Dear Readers,

This is the sixth 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
Recent Publications by CB PhD Students

Hind Hashwah - Group Prof. Anne Müller

Our research elucidates a tumor suppressive role of CREBBP/EP300 in diffuse large B-cell lymphoma. We show that both histone acetyl-transferases control MHCII expression; hence their mutational inactivation promotes immune evasion. Loss of Crebbp also induces hyperproliferation of germinal center B-cells, predisposing mice to MYC-driven lymphomagenesis.

Inactivation of CREBBP expands the germinal center B cell compartment, down-regulates MHCII expression and promotes DLBCL growth

Hind Hashwah, Corina A. Schmid, Sabrina Kasser, Kattrin Bertram, Anna Stelling, Markus G. Manz, and Anne Müller

Abstract:
The genes encoding the histone acetyl-transferases (HATs) CREB binding protein (CREBBP) and EP300 are recurrently mutated in the activated B cell-like and germinal center (GC) B cell-like subtypes of diffuse large B cell lymphoma (DLBCL). Here, we introduced a patient mutation into a human DLBCL cell line using CRISPR and deleted Crebbp and Ep300 in cell GC B cell compartment of mice. CREBBP-mutant DLBCL clones exhibited reduced histone H3 acetylation, expressed significantly less MHCII, and grew faster than wild-type clones in s.c. and orthotopic xenograft models. Mice lacking Crebbp in GC B cells exhibited hyperproliferation of their GC compartment upon immunization, had reduced MHCII surface expression on GC cells, and developed accelerated MYC-driven lymphomas. Ep300 inactivation reproduced some, but not all, consequences of Crebbp inactivation. MHCIIm deficiency phenocopied the effects of CREBBP loss in spontaneous and serial transplantation models of MYC-driven lymphomagenesis, supporting the idea that the mutational inactivation of CREBBP promotes immune evasion. Indeed, the depletion of CD4+ T cells greatly facilitated the engraftment of lymphoma cells in serial transplantation models. In summary, we provide evidence that both HATs are bona fide tumor suppressors that control MHCII expression and promote tumor immune control; mutational inactivation of CREBBP, but not of EP300, has additional cell-intrinsic engraftment and growth-promoting effects.

Read full article here
PNAS Sep 5, 2017; 114 (36): 9701-9706

Johanna Diener - Group Prof. Lukas Sommer

To test whether CD271 is a regulator of melanoma phenotype switching, we engineered a doxycycline-inducible CD271 expression system. To mimic phenotype switching, we used this system to overexpress CD271 temporally in human xenograft tumors growing on immunocompromised mice. By doing so, we could show that transient (but not permanent) overexpression of CD271 lead to reduced proliferation and adhesion in vitro and to increased metastasis formation in vivo, supporting the role of CD271 in melanoma phenotype switching.

Mechanistically we found that on one hand the CD271 intracellular domain (ICD) regulates proliferation. On the other hand the interaction of CD271 with the neurotrophin receptor Trk-A upregulates cholesterol and lipid biosynthesis genes, which is crucial for CD271-mediated changes in adhesion. Interestingly, high expression of those cholesterol and lipid biosynthesis genes correlates with bad prognosis of melanoma patients, suggesting a potential role of disrupted cholesterol homeostasis in cancer development.

The low affinity neurotrophin receptor CD271 regulates phenotype switching in melanoma

Gaetana Restivo, Johanna Diener, Phil F. Cheng, Gregor Kiowski, Mario Bonalli, Thomas Biedermann, Ernst Reichmann, Mitchell P. Levesque, Reinhard Dummer & Lukas Sommer

Abstract:
Cutaneous melanoma represents the most fatal skin cancer due to its high metastatic capacity. According to the “phenotype switching” model, the aggressive nature of melanoma cells results from their intrinsic potential to dynamically switch from a high-proliferative/low-invasive to a low-proliferative/high-invasive state. Here we identify the low affinity neurotrophin receptor CD271 as a key effector of phenotype switching in melanoma. CD271 plays a dual role in this process by decreasing proliferation, while simultaneously promoting invasiveness. Dynamic modification of CD271 expression allows tumor cells to grow at low levels of CD271, to reduce growth and invade when CD271 expression is high, and to re-expand at a distant site upon decrease of CD271 expression. Mechanistically, the cleaved intracellular domain of CD271 controls proliferation, while the interaction of CD271 with the neurotrophin receptor Trk-A modulates cell adhesiveness through dynamic regulation of a set of cholesterol synthesis genes relevant for patient survival.

Read full article here
Nat. Com. 07 Dec 2017; 10.1038
Collaborative Science: Speeding up the process from bench-to-bedside

The Comprehensive Cancer Center Zurich (CCC ZURICH) has been recently established by the University of Zurich (UZH) and the University Hospital Zürich (USZ). It aims to bring together people from areas of basic scientific research, clinical care, and educational practices to create a prominent hub for cancer research in Zürich. Within the CCC ZURICH, the Cancer Research Center (CRC) came into operation early this year. The CRC will facilitate a joint research strategy exploiting resources beyond those available in a single research laboratory to unravel the complexity of cancer and to develop novel diagnostics and therapeutics.

One major priority towards this goal is to combine clinical and basic research taking place across different physical entities in Zürich. The CRC should catalyze this interaction and promote the exchange of resources and information. The current activities of the Cancer Network Zürich, such as the Joint Cancer Meeting, the biennial retreat, and the MSc and PhD programs will be integrated into the CRC. Both students and principle investigators (PIs) are encouraged to support these events to keep the community alive. Ideas and suggestions to increase the appeal of attendance are very welcome! Feasible possibilities could be to arrange an interactive video seminar between Irchel and the USZ or to alternate the location each month between campuses.

The effort of the CRC will be to enhance crucial collaborations to drive translational research and to accelerate the process towards innovative findings in different aspects of cancer research. To achieve these goals and to conduct research between multidisciplinary teams, competitive funding opportunities are on offer. Each year, five 2-year fellowships will fund projects affiliated with two groups from basic research and clinical fields. A panel of external renowned scientists will review and rate the applications, which will be judged based on two principal components: scientific merit and synergistic potential.

Young scientists are encouraged to apply! Young scientists could team up with 2 PIs to apply for the CRC fellowship for him or herself, where one of the PIs should be a member of CRC. For the first round of applications, fourteen proposals were submitted of which five promising projects will be selected for funding. For more information on the CRC and adverts for funding please check the CRC website. The next round of applications will be open on 15 Dec 2018.

From the perspective of a PhD student, we aspire for the CRC to provide a platform to receive feedback on individual projects from a consortium of experts in the field through active discussions, presentations and seminars. This will be especially useful for students looking for a more translational aspect to be integrated into their projects. Ideally, the CRC should also encourage collaborations at the PhD level, and provide advice on possible job opportunities for students at the end of their doctorates. Such possibilities in translational research that don’t directly fall under the academic criteria are hard to find or require the applicant to know a person working in the company of interest. Our concerns about implementation of the planned actions of the CRC can be mainly attributed to the fact that clinical and basic research take place in separate locations across Zürich. Lastly, we hope that funding tools will provide opportunities for scientists from newly established and perhaps not renowned scientific groups.

- Hannah & Hind (Information source: CRC website, last accessed: 08 Jun 2018)

How does the world see cancer?

We are wondering how different societies perceive cancer, and how this might impact the psychological well-being of cancer patients. What are available resources and how much should schools educate pupils about such major killers in our current day world? Continued on page 4....
Transferable skills courses: Opinions

Voice training and presentation skills

The voice training and presentations skills course is a transferable skill course provided by the UZH Graduate Campus. This course is taught by Janneke van Woerden and Michael Berndonner and aims to instruct students on how to design and deliver poster and power point presentations. The course is not only focused on how to successfully structure your poster or power point presentation but also on how to give a great oral presentation. I personally found the course one of the most helpful transferable skills courses offered by the university and I highly recommend it to every student.

During the two day course, we covered the most important topics of poster design and of successful oral communication. For that purpose, we first scrutinized the posters provided by other students then and analyzed our own speech patterns. I believe that, with this course, I immensely improved my oral communication and speech patterns, which was reflected immediately in my subsequent power point presentations. We further learned how to structure and give feedback and became aware of our posture during a presentation.

The organizers of the course were extremely kind and answer all questions with precision and relatable examples. All in all, you can expect to become aware of the best practices for poster and power point presentation, you will be given the chance to practice your speech while being aware of your body posture and what they can reflect.

- Ana

Starting a professional career in industry: Matching market needs and self-presentation

This course was offered for the Life Science Graduate School Zurich by Dr. Monika Clausen & Netzwerkpartner. It was structured such that 16 people took part, which allowed one-on-one interactions with Dr. Clausen. Students often worked in teams of four, and this allowed individuals to have a rich experience.

In addition to receiving personalized feedback about our application packages (CV and cover letter) from Dr. Clausen, we arranged mock-interviews within our four-people group. This was designed in a way that allowed each student to take turns in the three different roles. For instance, the first role would be the applicant, and hence the student is interviewed for a position of his or her choice, be it for academia or industry. The main points. In the second day, the topic was how to plan and write the time schedule and finances for the set goals in an efficient and modest way. My personal favorite was that they put a lot of accent on the minute details that can get the applicant important points in the grading system of the application.

All in all, I believe this course can be beneficial for any PhD student that started writing a grant proposal or is thinking of writing one in the near future.

- Anca

How does the world see cancer? Switzerland’s perspective

Cancer awareness in Switzerland is highly sponsored by different organizations such as Krebsliga, the Swiss Cancer Foundation, Cancer Support, Swiss Cancer League, Kinderkrebs and others. Besides subsidizing cancer research, the Krebsliga offers support to cancer patients and their families. As you might have noticed in public transportation, Krebsliga has various advertisements promoting healthy behaviors and offering different counseling and support systems to cancer patients. Generally, cancer in Switzerland is not a taboo subject and the fight against cancer is highly supported with funding for research, prevention and early diagnosis campaigns, patient support, and cutting edge treatments. The success of investing in cancer treatments is reflected in the fact that despite high cancer incidence, the survival rates in Switzerland are among the highest in the world.

This is the opinion of one of our members - now we would like to hear your view. How do you think society in your country perceives cancer with regard to quality of life of patients, prevention and therapy. Tell us what you think; take part in our next issue!
Whatever became of...

...Andreas Kyburz - Medical Science Liaison Oncology at MSD

1) Could you tell us in which group you carried out your PhD, and how you proceeded after obtaining the degree?
I did my PhD in the group of Prof. Dr. Anne Müller. I already started looking for a job a couple of weeks before my defense by checking the Internet for advertisements and by setting up job-alerts (e.g. on jobs.ch).

2) Could you give us a short description of your current position, including daily responsibilities?
I’ve started just a couple of weeks ago as a Medical Science Liaison (MLS) in Immuno-Oncology. Thus, I’m not yet able to give an extensive description. In general MSls have to establish networks with external key opinion leaders in their specific scientific field. They should engage in scientific discussion with physician and medical doctors about the product and disease they are working for to produce valuable insights for the company. However, the aim of these discussions should never be to commercially promote a product like in sales but to exchange scientific facts.

3) Why did this particular position appeal to you?
In my opinion this position is extremely appealing because it is very versatile with scientific exchanges between the clinics and research institutions. Every week might look different and due to the fast evolution of drugs in oncology, one continuously has to learn new things. And, of course, I like that it is tightly connected to clinical science/research (i.e. PhD knowledge can be used), but also brings you in touch with the business side of the pharmaceutical industry. Additionally, I like the collaborative part of it, which provides you with valuable insights into other interesting departments in industry.

4) Where did you apply for your current position and how did the application process looked like?
I applied via the online tool provided by the company. Everyone has to submit the application there. Subsequently, I had 3 interviews: 2 in person (1 with a case presentation) and one telephone interview.

5) Are you happy with your current position and to whom would you recommend it?
Yes, I am happy with the position. Sometimes I miss the “creative spirit” found at universities but in general, I consider myself lucky having found a position in a very welcoming working environment. I would recommend such a position for all graduates who enjoy communication and interaction, like to plan and organize and who are interested in clinical research.

...Simon Schäfer - Clinical Project Manager (CPM)

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 the group of Prof. Lukas Sommer at the Institute of Anatomy. After I graduated, I was looking for job opportunities outside of basic research. Since I could imagine myself working in many different fields, like clinical research, scientific writing, regulatory affairs or teaching biology classes, I was also applying to jobs in different fields.

2) Could you give us a short description of your current position, including daily responsibilities?
I work as a clinical project manager (CPM) in a non-profit organization in Berne. I am responsible for developing trial protocols and conducting clinical cancer trials. The job contains a lot of planning, organization and communication. My daily responsibilities include writing trial protocols, coordinating drug delivery to the hospitals, documenting safety events, updating pharmaceutical companies and supporting clinical research organizations (CRO). Therefore, I spend a lot of time writing emails and participating in telephone conferences.

3) Why did you choose this position?
Working for a non-profit organization allows independent clinical research without financial interests enabling exceptionally high data quality as well as patient safety. It was also crucial that the job contains many different, versatile and interesting tasks and is not much repetitive. Further, an important point to me was the team spirit and the working environment.

4) Where did you apply for your current position and how did the application process looked like?
A friend of mine was working in the same organization and sent me the job application. I applied online with my CV, motivation letter, records and diplomas and was happy to receive an invitation for the first interview. After two interviews, I was invited for a trial day in Berne and luckily received a positive feedback half of a week later.

5) Are you happy with your current position and to whom would you recommend it?
Yes, I am happy with the position. Sometimes I miss the “creative spirit” found at universities but in general, I consider myself lucky having found a position in a very welcoming working environment. I would recommend such a position for all graduates who enjoy communication and interaction, like to plan and organize and who are interested in clinical research.
1) Can you give us a brief overview of your career?
After my Master in Biochemistry and Molecular Biology at the ETH of Zurich I did a PhD in Immunology at the Swiss Institute of Allergy and Asthma Research (SIAF) in Davos. For my postdoc, I moved to Oslo, Norway, where I addressed the role of T helper cells in chronic lymphocytic leukemia (CLL), a B cell cancer. Unexpectedly, we found that the T helper cells – instead of attacking the CLL cells – supported them, as they support normal B cells. Motivated by this finding, I was eager to investigate, whether such a cancer-supportive functions of T helper cells can be found in other B cell malignancies as well. Thus, I moved to the Children’s Hospital Zurich to study the role of T helper cells in precursor B acute lymphoblastic leukemia.

2) When did you move to Zurich?
I moved to the Children’s Hospital Zurich in November 2013.

3) How is it to be a part of the cancer research community?
Interacting and collaborating with smart and reliable researchers is crucial in science, and I feel Switzerland is the place to meet such people. Thus, I consider it to be important to be part of it, not only for me, but also for my group members.

4) How many people are currently working in your lab?
Currently, there is one Postdoc, two PhD students, a medical student and three Master students working in my lab.

5) What is the main focus of your research?
We are interested in the mechanism by which T-helper cells and infectious pathogens like the Epstein-Barr virus or Plasmodium falciparum promote the pathogenesis of B cell malignancies such as precursor B acute lymphoblastic leukemia and Burkitt’s lymphoma. Many of the projects address the role of AID/APOBEC enzymes in the generation of tumorsic translocations and drug resistance, and the mechanisms that regulate their expression and activity. Such mechanisms may be targets for future therapies that aim to prevent malignant transformation or drug resistance.

6) What was your most memorable lab experience?
I was supervising a new Master Student and we were assessing our T cells under the microscope. Before looking at them, I explained her that if they would be activated as we expected, the would be big and “banana-shaped”. She looked through the microscope, then at me, with eyes wide-open and exclaimed “oh, yes, I see it!”. This enthusiasm and fascination of a young scientist (which in her case never ceased throughout her master thesis) delighted and encouraged me enormously.

7) What is the motivation that keeps you going?
I greatly enjoy mentoring PhD and Master students and addressing research questions together with them. To see that all group members work hard and support each other makes it easier for me to push through busy days or less interesting tasks. Furthermore, I’m very motivated by interesting or unexpected results, or if we manage to establish a new assay or technique that initially seemed to be unfeasible or hard to achieve.

8) Which advice would you give a fresh PhD student?
Follow your own scientific interests and be brave enough to try out your ideas, even if your supervisor tells you they won’t work. He/she may turn out to be right, but at least it was your own decision and you will learn a lot from it, which is - in my mind - the most important part of doing a PhD.

9) What is the last book you have read?
It was “Tørst” by Jo Nesbø (english title “The Thirst”). I like to read detective stories from this author, since they most often play in Oslo, the city where I have been living for some years. Furthermore, it is a good way to preserve my Norwegian!

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
This year the PhD student retreat took place in March in Ascona-Locarno, Ticino. The organizing team did an amazing job of bringing to this retreat, both impressive research presentations and fascinating talks from all across the field of cancer research. The keynote speakers were: (1) Dr. Ilaria Malanchi from The Francis Crick Institute, UK. She presented her lab’s research on the process of tumor initiation and metastasis formation. (2) Dr. Tilmann Bürckstümmer from Horizon Discovery talked to us about career options and a novel technique of introducing foreign DNA sequences in a genomic locus using the CRISPR-Cas9 system and (3) Dr. Nicola Aceto from the University of Basel. He showed us a novel technique to capture and measure circulating tumor cells and how crucial they could be for the development of metastasis-tailored therapy. Another well-organized part of this event was the oral and poster-presentation sessions, where we had a chance to showcase our work and present it to our peers. This allowed us to broaden our scientific network, exchange ideas and share experiences with specific methods and techniques.

Oral presentation winners: Christoph Umbricht, Pharmaceutical sciences, ETH, Zürich, Rexhep Uka, Oncology, University Hospital Zürich

Poster Presentation winners: Anika Trenner, Institute of Molecular Cancer Research, University of Zürich, Anna Stelling, Institute of Molecular Cancer Research, University of Zürich, Giulia Lucchiari, Institute of Experimental Immunology, University of Zürich, Marco Gualandi, Department of Oncology, University Hospital Zürich

To wrap up, this was an excellent student retreat that gave us an update on the most recent ideas and discoveries of our peers and keynote speakers whilst enjoying the sightseeing of the beautiful surrounding area.

- Anca