lively talk, he guided the audience through the broad spectrum of adenoviruses presently known, but also stressed the abundance of discovered AdVs in reptiles and birds. The methods used in the Harrach / Benkö group involve the collection of animal samples followed by PCR analyses using degenerate primers to amplify adenovirus-related gene fragments. Sequencing and phylogenetic analyses then place the data into context of the known Adenovirus sequences. The laboratory maintains and also annotates these sequences on their web site (www.vmri.hu/mbenko.htm).

Eric KREMER (*Institut de Génétique Moléculaire de Montpellier,* **Montpellier**, France) and his colleagues work on the immune response against the trafficking of, and the receptors involved in, human and non-human adenovirus biology. One aim is to develop therapies for neurodegenerative disease using canine adenovirus (CAdV2 or better known as CAV-2) vectors. When incubating CAV-2 with neurons, they observed retrograde transport via uptake by CAR+ vescicles, and Rab5 to Rab7-dependent endosomal transport. Using CAV-2 vectors they study Parkinson's disease, a common, focal neurodegenerative disease, and MPS VII, an orphan disease affecting the entire CNS. With their colleagues they also developed a bioprocessing approach for creation, production and purification of CAV-2 vectors.

Ramón ALEMANY (*IDIBELL-ICO*, **Barcelona,** Spain) presented design strategies for new classes of oncolytic adenoviruses. His group works on the characterization of human adenovirus-based oncolytic vectors. Together with his team, he contributed with promoters and mutations to achieve tumor selective replication, capsid modifications to improve systemic tumor targeting, and transgenes to enhance oncolytic potency. However, with these optimizations there are major hurdles in the development of oncolytic adenoviruses, mainly virus interactions with blood and immune components, delivery to tumors limited intra-tumoral spread, and immune responses. Focusing on unraveling the characteristics of these processes, his group aims to translate this knowledge to produce more effective oncolytic viruses.

Pekka SIMULA (Oncos, **Helsinki**, Finland) presented the company Oncos and their translational research towards the clinic. Oncos' aim is to develop oncolytic viruses, but he is aware of the risks and past experience, saying that "Oncolytic viruses present a graveyard of failed projects". In a quick overview, he familiarized the audience with the obstacles that one faces when taking an interesting (oncolytic) therapeutical agent to the clinic. In this field, it is important to be aware of the many practical feasibility requirements, including large-scale production of this agent.

Andrew BAKER's presentation (*Institute for Cardiovascular Research*, *UGLA*, **Glasgow**, United Kingdom) focused on the manipulations of the adenovirus capsid to improve local and systemic gene delivery. Working on treatments for cardiovascular disease and more specifically atherosclerosis, his group employs HAdV5. In previous studies, they showed that blood coagulation factor X mediates liver targeting of Adenovirus in rodent models and non-human primates. Using the findings of this study, he succeeded in creating Adenovirus derivatives that bound specifically to veins of pigs and acted to block the formation of atherosclerotic plaques after putting the vein back into the animal. This study is now on its way to be translated into the clinic.

Silvio HEMMI (*Institute of Molecular Life Sciences*, *UZH*, **Zurich,** Switzerland) presented his research on human Adenovirus 3. Together with HAdV-B7 and 14, these three serotypes appear to be more virulent than others and also possess a broader tropism. He showed us data that illustrates that E3 from HAdV-B3 counteracts the host immune system and pIIIa is strongly phosphorylated.

Len SEYMOUR (*Department of Oncology*, **Oxford**, United Kingdom) discussed the importance of the tumor microenvironment in adenovirotherapy. One of the main interests of his group is

cancer immune editing or how cancer cells produce a tumor microenvironment that enables them to thrive without being detected by the immune system. In the first line, expression of cancer antigens is not actively suppressing the immune system, but other tumor cell mechanisms help these cells escape from eradication by the immune system. The aim is to target these mechanisms by armed viruses that are able to modulate the immune suppressed environment in situ. Eventually this might make it possible to combine virotherapy with cancer immunotherapy.

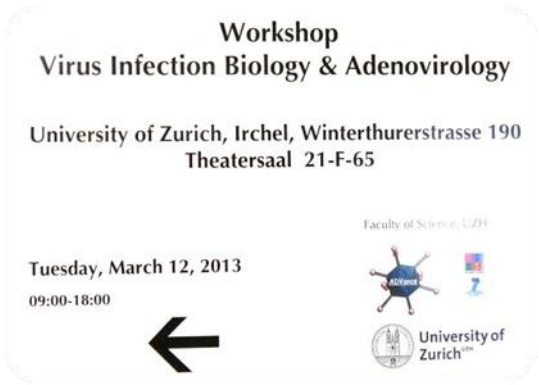
The last three talks of the symposium were given by representatives of the industrial partners within the ITN.

Jerome CUSTERS (*Crucell*, **Leiden**, The Netherlands) presented a line of research on the development of prophylactic and therapeutic Adenovirus-based vaccines. Whereas in earlier days, HAdV5 seemed to be a promising candidate, high seroprevalence of this type has hindered its further development for these purposes. Thus, he and his team are working on novel Adenovirus vectors such as HAdV26 and HAdV35 in order to eventually treat infectious diseases. The whole production relies on manufacturing in the E1-complemented PerC6- cell line that is approved by the EMEA for production of HAdV vectors. Viruses lacking the E1 region can be equipped with genes of interest and grown in these cells in large perfusion reactors supplying the necessary quantities of therapeutic vectors for clinical applications.

Kerry FISHER (*Psioxus*, **Oxford**, United Kingdom) talked about the importance of human blood interactions when considering using adenoviruses for systemic delivery. Pre-existing immunity, complement fixation and blood cell binding may adversely affect delivery and therapy. Many of these events can be measured in blood samples ex-vivo but it is important to work at physiological concentrations. Of particular interest to this group are low-seroprevalent viruses that do not bind to CAR which is abundant in human erythrocytes.

Representing *Batavia Biosciences* (For-profit company, **Leiden**, The Netherlands) **Angelique LEMCKERT** introduced the audience to the principles of adenoviral vector manufacturing. She emphasized the importance of large scale applications in which parameters such as medium formulation, cell density, MOI or time points of harvest are essential issues for a successful production of adenoviral vectors. In addition, proper development of assays measuring particle amounts, or grade of purity are crucial for manufacturing clinical grade adenoviruses.

Here are some images of the symposium:



Upper image:
Urs and Glen before the actual presentation

Middle image:
Audience during the discussion

Lower image:
Urs and Ari during the questions session

II. COMPLEMENTARY SKILLS TRAINING WITHIN THE ITN

In addition to gaining and developing practices that are related to laboratory skills, another important focus point of the Zurich meeting was to enhance transversal skills complementary to scientific and technical skills, such as management of research, scientific writing, knowing how and where to apply for funding, and approaches from science to business.

Monday 11th March 9:15 – 15:30

On the first day of our meeting, a comprehensive training session on these complementary skills was included in the schedule for all ERs and ESRs. EASCO had assembled a series of lectures, namely from **Stefan CONSTANTINESCU** (*Ludwig Institute of Cancer Research, Université Catholique de Louvain, De Duve Institute*, **Brussels**, Belgium), **Mauro MEZZINA** (*EASCO-CNRS*, **Paris**, France) and **Anne DOUAR** (*Gensight Biologics,* **Paris**, France). Below is a brief synopsis of their presentations.

Stefan Constantinescu

Management of Research and Careers of Researchers

To manage derives from the word *ménage* for households and describes how to deal with and organize one's self, other people and other things. Relating this to scientific research implies action, verification of the science and taking responsibility for those actions.

Within this context, Stefan introduced us to the management of research and research careers, looking at ways of solving problems, and simplifying complicated matters by disassembly into smaller units. He discussed ways of tackling the initial issues that everybody has to struggle with when starting at a lab, such as the choice of mentor or development of organizational skills, and also highlighted the need for appropriate social skills such as diplomacy and avoidance of procrastination in order to make projects fruitful and successful.

As regards developing good presentation skills, Stefan's advice was to capture your audience, perhaps by using powerful images, and developing a story throughout the presentation to keep the audience attentive and hungry for data He also provided us with tips on career development after the training period in the ITN. His recommendations included making contact with as many interesting PI's and labs of a slightly different background as possible, checking for personal skills that might be relevant to the lab in question or making a statement of long term goals. All in all, we were given the opportunity to hear a very interesting talk that was relevant for any researcher.

Mauro Mezzina

Bursaries and Grants for PhD Students and Post-docs

Mauro's talk was dedicated to potential future plans and undertakings of all ITN fellows. It comprised a detailed description of what training and support is possible through the training partner EASCO while in the ITN network and also beyond. Three big paths are open from a post-ADVance point of view: finding a post-doc position, a job in academia

or industry or building up a team, where each position offers different possibilities of inter-connection and further future steps. Regarding the search for a post-doc position, we were introduced to the requirements of different fellowships and grants, which are indispensable for this stage in a researcher's career. In the European Context we were acquainted with EMBO short and long term fellowships, Marie Curie fellowships (either within an ITN for the ESRs or Individual Fellowships for ERs) and European Research Council Grants (ERC). The proposal structure and evaluation criteria for the above mentioned grants and different subgroups such as Starting and Advanced Grants within the ERC category were particularly emphasized. Complementary to this talk we also had a session during the practical course chaired by Glen Nemerow on how to write a grant application according to NIH grant guidelines (see below).

Anne Douar

From Bench to Business: Career Development in Life Sciences

Anne's lecture focused mainly on what we can to do with a scientific degree, not only in the lab, but also in companies on a more applied basis, from basic research to the patient bedside.

The process starts with conducting a basic research project that leads to implementation of innovation in the form of new products or services which will enhance the quality of people's life. During this process, products go through different phases of pre-clinical and clinical development, then registration and entry into the market,. In each stage scientists have varying functions and responsibilities. When discussing the process of developing new products from prototypes to market-ready stages along with cash flows, Anne highlighted what considerations have to be taken into account when a product from basic research is launched as a fully usable product on the market. All along the product development chain, the importance of scientific personnel becomes obvious for the success of the enterprise e.g. Regulatory Affairs, Intellectual Property, Business Development or Project Management. Interdisciplinary working and thinking is highly important as well as skills in project management in all these domains

Putting emphasis on the fact that inventions only refer to a technical solution, but innovation is the translation of the invention into business, Anne familiarized the audience with entrepreneurial thinking and potential alternatives to academia after graduation or finalization of a post-doc position

Monday 11th, Thursday 14th and Sunday 19th March – Scientific Writing

An integral part of our schedule on complementary skills was an introduction to scientific writing by **Maarit SUOMALAINEN** (*Institute of Molecular Life Sciences*, *UZH*, **Zurich,** Switzerland) and **Hugo STOCKER** (*Institute of Molecular Systems Biology*, *ETH*, **Zurich,** Switzerland).

Maarit Suomalien

From the diversity of scientific publications, they acquainted us further with the body of a research paper and went into the details how every part links with each other. Another important point was the use of proper tense, grammatical structures and design of a flow from one paragraph to another. The specific requirements for all components were discussed as well as how to link ideas or contradict

Hugo Stocker

the current knowledge where there are existing gaps in knowledge. All in all, this course gave as fruitful input on how to design a research paper or the composition of a laboratory report, which we were required to deliver at the end of the course.

Thursday 14th and Monday 18th March: Grant Writing Tutorial

Glen Nemerow

A special treat for all the participants on the ADVance Lab Course in Zurich. was the Grant Writing Tutorial with **Glen NEMEROW** (*Department of Immunology and Microbial Science*, *The Scripps Research Institute*, **La Jolla**, California, USA) Glen introduced us to the most important points when applying for a grant and all the planning that has to go hand in hand with it. Depicting everything from the point of view of a NIH grant, we learned about the main components of such an application, general considerations that should be taken into account and of course how to deal with potential pitfalls and problems if strategy no 1 fails.

III. PRACTICAL COURSE ON AUTOMATED MICROSCOPY PERTURBATION SCREENS IN ADENOVIRUS ENTRY

Nina Wolfrum

For all ESRs and ERs involved in the ADVance initial training network, the Zurich workshop was an opportunity to learn about the potentials and pitfalls of high-throughput screenings in relation to HAdV entry. This practical course organized by **Nina WOLFRUM** and **Urs GREBER** started in the first week and comprised data mining as well as comparisons of the conceptual biological replicates amongst the groups.

Urs Greber

In total, two big sets of wet bench experiments were performed: a compound screen, a siRNA knockdown screen alongside with its checkerboard in a 96-well plate format. In particular, these screens aim at the comparison of RNA-based and chemical compound interference with cultured cells and scoring of the infection efficiency by either direct GFP or immune-staining readout. The technical environment allowed for automated microscopy, and subsequently the fraction of infected to total cells was calculated and the therapeutic index of the respective interfering compound or siRNA determined. Having done these infection analyses and the generation of a raw hit list, bioinformatics approaches such as the pathway and clustering software STRING.

Summarizing the hypothesis and results, siRNA interference and small chemical interference results were put in correlation to each other, in particular with regard to the common targets and pathways.

In terms of learning objectives, this practical course featured:

- Learning to formulate and test a scientific hypothesis based on existing literature,
- Learning how to carry out an infection experiment at small scale in high throughput mode, thereby testing the hypothesis,
- Learning aspects of liquid handling and fluorescence imaging,
- Learning to choose appropriate experimental controls, positive, negative and background controls.
- Gaining basics in 'scientific writing' and the salient features of grant writing

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The compounds utilized were categorized according to their expected effects on subcellular components or events:

- Cytoskeleton & Motors
- Replication
- Endocytosis & Trafficking
- Kinases & Phosphatases
- Nuclear Transport
- Lipid Metabolism.

This same classification was later on applied for the siRNA's used in the small screen. In addition, some groups dealt with plates with the single siRNA's and also pools of those that targeted the same gene for knock-down.

In general, the experimental design favored the six groups doing the same experiments with the only exception being having either wild type HAdV-C5 or HadV-ΔE1A-GFP-C5. Hereby reproducibility of results between groups with the same virus and comparison of a replicating vs. a non-replicating virus could be assessed.

Mini-Compound Screen

The cells were pre-seeded by Nina Wolfrum and so drug treatment of the cells was possible on day 3. To do so, the compounds were added to the HeLa ATCC cells (the cell line used throughout the practical) and incubated at 37°C for 1 hr. After this incubation, the respective virus was added and cold-bound to the cells during 30 minutes. The plates were then washed once, medium replaced and supplemented again with the specific compounds. The cells were incubated at 37°C for 3hrs in presence of both the compounds and still-bound virus. After that cells were washed again, replenished with compound-free medium and incubated overnight at 37°C. The next day, cells were fixed and stained according to what virus had been applied to the cells (i.e. simple DAPI stain for GFP-expressing virus or DAPI and immunostain for wild type virus). Imaging was done on a Molecular Devices High-Throughput Microscope with the aid of a

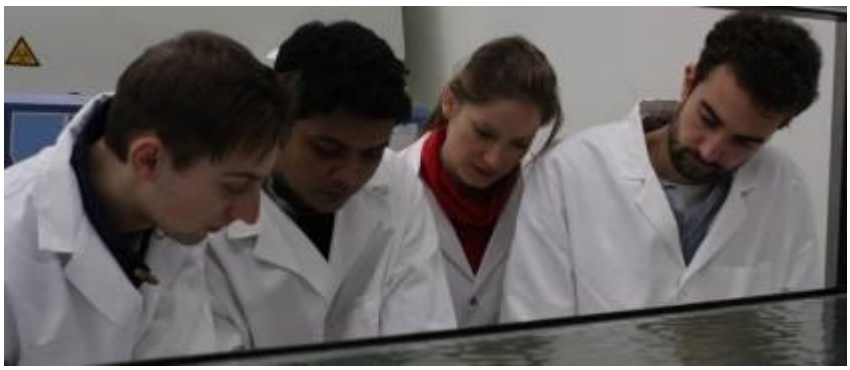
robotic arm to load plates overnight. Acquired data were then analyzed with the help of CellProfiler and KNIME software and graphically displayed with Excel diagrams.

siRNA-Mini-Screen

On day 3, the siRNA perturbation screen was performed. Before this, a checkerboard plate assay was carried out alongside the actual experiment to get an estimation of how the infection index is influenced by the cell number (ie, seeding density or amount of perturbation-surviving cells). Plates pre-spotted with different siRNAs were used for reverse transfection of HeLa ATCC cells and RNAiMAX. Knockdown of the targeted genes was for 72 hours, when the virus was added to both the checkerboard and the siRNA plates. Again for reasons of experimental design one half of the groups utilized wild type virus, the other half GFP-expressing, non-replicating virus. After an overnight incubation with virus, the plates were fixed and stained, and then again imaging was done with the aid of the high-throughput microscope.

Before we started the data analysis, Artur Yakimovich gave a comprehensive tutorial for imaging analysis in general and in particular more specific insights into the software of CellProfiler and KNIME, two freely available tools for the specific analysis requirements of this course and its datasets. The data for each group and each experiment were processed separately. During the analysis, each group focused on one of the different effector groups mentioned above. Our results were later on presented with a short informal presentation and a written report.

On analyzing all the data, we noticed that the results overall were inconclusive, as compared to the control data obtained in an identical test run before the lab course. We speculated that the multitude of experimenters or the unfamiliar protocols impacted on the reproducibility of the manipulations. Nevertheless the course was successful in demonstrating how to use the power of interference strategies, quantitative image acquisition and analyses to acquire new knowledge on host factors for Adenovirus infections in cultured cells.



Students in action during the practical course focusing on a cellular perturbation screen in a high throughput mode

V. NETWORKING AND SOCIALIZING EVENTS

As the Zurich meeting was the first opportunity of the ESR's, ER's and PI's to meet each other, social events were very important, and a cornerstone for the success of the meeting.

Sunday 10th March – Dinner Reithalle

Just after the arrival of almost all ESR's and ER's and some PI's to Zurich, a dinner at Restaurant Reithalle by the river Sihl was organized by Urs for our first get-together. We all gathered downtown Zurich at 6.30 pm and after a short introduction the group was divided over three tables. Here we continued our talks and discussions while enjoying a nice meal.

Monday 11th March – Business meeting of the PI's and Dinner Commihalle

Before the dinner with all participants, a business meeting of the PI's took place which allowed discussion on the routes to be pursued, actual developments in the field, and also the chance for networking and building up collaborative projects.

Afterwards all ESRs, ERs and PIs met for dinner at restaurant Commihalle. This provided an excellent opportunity to review the day and continue discussions. It was a delicious dinner in a relaxed atmosphere which we all enjoyed.





Wednesday 13th March – Presentation of the individual ESR/ER projects

In order to get to know each other better from a scientific point of view, a session of presentations by all ESR's and ER's was organized and chaired by Urs.

ESR/ ER	First name / Surname	Principal Investigator, Institution, Country	Topic
ESR	Estrella Lopez Gordo	Andrew Baker, UGLA, United Kingdom	Tropism-modification of adenoviral vectors for targeted gene delivery
	Karsten Eichholz	Eric Kremer, CNRS Montpellier, France	Adenovirus immune complex induced maturation of dendritic cells – cell biology and down-stream interaction with other players of the immune network
	Nicole Stichling	Urs Greber, UZH, Switzerland	Innate immune sensing mechanisms during Adenovirus entry
	Rodinde Hendrickx	Silvio Hemmi, UZH, Switzerland	Using Mouse Adenovirus as an oncolytic agent
	Anandi Rajan	Niklas Arnberg, Umeå, Sweden	Identifying binding partners for Human Adenovirus 40 and 41 penton base proteins and characterizing their roles in the life cycle of the virus
	Naresh Chandra	Niklas Arnberg, Umeå, Sweden	Identification and characterization of soluble components that regulate Adenovirus tropism
	Jorien Koelen	Len Seymour, UOx, United Kingdom	Effects of TNF and LTA on colorectal cancer and the tumor microenvironment
	Carlos A. Fajardo	Ramón Alemany IDIBELL-ICO, Spain	Arming oncolytic Adenoviruses to improve antitumor immunity
	Nicholas Downes	Seppo Ylä-Herttuala, UEF, Finland	Modulation of gene expression via ncRNA induced epigenetic modifications
	Hugo Calderón	Kerry Fisher, Psioxius, United Kingdom	Elucidating the mechanism of action for the oncolytic Adenovirus ColoAd1
	Lukas Kuryk	Akseli Hemminki, Oncos, Finland	Production and analytical assays of CGTG-401
	Iva Podgorski	Maria Benkö, VMRI, Hungary	Screening for new Adenoviruses
ER	Raquel Garcia	Andrew Baker, UGLA, United Kingdom	Identification of small molecules enhancers of Factor X-mediated Adenovirus-5 transfer; Adenovirus as a tool to deliver microRNAs in vein graft failure
	Dragomira Majhen	Jerome Custers, Crucell, Netherlands	Anti-vector response and basic biology of AdV type 26
	Agnieszka Lipiec	Menzo Havenga Batavia, Netherlands	Helping to accelerate biopharmaceutical development from discovery to the clinic

Sunday 17th March – Luzern & Pilatus

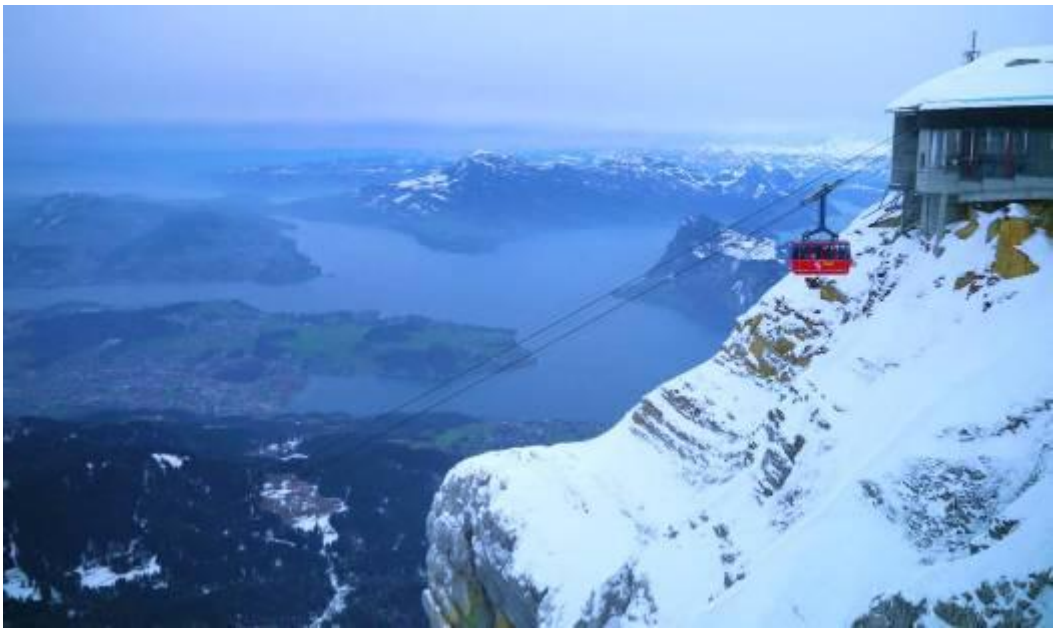
On a cold Sunday morning, all the participants gathered at the Central Station of Zurich for our trip to Luzerne. During the one hour train ride to Luzerne some enjoyed the beautiful view over Lake Zurich with the still snowcapped mountains all around, while others needed more time to wake up! Upon arrival in Luzerne, we walked past the famous Kapellbrücke towards the National History Museum. Once inside to the warmth, we had the opportunity to explore the huge variety of displayed objects. This was achieved with the help of a barcode scanning guide that organized

an individual subject-oriented tour through the museum. Equipped with our new gadget, we walked through the museum to find interesting exhibits. After an hour of discovering historical treasures, we went for a walk through the city to see the famous Luzerne monument: the carving of the dying lion. After these two cultural highlights the group splintered to smaller ones to have lunch before we would continue the trip to mountain Pilatus.

Group picture of all participants in front of the carving of the dying lion at Lucerne

Around 1.30 pm, we met again at the main station of Luzerne to take the bus to the gondolas. After a short ride through the city, we arrived at the cable cars that would take us up part of Mount Pilatus. On the way up, we had a great view over both Luzerne and its lake. After twenty minutes in the first cable car, we arrived at the station for the gondola that would take us up to Pilatus peak.

At the highest accessible point, we felt a sudden drop in temperature, especially because of the strong wind. This made it tricky to get to the viewpoint. Nevertheless, most of us went up there to enjoy the beautiful view over Lucerne and Lake Lucerne. The warmth of the visitors' center however, was too tempting to resist after a while outside in the cold. There, we enjoyed the view from behind the glass, until it was time to return to Zurich. On the train on our way back, we celebrated Urs` birthday with a spontaneous `happy birthday` song, cake and Luxemburgerli. It was a great trip and we all got a sneak peak of the beauty of Switzerland.



View from Pilatus peak over Lake of Lucerne and Lucerne itself

Leisure time and Evenings spent together throughout the course

Fortunately, there was also some time for leisure activities for the students in the wonderful city Zurich.

Main Entrance of the University of Zurich at the central campus

On the Saturday most of us enjoyed a stroll through the city and along the lakeside. Shopping Sprüngli chocolate and other delicious food was of course not to be missed, as well as a coffee on top of Zurich's highest sky scraper Prime Tower.

For the farewell dinner on Thursday 21st March we had chosen Zeughauskeller, a restaurant that offers typical swiss dishes in a beautiful atmosphere near Paradeplatz.





Upper left image: Tuesday night out at a pizzeria downtown **Upper right image:** Atrium of Irchel Campus **Lower left image:** View from Prime Tower's Clouds Bar over the city of Zurich **Middle image:** Friday Beer at Les Halles **Lower right image:** Cheese Fondue Night - not to be missed by anyone

In conclusion, we would like to express our sincere thanks to the organizers and especially the people behind the scenes who contributed to the overall success of the event. We would also like to thank Carlos, Anandi, Naresh, Iva, Andrea and Bettina for sharing their pictures and all the ERs and ESRs for making the first ADVance training event so special.