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Dear Readers,

This is the fifth 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 :) 

The SCOOPED Team

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Piled Higher and Deeper by Jorge Chan - www.phdcomics.com
Iron-sulfur (Fe-S) clusters are inorganic cofactors found in a wide variety of proteins carrying out fundamental biological processes, such as electron transfer (e.g. in respiratory complexes I, II, III), catalysis (mitochondrial aconitase), and cellular iron homeostasis (IRP1). During the past years many nuclear proteins involved in essential steps of DNA replication and repair were also found to coordinate an Fe-S cluster (e.g. Pol α, Pol δ, Pol ε, DNA2, XPD, FANCJ, RTEL1, ChlR1). This finding was rather surprising, since Fe-S clusters may generate reactive oxygen species upon oxidation and potentially damage DNA.

The maturation of nuclear FeS cluster proteins is a multi-step process that finishes with the transfer of an Fe-S cluster to client Fe-S proteins. This step is carried out by the so-called CIA (cytosolic iron-sulfur cluster assembly) targeting complex. In this project we investigated the composition of the CIA targeting complex and its interaction with client Fe-S proteins.

**The CIA Targeting Complex Is Highly Regulated and Provides Two Distinct Binding Sites for Client Iron-Sulfur Proteins**

Odermatt DC, Gari K

**Abstract:**

The cytoplasmic iron-sulfur assembly (CIA) targeting complex is required for the transfer of an iron-sulfur (Fe-S) cluster to cytoplasmic and nuclear proteins, but how it engages with client proteins is unknown. Here, we show that the complex members MIP18 and CIAO1 associate with the C terminus of MMS19. By doing so, they form a docking site for Fe-S proteins that is disrupted in the absence of either MMS19 or MIP18. The Fe-S helicase XPD seems to be the only exception, since it can interact with MMS19 independently of MIP18 and CIAO1. We further show that the direct interaction between MMS19 and MIP18 is required to protect MIP18 from proteasomal degradation. Taken together, these data suggest a remarkably regulated interaction between the CIA targeting complex and client proteins and raise the possibility that Fe-S cluster transfer is controlled, at least in part, by the stability of the CIA targeting complex itself.

**Probing the Canonicity of the Wnt/Wingless Signaling Pathway**

Alexandra Franz, Daria Shlyueva, Erich Brunner, Alexander Stark and Konrad Basler

**Abstract:**

The hallmark of canonical Wnt signaling is the transcriptional induction of Wnt target genes by the beta-catenin/TCF complex. Several studies have proposed alternative interaction partners for beta-catenin or TCF, but the relevance of potential bifurcations in the distal Wnt pathway remains unclear. Here we study on a genome-wide scale the requirement for Armadillo (Arm, homolog of beta-catenin) and Pangolin (Pan, Drosophila’s TCF) in the Wnt/Wingless(Wg)-induced transcriptional response of Drosophila Kc cells. Using somatic genetics, we demonstrate that both Arm and Pan are absolutely required for mediating activation and repression of target genes. Furthermore, by means of STARR-sequencing we identified Wnt/Wg-responsive enhancer elements and found that all responsive enhancers depend on Pan. Together, our results confirm the dogma of canonical Wnt/Wg signaling and argue against the existence of distal pathway branches in this system.
Recent Publications by CB PhD Students

Martin Schwill - Group Prof. Andreas Plückthun

In the Plückthun lab we focus on protein engineering and crystallography to unravel nature’s secrets in the structure and function of proteins, as well as to create novel proteins for therapy. Using designed ankyrin repeat proteins (DARPins) libraries, we are able to generate specific binding reagents against virtually any epitope on a target protein, which opens up a myriad of possibilities to engage protein oncogenes. By combining a wide range of technologies, from proteins design over cells to in vivo experiments, we seek to find answers for unmet medical needs. In particular, we aim to shed light on the hyper-activation of receptor tyrosine kinases such as EGFR, HER2, HER3 and MET that cause cancers in various tissues.

Intermolecular Trapping of ErbB2/HER2 Receptor Induces pan-ErbB

Rastislav Tamaskovic1,*, Martin Schwill1,*, Gabriela Nagy-Davidescu1, Christian Jost1,*, Dagmar C. Schaefer2, Wouter P.R. Verdurmen1, Jonas V. Schaefer1, Annemarie Honegger1 & Andreas Plückthun1

Abstract:
ErbB2 is a receptor tyrosine kinase directly linked to malignancies and the target of the therapeutic monoclonal antibodies trastuzumab and pertuzumab as well as kinase inhibitors such as lapatinib. Although targeted agents against ErbB2 show high response rates in first line therapy, tumors develop therapeutic resistance within several months and cancer drug resistance remains one of the major clinical challenges. Compensatory mechanisms, such as relief of AKT-ErbB3-negative feedback, are known to desensitize ErbB2-dependent tumours to targeted therapy. Recently, we have described yet another adaptation route leading to reactivation of the PI3K/AKT pathway, which acts independently of ErbB3 re-phosphorylation. This signaling bypass of phospho-ErbB3 operates in HER2-positive cancer cells via RAS-PI3K crosstalk and is attributable to ErbB2 homodimers. Consequently, blocking these compensatory mechanisms is predicted to potentiate the effect of incomplete ErbB2/3 blockade as it occurs during treatment by trastuzumab and pertuzumab. In the present work, we have developed a novel class of biparatopic anti-ErbB2 Designed Ankyrin Repeat Proteins (DARPins), which effectively downregulate oncogenic ErbB2/3 signaling and exert tumoricidal activity in 2D- and 3D-cell culture models as well as in orthotopically xenografted animals. By creating an intermolecular trap with biparatopic DARPin agents, which simultaneously engages two distinct ectodomain epitopes of ErbB2, the receptors adopts an inactive conformation resulting in kinase domains incapable of forming productive interactions. Such a trapping obstructs signaling from all functional ErbB2 homodimers, thereby achieving a pan-ErbB inhibition. The ensuing dephosphorylation of both ErbB2 and ErbB3 results in persistent attenuation of downstream signaling and overcomes adaptive responses incorporated into the ErbB oncogenic network. These novel insights into the mechanisms underlying oncogenic network robustness provide a guide to overcome adaptive resistance to current ErbB2/ErbB3-targeted therapy and we demonstrate a novel approach to engineer cell-specific apoptosis based on a structurally and mechanistically understood principle.

Read full article here
Nat Commun. 2016; 7: 11672

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
Tips for CANDOC Forschungskredit grant:

I learned about the CANDOC Forschungskredit grant from my supervisor. I applied for this grant during the first 6 months of my PhD, which was a challenge. I learned how to present the aims of my work in a structured manner and how to convey the importance of my research. It also helped me structure my project and plan experiments beyond the near future. Receiving a grant is also a good point for my CV. The overall experience with this grant was very positive.

Júlia Aguadé Gorgorió
Postdoctoral researcher
Lab of PD Dr. Jean-Pierre Bourquin
EICR, UZH

*Click on the grant names for more information
Tips for EMBO Long Term Fellowships:

My overall experience with the EMBO Long Term Fellowship was very positive. In general, I think this is a great fellowship for anyone doing basic research in the life science field in Europe. The application for this fellowship was straightforward and clearly focused on the scientific merits of your proposed research project. One unique part of this fellowship, which could be a pro or a con depending on the degree of your fear of public speaking, is the oral interview. If your written application passes the first round (I think they take the top 50%), you will have the opportunity to describe your research in person to an EMBO member. Personally, I appreciated the chance to interact with a real human and demonstrate my excitement for science, which does not always come across in writing. I highly encourage anyone thinking of pursuing a postdoc in the life science field to apply. Good luck!

Sean Howard
Postdoctoral Fellow
Lab of Prof. Petr Cejka
Institute for Research in Biomedicine
Bellinzona, Switzerland

Tips for travel grant – CNZ:

I applied for the CNZ travel grant to fund my expenses for the ‘ISPNO 2016’ conference. The application process was straightforward and easy. You have to apply for this grant before the conference, where you have an oral or poster presentation. After the conference, the bills have to be submitted along with a short summary of the conference. Based on the aforementioned documents submitted, the grant will be approved. You get extra brownie points if you have a significant contribution to the Cancer Biology PhD program.

Karthiga Santhana Kumar
PhD student
Lab of PD Dr. Martin Baumgartner
EICR, UZH

*Click on the grant names for more information
**Whatever became of...**

...Christine-Marie Weller - Lecturer position at the LMU in Munich

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 in Prof. Jiricny’s lab, continued with a short Post-Doc in the same lab and then went on to the LMU in Munich, where I obtained a Lecturer Position.

2) Could you give us a short description of your current position, including daily responsibilities?
As a Lecturer I am responsible for Biochemistry II Seminars at the LMU. It’s a seminar given by Professors, Group Leaders and external Lecturers like me in addition to the general main lectures. We teach the entire spectrum of Biochemistry II from Molecular Biology to Metabolism of the cell and repeat the basics in Chemistry, Kinetics of biochemical reactions, Biology, ... I prepare and give the daily seminar and must be ready to answer questions, clear up misunderstandings from the main lectures and help to solve other issues that are not understood well. Furthermore, I try to guide the students through the complex material and point out important key questions for them to understand the basics of biochemistry as well as in depth facts.

3) Why did you choose this position?
Teaching is something that I always enjoyed and it comes very naturally to me. However, instead of becoming a highschool teacher I chose Science first and did a PhD.

...Corina Schmid - Postdoctoral researcher at Roche Glycart in Schlieren

1) Could you tell us in which group of the CNZ you graduated, and how you proceeded after obtaining your PhD?
I completed my PhD in the group of Prof. Anne Müller at the IMCR in 2015. I stayed in her lab as a Postdoc for another 7 month while I was looking for new opportunities in the field of translational cancer research. I applied for Postdoc positions in academia as well as in industry and in the end decided to join the Roche Postdoc Fellowship program in cancer immunotherapy.

2) Could you give us a short description of your current position, including daily responsibilities?
The daily work of a Postdoc at Roche is pretty similar to that of an academic Postdoc...Planning and executing experiments, troubleshooting and presenting results in lab and department meetings. In addition to that there are several opportunities to attend courses and conferences as well as to get an insight in the structures of pharmaceutical research and drug development.

3) Why did you choose this position?
I guess a lot of graduates wonder whether they should stay in academia or rather try an industry environment. For me the Postdoc position at Roche offered an insight into translational research and “big pharma”, while still working on the bench and performing hands on cancer research.

I’m happy that I found a position where I can combine both and teach at a very high level, using the knowledge I have acquired during my studies.

4) Where did you apply for your current position and how did the application process look like?
I applied directly at the LMU, Molecular Biology department that offered the position. Shortly after my application I was invited for an interview, where I was asked to prepare two specific seminar presentations, one in molecular biology, the other in metabolism. During these short presentations three Professors addressed very specific questions about the topics at hand and basic Biochemistry questions to test my expertise and afterwards I was asked about my motivation and qualifications for the job. I was offered the position within a few weeks, after all applicants had been interviewed; so it was a very fast process with only one interview.

5) Are you happy with your current position and to whom would you recommend it? I’m quite happy with my position right now. It’s very challenging and demanding, especially because it’s new for me this first year as a lecturer. It’s also quite exciting and incredibly rewarding to see how helpful our seminar is for the students and to hear how thankful and appreciative they are. This job is something for a transition period, because the Academic education system in German-speaking countries does very rarely offer full-time, permanent lecturer positions at the university (other than professorships).

I think it is a good way of getting to know the world of pharma industry but still having the opportunity to go back to academia.

4) Where did you apply for your current position and how did the application process look like?
I actually applied for a Scientist position at Roche Glycart in Schlieren, which they advertised on their homepage. The application process included the standard documents (CV, letter of motivation), a phone interview and ultimately a personal on site interview with HR, the department head, several group leaders and I also had to give a talk about my PhD work. In the end they decided to take some one else for this scientist position, but offered me the Postdoc position instead.

5) Are you happy with your current position and to whom would you recommend it?
I am super happy with my decision to do a postdoc at Roche and I would recommend this position to people who are passionate about the translational aspect of cancer research, willing to work as part of a team and who don’t mind the confidentiality of the research and that the interests of the company is not primarily to publish the work but to bring novel therapies to the market.

6) What are your plans for the future?
I would like to continue my career in cancer research in an industry environment. I see myself in a Scientist position with the ultimate goal to lead my own research group one day.
New CNZ Members 2016

Prof. Tuncay Baubec - Department of Molecular Mechanisms of Disease, UZH

1) Can you give us a brief overview of your career (where/what did you study, what were the different stages of education/work you passed until you moved to Zurich)? I started as a biology student at the University of Vienna in 2000 and specialised in genetics and microbiology. For my masters I have joined Prof. Denise Barlow at the Centre of Molecular Medicine in Vienna to study the role of DNA methylation in replication asynchrony and chromatin compaction using the mouse imprinted gene cluster Aim/lgf2r as a model. I started my PhD studies in 2004 as a part of the Vienna Biocenter PhD Programme. I remained interested in epigenetics, but decided to change the model organism and joined Prof. Ortrun Mittelsten Scheid at the Gregor Mendel Institute to work on transcriptional gene silencing and paramutation in plants. After my PhD I moved to Basel to join Prof. Dirk Schübeler at the Friedrich Miescher Institute. As a postdoctoral fellow I combined genomics and computational approaches to study DNA methylation in embryonic stem cells. In 2015, I have received an SNF professorship to carry out my independent research at the Department of Molecular Mechanisms of Disease at UZH.

2) When did you move to Zurich? I have started my group in June 2015.

3) When did you join the Cancer Network Zurich and why? My group joined the CNZ in August 2016. I saw this as a great opportunity to place our basic research questions in a disease-relevant setting.

4) How many people are currently working in your lab? Two postdocs, three PhD students and one technician.

5) What is the main focus of your research? In my research group we study the fundamental aspects of eukaryotic gene regulation. In particular we focus our research to understand how genetic and epigenetic regulatory mechanisms give rise to tissue-specific gene expression programs, and how these become disturbed in human diseases, including cancer. Towards this we utilise high-throughput genome engineering in mouse stem cell models, functional genomics, proteomics and computational biology approaches.

6) What was your most memorable lab experience? In general the type of Eureka! moments, where results finally start to make sense and something which has not been described before comes to surface. That type of experience was always very rewarding and motivating for me.

7) What is the motivation that keeps you going? A constant curiosity to understand how we function, paired with an amazement at the complexity of biological systems. This results in an interplay of interesting questions and cool, sometimes unexpected answers, even if the latter usually are again only a part of the story.

8) Which advice would you give a fresh PhD student? Stay curious and follow your interests, and most importantly: enjoy science.

9) What is the last book you have read? “Herr Lehmman” from Sven Regener - the English title is “Berlin Blues”

Dr. Beat Bornhauser - Kinderspital, UZH

1) Can you give us a brief overview of your career (where/what did you study, what were the different stages of education/work you passed until you moved to Zurich)? I did my master of science at the Institute of Zoology at UZH, and obtained a PhD in molecular biology also at UZH, in the Division of Pharmacology. I then went to the Biomedical Center of the University of Uppsala, Sweden, for a 5 year postdoc, from where I came back to Zurich. Together with Jean-Pierre Bourquin we have then built up the leukemia group in the oncology department at the Children’s Hospital Zurich.

2) When did you move to Zurich? 2005

3) When did you join the Cancer Network Zurich and why? I joined the CNZ in 2016. I am happy to contribute to exchange and support further development of the cancer research community in Zurich.

4) How many people are currently working in your lab? We are currently two Postdocs, one PhD student, one master student and myself. We are closely working together with the group of Jean-Pierre Bourquin.

5) What is the main focus of your research? We are interested in cellular decisions that determine the switch from cell survival to cell death. Recent discoveries have identified a number of different programmed cell death mechanisms, distinct from the well-known apoptotic machinery. We think that the potential to activate one or several of these is a vulnerability of many cancer cells, in particular also of those that are resistant to current chemotherapy. Indeed, we could show that a subgroup of refractory leukemia cases is highly sensitive to necroptosis induction by small molecules. We follow this approach and decipher the molecular mechanisms that drive sensitivity to alternative cell death mechanisms to exploit them for cancer therapy.

6) What was your most memorable lab experience? There are several, but one particular was the moment we realized that the activity of a specific molecule was not just random toxicity as was claimed at the time by almost the whole rest of the world, but controlled non-apoptotic cell death. We could subsequently decipher the mechanisms of action.

7) What is the motivation that keeps you going? A constant curiosity to understand how we function, paired with an amazement at the complexity of biological systems. This results in an interplay of interesting questions and cool, sometimes unexpected answers, even if the latter usually are again only a part of the story.

8) Which advice would you give a fresh PhD student? I try to encourage them not to loose the focus by having to overcome smaller obstacles. One thing that we should not forget is also that we should have some fun at what we do.

9) What is the last book you have read? “The Golden Egg”, from Donna Leon
The Center for Microscopy and Image Analysis is an open imaging core facility at the University of Zurich. The center operates microscopy-related resources, collaborates with scientists in microscopy-related projects and teaches microscopy in courses, lectures and trains users in using specific microscope techniques required for their research projects.

Light microscopy-related resources range from advanced widefield fluorescence, lightsheet, confocal laser-scanning, multiphoton and superresolution microscopes. Imaging of cells, tissue but also of organisms like zebrafish, drosophila or small rodents can be performed. Dedicated light microscopes can be used to image live organisms in an unattended, automatic fashion to allow the acquisition of statistically relevant data. In electron microscopy state-of-the-art systems range from scanning to transmission electron microscopes allowing high resolution ultrastructural investigations also in the third dimension using focused ion beam scanning electron microscopy or cryo-electron tomography. Integrated approaches using light and electron microscopy are also supported to gain additional information from an experiment.

We assist users in using complex microscopes, planning imaging projects, sample preparation, image processing, data analysis, and storage of data as well as establishing new imaging infrastructure. The Center for Microscopy and Image Analysis also operates a virtualized image and data processing infrastructure optimized for microscopy data. This infrastructure can be accessed by all scientists of the UZH.

Lectures and practical courses organized by the Center aim to help scientists gain a better understanding in using modern concepts in microscopy for their research. Sample preparation for light and electron microscopy are covered with a special focus on practical hands-on courses. These topics are complemented with extensive in-depth training at microscopes to achieve optimal results for various projects.

Our lectures, courses and trainings can be found: http://www.zmb.uzh.ch/en/teaching.html. Individual trainings and introductions to microscope systems and image processing as well as project discussion can be arranged directly.

Further information can be found at http://www.zmb.uzh.ch.

COS-7 cells stained for DNA (cyan, DAPI), mitochondria (green, TOM-20—Oregon Green488), microtubules (red, tubulin—TMR) and actin (magenta, actin-SiR) a) Large area overview to allow selection of cells for higher resolution imaging. b) high resolution imaging of the boxed area in a). c) magnification of b. d) deconvolved data of b) to reduce noise and to increase resolution.
New CB PhD Student Representatives

Julia Godau and David Vukovic introduce themselves as the new PhD Student Representatives

Where are you from?
Julia Hamburg, from the North of Germany
David I am from Vienna, Austria - one of the larger cities on the Danube River

Which lab are you currently working in?
Julia I am working in the Institute of Molecular Cancer Research in the group of Prof. Sartori
David I’m working in the group of Andreas Plückthun at the Department of Biochemistry

What will your tasks be as the new representatives?
We are representing the collective interests of the Cancer biology PhD students - for example at the steering committees. In that role it is our duty to first understand, and second to communicate new ideas, concerns or problems brought forward to us efficiently within the graduate school. The less serious component of our duties includes channeling our combined creativity into organizing events like the Come together with new PhD candidates, the traditional barbecue as well as the annual Christmas event. In that regard we’re doing everything we can to involve a bouncy castle at some point in the future - but we’ll need serious support from everyone to get this through.

On a serious note, feel free to come forward with any questions arising. Us two having lived and studied here for a while now, we’re also happy to share a few tips and tricks – so never hesitate to come forward!

What is your favourite dish?
Julia Mmh, depending on my mood. But I would say any kind of cake I could eat every day...
David In my case it’s stuffed paprika, or “punjena paprika” as my grandmother calls them. I’ve never quite succeeded in reproducing her results following her very own protocol – for me the reproducibility crisis starts right there.

Where is your favourite place in Switzerland/Zurich?
Julia Somewhere at the water. In Zurich I like the Werndinsel or Rote Fabrik.
David For me it’s high up on the mountains. I can’t even pin down a specific spot – you get spoiled with amazing views wherever you go!

Tell us one interesting fact about yourself.
David I have yet to find someone who also succeeded in hitting himself in the head with an axe. Quite a feat I was told.

Dates for your diary...

27th - 30th June 2017 & 26th - 29th September 2017: Transcriptomics RNA-seq course, Functional Genomics Centre, Zurich
27th June 2017: London Cell Cycle club, The Francis Crick Institute London, UK - it’s free to attend!
25th - 28th June 2017: 3rd EACR Conference on Cancer Genomics, Cambridge, UK
9th - 13th July 2017: 2nd Zing Genomic Integrity Conference, Dublin, Ireland
10th - 14th October 2017: Biology of Cancer: Microenvironment & Metastasis, Cold Spring Harbour, USA
18th - 21st October 2017: 9th World Congress of Melanoma, Brisbane, Australia
5th - 8th November 2017: Cancer Genomics, EMBL, Heidelberg, Germany
13th - 17th November 2017: Integrative -Oomics practical course: «From the transcriptome to the proteome» Functional Genomics Centre, Zurich
CB PhD Program Christmas Event

Every year the Cancer Biology PhD program organizes a Christmas event for all its PhD students. This conventional social event is a wonderful way to meet, chat and get to know old and new PhD students in a non-scientific environment. Almost 85 PhD students participated in the Christmas dinner 2016. The cold winter evening was turned into a fun-filled bowling tournament at the Bowling west center. With some good wine keeping up the game spirit, initial ‘gutters’ lead to professional ‘strikes’ and friendly competition among the teams. Following a phenomenal bowling session, the players were treated with a delicious cheese fondue for dinner. With perfect prior arrangements in place, the students enjoyed the dinner and hospitality and left the place with pleasant memories.

CNZ Retreat 2017

The 7th Cancer Network Zurich retreat was organized together with the Cancer Biology PhD program and the URPP Translational Cancer Research from March 26-28, 2017. It was held at Hotel Seeblick, Emmetten, a beautiful location overlooking Lake Lucerne. We had seven keynote lectures highlighting recent advances in the field of cancer research. Eminent scientists were also invited for the cancer biology PhD program mini-symposium as well as the URPP translational cancer session. Every session included speakers selected by the CNZ steering committee from top-scoring abstracts. The talks were engaging and were followed by some stimulating discussions. Poster sessions held on both evenings, were very interactive with everyone sharing ideas and giving inputs. Prizes for the best presented posters were awarded to Andrej Besse, Hind Hashwah, Rodrigo Pena, Karina Silina and Daniel Zingg.