University of Zurich[UZH] | ETH zürich

SCOOPED

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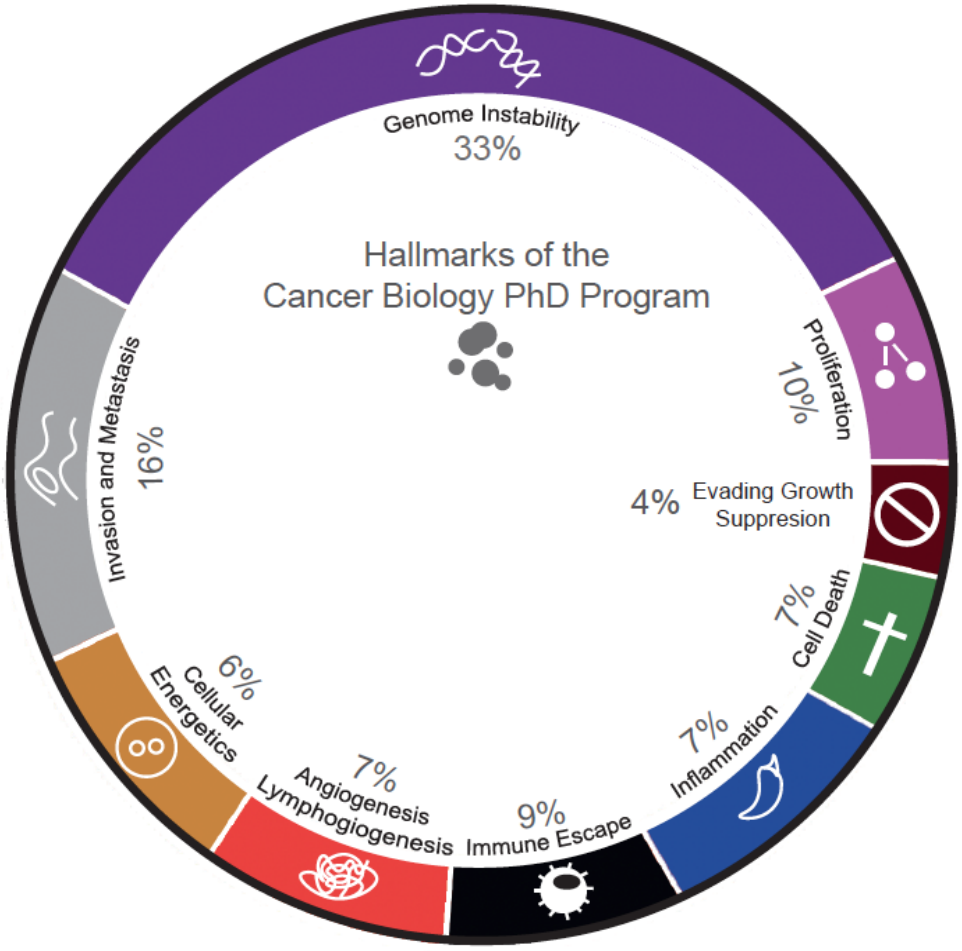
The Cancer Biology PhD Program Newsletter



Dear Readers,

This is the fourth issue of SCOOPED, the biannual Cancer Biology PhD program newsletter.

So far, contribution to the newsletter has been fantastic and we would like to thank everybody involved for making the effort. However, the success of this newsletter will always depend on your assistance, ideas and feedback. We therefore encourage you to contact us when:

- **you publish a paper you would like to share with the cancer research community in our «Research Highlights» section**
- **you develop an exceptional technique other labs could profit from, which you would like to explain in more detail**
- **you go to a conference and would like to write a brief report about the highlights of the meeting**
- **you have some other type of information you would like to communicate**
- **you want to give us some general feedback**

In addition we are looking for motivated people who are interested in joining the newsletter team. Please contact us if you would like to contribute to the next issue of SCOOPED by collecting information, conducting interviews or writing articles:

CancerBioNews@gmail.com

We hope you enjoy reading this issue :)

Ana Antunes, Karthiga Kumar and Hannah Parker

"Piled Higher and Deeper" by Jorge Chan www.phdcomics.com

Recent Publications by CB PhD Students

Ashisha Sharma & Sabine Bender - Group Prof. Martin Pruschy

Intrinsic and acquired resistances to radiotherapy represent a major challenge in the treatment of NSCLC. Here we demonstrate that genetic and pharmacological inhibition of ADAM17 radiosensitizes NSCLC tumors in vitro and in vivo. We provide a sound rationale for repositioning ADAM17 inhibitors as short-term adjuvants to improve the radiotherapy outcome of NSCLC patients.

Secretome Signature Identifies ADAM17 as Novel Target for Radiosensitization of Non-Small Cell Lung Cancer

Sharma A[1], Bender S[1], Zimmermann M[1], Riesterer O[1], Broggini-Tenzer A[2], Pruschy MN[3]

Summary: Ionizing radiation (IR) induces intracellular signaling processes as part of a treatment-induced stress response. Here we investigate IR-induced ADAM17 activation and the role of ADAM17-shed factors for radiation resistance in non-small cell lung cancer. Experimental **Design:** Large scale secretome profiling was performed using antibody arrays. Secretion kinetics of ADAM17 substrates was determined using ELISA across multiple in vitro and in vivo models of non-small cell lung cancer. Clonogenic survival and tumor xenograft assays were performed to determine radiosensitization by ADAM17 inhibition. **Results:** Based on a large scale secretome screening, we investigated secretion of auto- or paracrine factors in non-small cell lung cancer in response to irradiation and discovered the ADAM17 network as crucial mediator of resistance to IR. Irradiation induced a dose-dependent increase of furin-mediated cleavage of the ADAM17 proform to active ADAM17, which resulted in enhanced ADAM17 activity in vitro and in vivo. Genetic or pharmacologic targeting of ADAM17 suppressed IR-induced shedding of secreted factors, downregulated ErbB signaling in otherwise cetuximab-resistant target cells and enhanced IR-induced cytotoxicity. The combined treatment modality of IR with the ADAM17 inhibitor TMI-005 resulted in a supra-additive antitumor response in vivo demonstrating the potential of ADAM17 targeting in combination with radiotherapy. **Conclusions:** Radiotherapy activates ADAM17 in non-small cell lung cancer, which results in shedding of multiple survival factors, growth factor pathway activation and IR-induced treatment resistance. We provide a sound rationale for repositioning ADAM17 inhibitors as short-term adjuvants to improve the radiotherapy outcome of non-small cell lung cancer.

Read full article here
Clincanres. 2016 Apr 13; 2449

Júlia Aguadé-Gorgorió - Group Jean-Pierre Bourquin

Defects in the apoptosis machinery are major contributors to drug resistance in cancer. We found that simultaneous activation of different cell death programs, apoptosis and necroptosis, by SMAC mimetics effectively killed leukemia cells from highly resistant leukemia patients. Using CRISPR/Cas9-based genome editing in primary patient cells, we identified RIP1 Kinase as a primary target of the SMAC mimetics. Furthermore, only disruption of both apoptotic and necroptotic genes lead to complete protection against death by SMAC mimetics, supporting the notion of dual killing activity of these compounds. None of the currently used chemotherapeutic agents exploited this RIP1 Kinase dependent death pathway, suggesting that resistance to RIP1 targeting is not to be expected.

Activation of concurrent apoptosis and necroptosis by SMAC mimetics for the treatment of refractory and relapsed ALL

Scott McComb[1],*, Júlia Aguadé-Gorgorió[1],*, Lena Harder[1], Blerim Marovca[1], Gunnar Cario[2], Cornelia Eckert[3], Martin Schrappe[2], Martin Stanulla[4], Arend von Stackelberg[3], Jean-Pierre Bourquin[1],* and Beat C. Bornhauser[1],*,† * These authors contributed equally to this work.

Abstract: More precise treatment strategies are urgently needed to decrease toxicity and improve outcomes for treatment-refractory leukemia. We used ex vivo drug response profiling of high-risk, relapsed, or refractory acute lymphoblastic leukemia (ALL) cases and identified a subset with exquisite sensitivity to small-molecule mimetics of the second mitochondria-derived activator of caspases (SMAC) protein. Potent ex vivo activity of the SMAC mimetic (SM) birinapant correlated with marked in vivo antileukemic effects, as indicated by delayed engraftment, decreased leukemia burden, and prolonged survival of xenografted mice. Antileukemic activity was dependent on simultaneous execution of apoptosis and necroptosis, as demonstrated by functional genomic dissection with a multicolored lentiCRISPR approach to simultaneously disrupt multiple genes in patient-derived ALL. SM specifically targeted receptor-interacting protein kinase 1 (RIP1)-dependent death, and CRISPR-mediated disruption of RIP1 completely blocked SM-induced death yet had no impact on the response to standard antileukemic agents. Thus, SM compounds such as birinapant circumvent escape from apoptosis in leukemia by activating a potent dual RIP1-dependent apoptotic and necroptotic cell death, which is not exploited by current therapy. Ex vivo drug activity profiling could provide important functional diagnostic information to identify patients who may benefit from targeted treatment with birinapant in early clinical trials.

Read full article here
Scitransmed. 2016 May 18;8(339):339ra70

Recent Publications by CB PhD Students

Chiara Giorgi - Group of Prof. Beat Schaefer

In our group we investigate new systems to target EWS/FLI1 fusion protein in Ewing sarcoma, a rare tumor that affects bones and soft tissues in children and young adults. EWS/FLI1 is a fusion protein found only in tumor cells and being a transcription factor is difficult to target directly, therefore new therapeutic approaches are needed. From a drug screening with targeted compounds we identified PI3K inhibitors (BEZ235) as modulator of EWS/FLI1 activity and gene expression itself, through regulation at the promoter level via SP1. In collaboration with a research group in Munich we also described JQ1, a bromodomain inhibitor, as a potent regulator of EWS/FLI1 level. A combined therapy with both BEZ235 and JQ1 together with the standard treatments might lead to an increase of survival rate of those patients that present metastasis or relapse.

Targeting the EWS-ETS transcriptional program by BET bromodomain inhibition in Ewing sarcoma.
Hensel T [1,2] , Giorgi C [3] , Schmidt O [1,2] , Calzada-Wack J [4] , Neff F [4] , Buch T [4,5] , Niggli FK [3] , Schäfer BW [3] , Burdach S [1,2] , Richter GH [1,2]

Abstract:
Ewing sarcomas (ES) are highly malignant bone or soft tissue tumors. Genetically, ES are defined by balanced chromosomal EWS/ETS translocations, which give rise to chimeric proteins (EWS-ETS) that generate an oncogenic transcriptional program associated with altered epigenetic marks throughout the genome. By use of an inhibitor (JQ1) blocking BET bromodomain binding proteins (BRDs) we strikingly observed a strong down-regulation of the predominant EWS-ETS protein EWS-FLI1 in a dose dependent manner. This was further enhanced by co-treatment with an inhibitor of the PI3K pathway. Microarray analysis further revealed JQ1 treatment to block a typical ES associated expression program. The effect on this expression program was mimicked by RNA interference with BRD3 or BRD4 expression, indicating that the EWS-FLI1 mediated expression profile is at least in part mediated via such epigenetic readers. Consequently, contact dependent and independent proliferation of different ES lines was strongly inhibited. Mechanistically, treatment of ES resulted in a partial arrest of the cell cycle as well as induction of apoptosis. Tumor development was suppressed dose dependently in a xeno-transplant model in immune deficient mice, overall indicating that ES may be susceptible to treatment with epigenetic inhibitors blocking BET bromodomain activity and the associated pathognomonic EWS-ETS transcriptional program.

PI3K/AKT signaling modulates transcriptional expression of EWS/FLI1 through specificity protein 1
Giorgi C [1] , Boro A [1] , Rechfeld F [1] , Lopez-Garcia LA [1] , Gierisch ME [1] , Schäfer BW [1] , Niggli FK [1]

Abstract:
Ewing sarcoma (ES) is the second most frequent bone cancer in childhood and is characterized by the presence of the balanced translocation t(11;22)(q24;q12) in more than 85% of cases, generating a dysregulated transcription factor EWS/FLI1. This fusion protein is an essential oncogenic component of ES development which is necessary for tumor cell maintenance and represents an attractive therapeutic target. To search for modulators of EWS/FLI1 activity we screened a library of 153 targeted compounds and identified inhibitors of the PI3K pathway to directly modulate EWS/FLI1 transcription. Surprisingly, treatment of four different ES cell lines with BEZ235 resulted in down regulation of EWS/FLI1 mRNA and protein by ~50% with subsequent modulation of target gene expression. Analysis of the EWS/FLI1 promoter region (−2239/+67) using various deletion constructs identified two 14bp minimal elements as being important for EWS/FLI1 transcription. We identified SP1 as modulator of EWS/FLI1 gene expression and demonstrated direct binding to one of these regions in the EWS/FLI1 promoter by EMSA and ChIP experiments.

Read full article here
Oncotarget. 2016 Jan 12;7(2):1451

Read full article here
Oncotarget. 2015 Oct 6; 6(30): 28895–28910.

Call for Papers

We would like to continue the section «Research Highlights» in the next issue of SCOOPED. The idea is to briefly highlight work that you have published as first author during your PhD in order to provide others with an overview of the research topics of the PhD program.

If you would like to share your recent publication with the cancer research community using this platform, please send the abstract and concise summary/significance (no more than 300 characters) of your work to:

CancerBioNews@gmail.com

RuII-polypyridyl complexes: new promising cancer therapeutics

Vanessa Pierroz - Group PD Dr. Stefano Ferrari

Photodynamic therapy (PDT) is a medical technique employed in several countries for the treatment of dermatological diseases and some types of cancer. PDT consists in the light-dependent triggering of reactive oxygen species (ROS) such as singlet oxygen ($^1O_2$) by a photoactive compound or photosensitizer (PS) and results in cell death [1]. $^1O_2$ is a very reactive species with half-life in a biological environment estimated to ~40 ns, corresponding to a range of action of around 20 nm. Ideal properties of PS are:

1. High phototoxic index (calculated as ratio of IC50 in the dark/IC50 upon irradiation);
2. Activation at a specific wavelength (preferably in the red or near-IR region due to deeper penetration of light into tissues and better tolerance by patients);
3. Good chemical and biological stability as well as photostability;
4. Excellent efficiency in the photosensitization of molecular oxygen.

PS currently in the clinic are porphyrins, phthalocyanines or chlorins, with Photofrin® approved as PDT drug for the treatment of esophageal and non-small cell lung cancers [1]. Deployment of such PS, however, is clearly limited by important side effects, among which is the long-lasting light sensitivity caused by porphyrins due to their slow clearance. Ruthenium complexes have gained momentum as PS thanks to their tunable photophysics, their geometry (allowing to tailor compounds for binding to specific targets), the high uptake in cells and the low systemic toxicity. Two prominent Ru-based drugs, NAMI-A and KP1339, are currently in clinical trials [1].

Considering the peculiar affinity of RuII-polypyridyl derivatives for DNA, we recently embarked on a program aimed at investigating biochemical properties and cellular responses to such compounds. The first study, conducted in 2014, was centered on the synthesis and chemical characterization of RuII-polypyridyl complexes [2]. This study came to the conclusion that all the six RuII-polypyridyl derivatives synthesized had promising quantum yields for singlet oxygen production and displayed the ability to intercalate in DNA causing single strand cleavage upon light activation.

In a follow up study entitled «Dual mode of cell death upon photo-irradiation of a RuII polypyridyl complex in interphase or mitosis» that was recently published in the prestigious Royal Society Journal «Chemical Science» (http://pubs.rsc.org/en/content/articlelanding/2016/SC/C6SC00387G#!divAbstract), we explored biological properties and mechanism of action of the most promising RuII-polypyridyl complex, namely [Ru(bipy)2-dppz-7-methoxy][PF6]2 (hereafter Ru65). We first confirmed that Ru65 localized in the nucleus of various cancer and normal cells, displaying cytotoxicity only upon UV-A irradiation. Next, we examined the molecular mechanism of the UV-A mediated cytotoxic action of Ru65. In a series of in vitro studies, we were able to demonstrate that the complex intercalates in plasmid DNA and, upon light irradiation, causes nicks in the double helix. Most importantly, photo-activation of Ru65 promoted extensive guanine oxidation, as indicated by studies conducted with formamido-pyrimidine DNA glycosylase (Fpg or 8-oxoguanine DNA glycosylase), an enzyme that releases damaged guanines from dsDNA leaving a one-base gap: these experiments showed that supercoiled plasmid DNA in which intercalated Ru65 was photo-activated, was almost fully converted in the nicked form. In the next step, we confirmed this mechanism of action in living cells showing that UV-A irradiation of cells loaded with Ru65 resulted in a transient DNA damage response and cell death. We observed that cells underwent cell cycle arrest at the G2/M phase displaying massive cytoplasmic vacuolation, which was paralleled by an unfolded-protein stress-response, resulting in reduction of viability and cell death through a paraptosis-like mechanism. Strikingly, in cells synchronized at G2/M with a selective CDK1 inhibitor and that were released to progress to mitosis, photo-irradiation of Ru65 impaired mitotic entry, causing rapid cell death through classic apoptotic pathways. Importantly, targeting mitotic cells with Ru65 allowed increasing its photo-toxicity by a factor of 3.6.

As a whole, this study reached two important conclusions. The first consists in the elucidation of the mechanism of action of a Ru(II) polypyridyl complex upon irradiation with innocuous UV-A light. The second consists in the fact that photo-irradiation of Ru65 in mitotic cells results in rapid induction of cell death at a concentration 3.6-fold lower with respect to the dose causing loss of viability in non-synchronized cells. This finding paves the way to the implementation of novel therapeutic protocols according to which cancer patients could be treated with a combination of cell cycle inhibitors and Ru65/light for an effective clearance of tumors.

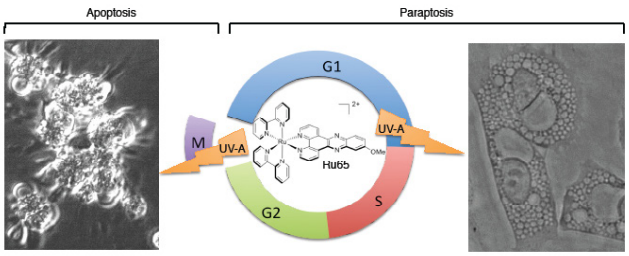


Figure 1 - Scheme of the different cell death modes triggered by UV-A irradiation of Ru65 in interphase (right) or at mitosis (left).

References

1. Mari, C., et al., Combination of Ru(II) complexes and light: new frontiers in cancer therapy. Chemical Science, 2015. 6: p. 2660-2686.
2. Mari, C., et al., DNA Intercalating Ru(II) Polypyridyl Complexes as Effective Photosensitizers in Photodynmic Therapy. Chem. Eur. J., 2014. 20(44): p. 14421-36.

107th AACR Annual Meeting

by Julia Aguade, Gabriele Manzella and Joana Marques



The 107th AACR Annual Meeting took place in the vibrant city of New Orleans from the 16th to the 20th of April. This year's theme was "Delivering cures through cancer science", and thousands of scientists from all around the world attended the conference.
The multidisciplinary program included outstanding speakers and more than 6,000 proffered papers. During these 5 days, you could attend talks and symposiums on a broad spectrum of topics, from basic chemistry to clinical studies and patient care, literally from bench to bedside.
The star topic of this year's AACR was, of course, CRISPR. There were talks about new Cas9 proteins with different functions such as RNA targeting and modifications of the standard Cas9 to induce gene knockdown. Also strategies to knockout specific domains of proteins to study their function and using CRISPR to generate knockout mouse models. Other big topics were epigenetics, metastasis, drug resistance and novel combination options for cancer treatment.

The best of AACR:
- You will always find something that is interesting for you, there are always talks from different themes taking place.
- It's very international, which allows you to meet people that you would not usually meet in European conferences.
- The last year of your PhD is a good time to go for networking opportunities, especially for those looking for a postdoc position. But email the people first, you will not find them by chance!
- There are many big pharma and biotech companies, so you can get a feeling of what's happening outside of academia (and get some free samples at the same time).
- The free coffee and cookies at the Bayer stand, definitely worth a visit.

The worst of AACR:
- It is quite overwhelming and easy to lose focus. There are a lot of topics and many talks going on at the same time. In order to get to the next talk you may have to miss the end of the previous talk.
- Don't go if you are looking for something specific. In that case it's better to find a small conference focused on your topic of interest.
- The poster sessions are huge, it is impossible to look at all of them.
- It is more difficult to be noticed and very difficult to get a talk.
- Most of the talks are given by PIs and are very broad summaries of their work over the last 20 years, not detailed.
- The air conditioning at the conference halls. Be ready to go from 30 to 15 ºC when you walk inside. Bring a jacket!

Overall, we would highly recommend to go to the AACR annual meeting or any other big international conferences at least once during your PhD. It's a unique chance to see the big guys presenting their work and meet people working in all aspects of cancer. How often will you have the chance to be lectured by Weinberg (yes, the one from the Hallmarks of Cancer) about what has gone wrong with science? You will leave with a different perspective on cancer research, new ideas for your own projects and some new contacts. And if you are lucky, you might even hear Vice-President Joe Biden speak about the Cancer Initiative!

Whatever became of...

...Mattia Bordoli - Senior Scientist at ETH, Group Prof. Dr. Sabine Werner

1) Could you tell us in which group of the CNZ you graduated, and how you proceeded after obtaining your PhD? I performed my PhD thesis in the group of Prof. Roland Wenger (Institute of Physiology, UZH). Following my thesis defense, while still working in Prof. Wenger's lab, I started looking for a Post Doc position in the United States or Canada I decided to join the group of Prof. Malcolm Whitman at Harvard University. I then successfully applied for the SNF postdoctoral fellowship and moved to Boston roughly half year after obtaining my PhD.

2) Could you give us a short description of your current position, including daily responsibilities? Since June 1st 2016 I am a Senior Scientist and Junior Group Leader in the research unit of Prof. Sabine Werner (ETH, Zurich). My position is funded by the SNF Ambizione grant. Currently I am mostly optimizing techniques I established previously and learning novel procedures. I am also busy building my own independent research group, which involves networking, establishing collaborations, looking for and interviewing potential students as well as of course plan and apply for future funding.

3) Why did you choose this position? The Ambizione grant represents for me a transition time in which I have the opportunity to learn new techniques and perform more applied research using in vivo disease models. This will allow me in the near future to establish my own independent research group combining my deep biochemical and molecular knowledge with a more translational approach.

4) Where did you apply for you current position and how did the application process look like? First, I needed to find a host group, willing to provide me with lab space and access to lab infrastructure in order to perform my research. I directly contacted Prof. Sabine Werner at ETH Zurich, who kindly accepted to host me in her research unit generously giving me full access to all the lab infrastructure. At this point I applied for the SNF Ambizione grant to secure my funding for the next three years.

5) Are you happy with you current position and to whom would you recommend it? Yes, I am happy with my choice. I have the opportunity to work in a highly competitive environment, to have access to a vast and modern research infrastructure, to network with people who share passion for science and discovery, to mentor PhD students and to lead my own projects.

6) What are your plans for the future? I am definitely aiming to establish my own research group focusing on extracellular matrix biology. In particular, I would like to understand how matrix modifications during disease progression (e.g. fibrosis, tumor invasion) are regulated at the molecular level. This will provide important information to develop new therapeutic options for diseases characterized by matrix rearrangements or excessive matrix deposition.

... Flurina Hari - Deputy manager at CLS Behring, Bern

1) Could you tell us in which group of the CNZ you graduated, and how you proceeded after obtaining your PhD? I did my PhD with Dr. Manuel Stucki, when he was still a group leader at the Institute of Veterinary Biochemistry. I stayed with him for five more months to help him to move his Lab to the Department of Gynaecology of the University Hospital. I applied then for several positions in the industry and choose the one at CSL Behring.

2) Could you give us a short description of your current position, including daily responsibilities? I am a senior scientist in the unit Operations Support, R&D at CLS Behring in Bern. Our group is responsible for R&D characterisation studies of process intermediates and of the final product of fullscale batches upon process changes or deviations. To my daily responsibilities belong statistical data evaluation, writing scientific reports, databases set up and maintenance, taking part in project team meetings.

3) Why did you choose this position? When I joined CSL Behring, I was the first to be mainly only responsible for these characterisation studies and my task was to develop these studies further, including statistical analysis, establishing databases and templates. To be able to improve or set up a system was an interesting challenge for me. In addition, my position requires contact to production, quality control, release, regulatory affairs - I liked the idea to be an expert for a specific field and contribute with this expertise to the manufacture of biotherapeutical drugs.

4) Where did you apply for you current position and how did the application process look like? My current position was advertised on jobs.ch. However, I was already observing CSL Behring AG because they produce products for biotherapies and because I heard about their cooperative working atmosphere. After sending my application by email, I was invited for two interviews.

5) Are you happy with you current position and to whom would you recommend it? During my PhD I realised that I like to acquire expertise and do research but need to have more structures and be involved as a team member; therefore, the choice to move to industry was really right for me. The current position allows me to work scientifically as a team member with achievable goals, timelines and visual outcome. I would recommend it to anyone that liked to work scientifically in the context of manufacturing drugs.

6) What are your plans for the future? I realise that I liked to set up new systems/databases and optimize processes. I could imagine any job where I can be involved in that.

New CNZ Members 2016

Prof. Dr. med. vet Carla Rohrer Biey, Division of Radiation Oncology, UZH

1) Can you give us a brief overview of your career (where/what did you study, what where the different stages of education/work you passed until you moved to Zurich)? After Veterinary School at the University of Bern (Switzerland), I did my dissertation thesis on opioid analgetics in cats at the University of Bern. Afterwards, as a further specialization, I pursued a residency in radiation oncology at the Vetsuisse Faculty, University of Zurich, receiving the Diplomate title for Radiation Oncology of the American College of Veterinary Radiology in 2003. After a couple of years as clinician (staff radiation oncologist), I spent almost four years as a Post-Doc in the Laboratory of Molecular Radiobiology at the University Hospital in Zurich in order to complete my research projects of my habilitation thesis on tumor hypoxia. In parallel and ongoing I am a consulting radiation oncologist in a Veterinary Oncology Specialty Clinic in Bologna, Italy. Since 2007 I am head of the Division of Radiation Oncology at the Vetsuisse Faculty, University of Zurich and as of 2015 Professor for Radiation Oncology.

2) When did you move to Zurich? I have had various positions at the Vetsuisse Faculty, University of Zurich since 2000.

3) When did you join the Cancer Network Zurich and why? I joined the Cancer Network Zurich at the End of 2015. With my professorship I will have the means to dive deeper into radiobiologic research topics with my team and I welcome the idea of being part of a specialized network.

4) How many people are currently working in your lab? My academic group of nine mainly consists of veterinary doctors that work in the clinical area. However, some of my doctoral students are planned to also spend quite some time in the lab in the future. The labgroup is headed by an experienced PostDoc and supported by our future PhD-student.

5) What is the main focus of your research?
For our lab-focused part of the research, we are interested in the behavior of tumors or normal tissues upon anticancer treatment, mainly radiotherapy: we investigate ionizing radiation induced cellular and tissue damage with two approaches. On the cellular or biopsy sample level we follow the extent on DNA damage produced by radiation, its speed of recovery and repair after radiation and the pathways involved in repair of the damage. At the tissue and functional level, we follow the damage produced by radiation (side effects), especially when large fractions of radiation doses are applied, such as in stereotactic hypofractionated radiotherapy.

6) What was your most memorable lab experience?
Whenever a publication from one of the group members was accepted for publication, we had a small pop-up celebration with prosecco and some snacks in the lab. This spontaneous honoration of the authors, after often many hours of drudgery is a very nice memory I have!

7) What is the motivation that keeps you going?
Luckily, I am looking forward to work every workday morning! The various aspects of my job including complex clinical work in radiation oncology, exciting research on the radiobiological aspect of cancer and teaching of assistants and students about cancer, the "emperor of all maladies", are very stimulating.

8) Which advice would you give a fresh PhD student?
The aim of this period is to cultivate the "craftsmanship" of your work you studied for the last years. Any PhD student is expected to work diligently, often resulting in long days. Teach yourself to think and focus while you work, e.g. work when you work and to be done when you are done. This will allow you to get work done in a satisfactory way and by fostering also the time of recovery, be sharp again on the next day.

9) What is the last book you have read?
I always have 5-7 books concurrently ongoing. However, over the last four years, I keep re-reading passages from Daniel Kahnemanns "Thinking, Fast and Slow". It amazes me over and over again, how our intuitive versus deliberate thinking influences our choices in life.

Dates for your diary...

13th-16th September 2016: Genomics course, Functional Genomics Centre, Zurich

4th-6th October 2016: EMBO conference - Translational Research in Cancer Cell Metabolism. For more info: Click here

1st-23rd November 2016: 25 hour teaching assistance in bloc course BIO319, PhD students of the CB PhD program can apply till 10th september 2016. For more info: Click here. Contact: martin.baumgartner@kispi.uzh.ch

14th-18th November 2016: Integrative -omics course «From the Transcriptome to the Proteome» - Functional Genomics Centre, Zurich

6th-9th December: Transcriptomics Course, Functional Genomics Centre, Zurich

New CNZ members 2016

Dr. César Nombela-Arrieta, Department of Experimental Hematology, University Hospital Zurich

1) Can you give us a brief overview of your career (where/what did you study, what where the different stages of education/work you passed until you moved to Zurich)?
I was trained as a Pharmacist in the Universidad Complutense of Madrid. In 2001 I started my predoctoral studies in the same city, in the National Center for Biotechnology. My supervisor was Jens Stein, who at the time was working in a large immunology group as a senior postdoc. Half-way through my PhD Jens got an independent position in the Theodor Kocher Institute in Bern. I loved my project, things were going well, and Jens was an excellent supervisor, so I moved to Switzerland and completed my doctoral studies. The group was working in dissecting intracellular pathways involved in lymphocyte recirculation, and for this we used intravital imaging techniques. As a postdoc I moved to the USA in 2007 to work in Leslie Silberstein's lab in the department of Transfusion Medicine of Children's Hospital Boston and Harvard Medical School. It meant quite a change in research topic, as I started focusing in understanding how blood stem cells were maintained in the bone marrow. My time in Boston was a great personal experience that taught me a lot about how academic research works, it helped me build up some endurance and to decide the type of scientist I wanted to be.

2) When did you move to Zurich?
I have lived in Zurich since late 2013. However, in a way I feel that I only got to settle here in July 2015, when my wife eventually moved to Zurich. Before then I was frequently traveling to Madrid in the weekends, and besides work I didn't have much time to enjoy the city.

3) When did you join the Cancer Network Zurich and why? I joined CNZ in January 2016. I think it is essential to find forums to discuss our projects, exchange ideas, and collaborate with people from different backgrounds. When I heard about the CNZ I had no doubt that I would like to be a part of it. Also, from the perspective of a PI I believe that for PhD students in my group it is really useful to belong to such a community and participate actively in its many activities.

4) How many people are currently working in your lab? Currently we are five people including myself. Stephan, Ute and Patrick are PhD students, and Álvaro, is a Master student from the ETH. It is a small group but we benefit from belonging to the Division of Experimental Hematology, the head of which is Prof. Markus Manz. We share labspace, labmeetings and journal clubs with other groups working in similar topics. This is absolutely critical for us as it favors close interactions, fosters collaborations and allows us to benefit from their work and expertise.

5) What is the main focus of your research?
In our lab we are investigating how hematopoiesis, which is an extremely complex, dynamic and plastic process, is regulated by the tissue microenvironment found in the different blood-forming organs. We are interested in defining the specific niches in which hematopoietic stem cells reside, the regulatory signals they receive from neighboring cells, and how these are altered as a result of pathological conditions such as inflammation, infections or leukemias.

6) What was your most memorable lab experience?
I have had many rewarding moments in the lab. If I had to choose I would pick those few moments in which I realized I was observing something that probably nobody else had before. Independently on how significant the finding maybe, it actually feels wonderful. During my time as a PhD student I remember experiencing this when while doing experiments that demonstrated the role of one of the signaling molecules we were studying, as a mediator of lymphocyte egress from lymph nodes.

7) What is the motivation that keeps you going?
I feel incredibly fortunate to have a career in academic research. It is wonderful to have a job in which the fundamental goal is to understand the ways in which nature works. It is a challenge and a huge incentive to aim for excellence in what I do everyday. Of course, as most scientists I would like to eventually contribute with a significant game-changing discovery.

8) Which advice would you give a fresh PhD student?
I can only give some tips that I believe have worked for me along the way. Be passionate about your work and always try to do a fine job, do not be sloppy. Try to be resilient. Don't let negative results, failed experiments or manuscript rejections bring you down. Finally, something that is easy to forget sometimes but is very important: science has to be fun, so be playful and take some risks.

9) What is the last book you have read?
"Why information grows", from César Hidalgo who is a Professor in the Media lab, at the Massachussetts Institute of Technology.

Core Facilities

Educational Facility at the Functional Genomics Center, Zurich

As a joint state-of-the-art research and training facility of the ETH and of the University of Zurich, the Functional Genomics Center Zurich (FGCZ) offers courses with hands-on practical in the most advanced experimental and analytical methodologies. These involve Next Generation Sequencing and Mass Spectrometry technologies used in the areas of genomics, transcriptomics, proteomics and metabolomics.
The practical courses that the FGCZ offers drifts away from a purely theoretical approach and students get a hands-on experience on this array of different -omics techniques.
We offer dedicated genomics and transcriptomics courses based in NGS technologies, to help scientists interested to gain a better understanding of the techniques available and their applications. Short lectures cover present technologies, their applications and the principles of downstream data analysis. The practical consists of a complete workflow which involves, the library preparation and sequencing run, followed by processing of the data and analysis.
Moreover, bearing in mind the significance of systems biology, we designed a new course which incorporates a proteomics component by nanoLC–MS/MS. The aim of this course is to help scientists interested in these cross -omics technologies and their data integration not only to gain a better understanding, of the available techniques and applications, but also to assist in the interpretation and characteristics of these –omics data. In this specific practical course, transcriptomics and proteomics data are generated and integrated together in several aspects. The integrated data analysis consists of direct feature and functional overlap as well as a joint pathway analysis.

Our next courses are as follows:

Transcriptomics course:
6th-9th of December 2016
Genomics course:
13th-16th of September 2016
Integrative –omics course: 'From the transcriptome to the proteome':
14th-18th of November 2016

Keep an eye on our 2017 courses as the new dates will be published in our website at the start of November 2016: http://www.fgcz.ch/education0.html
For further information regarding our courses, please-contact ngs.courses@fgcz.ethz.ch

The Viral Vector Facility, Neuroscience Centre Zurich

The Viral Vector Facility (VVF) is a service facility founded 2015 by the Neuroscience Center Zurich (ZNZ) and located at the Irchel campus. The VVF provides the production of custom viral vectors as well as cloning of custom viral and non-viral plasmids and consultation. Furthermore, the VVF maintains a repository for reporter viral vectors and for plasmids.
For in vivo gene delivery into mammalian cells, transduction by viral vectors is generally more efficient than transfection by plasmid DNA. Thus, many scientists use viral vectors as their tool of choice. Production, purification and characterization of high titer viral vectors depend on multi-step, time-consuming procedures with many pitfalls for the untrained Ph.D. student (see figure). The VVF offers competent and rapid production of viral vectors based on adenovirus-associated virus (AAV), lentivirus (LV) and γ-retrovirus (gRV). The production of other viral vectors (such as rabies virus) is possible.
AAV vectors became very popular, as they efficiently and stably transduce mitotic and postmitotic cells without toxicity, can be produced at high titers in the absence of helper viruses, are classified as BSL 1 and can be stored for extended periods without loss of transduction efficiency. Furthermore, several serotypes and variants of AAV vectors exist, which differ in their capsid proteins and thus in their tropism (transduction efficiency for a certain cell type or tissue). In order to facilitate the determination of the most efficient serotype and promoter combination for a particular project, the VVF maintains a repository consisting of small aliquots of pre-made AAV-based vectors that are available instantly. Currently, these aliquots are offered free of charge.
BSL 2-classified LV vectors are applied, when stable integration into the host genome is required or when the expression cassette is exceeding the packaging capacity of AAV vectors. The envelope of LV vectors is usually pseudotyped with VSV-G, leading to broad tropism and enhanced physical stability of the lentiviral vectors. As for AAV vectors, the VVF currently offers aliquots of reporter LV vectors free of charge.
Besides viral vector preparations, the VVF also covers the cloning of customized plasmids and offers consultation. An initial consultation is free of charge.
Further information, including prices and benefits from our annual membership, can be found on our homepage: www.vvf.uzh.ch
Please contact us via email at vvf@neuroscience.uzh.ch for free viral vector aliquots or to make an appointment for a consultation.

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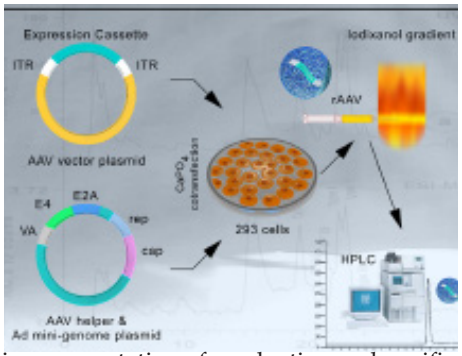

Schematic representation of production and purification of rAAV-2 vectors.

CB PhD Program Retreat

The 6th Cancer Biology PhD Program student retreat took place from 29th March 2016 to 31st March 2016 in Davos, Switzerland. The retreat was organized by 5 PhD students: Sabine Bender, Karthiga Santhana Kumar, Martin Falke, Ivo Grgic and Jelena Kresoja-Rakic. A total of 85 participants joined this event.

We had an outstanding scientific program with interesting and fruitful discussions in a beautiful location with perfect weather. Our keynote lectures were delivered by Prof. Dr. Anindya Dutta (University of Virginia Medical school), Gill Logan (Takeda Oncology) and Dr. Claudio Sustmann (Roche, Germany). The eminent speakers made sure that we had a great scientific input from the cancer community outside the Cancer Biology PhD program. Furthermore, one of our sponsors 'NEBION' held a training session for their versatile tool 'Genvestigator'. NEBION generously provided all the retreat participants with a one year free license to use Genevestigator.

Thirteen final year PhD students shared their exciting research work with the participants via oral presentations. During both evenings we had our poster sessions with approximately 40 poster presentations per session. The oral and poster presentations were of impecable quality which made it difficult to decide on the poster and oral presentation prizes. Prof. Dr. Anindya Dutta kindly helped us in judging the talks and the posters.

Our silver sponsor of 2016 retreat, SytemsX.ch, sponsored the poster presentation prizes. We had 3 oral presenation winners: Willy Decurtins, Simon Schäfer, Chiara Balbo and 6 poster presenation winners (3 from each session): Joana Marques, Simon Schwager, Viktoras Frismantas, Veronika Lysenko, Hind Hashwah, Brice Mouttet.

As a part of the social activity, we had a short hike to Schaztalp Hotel, Davos which completed our outstanding scientific program.

Impressum

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