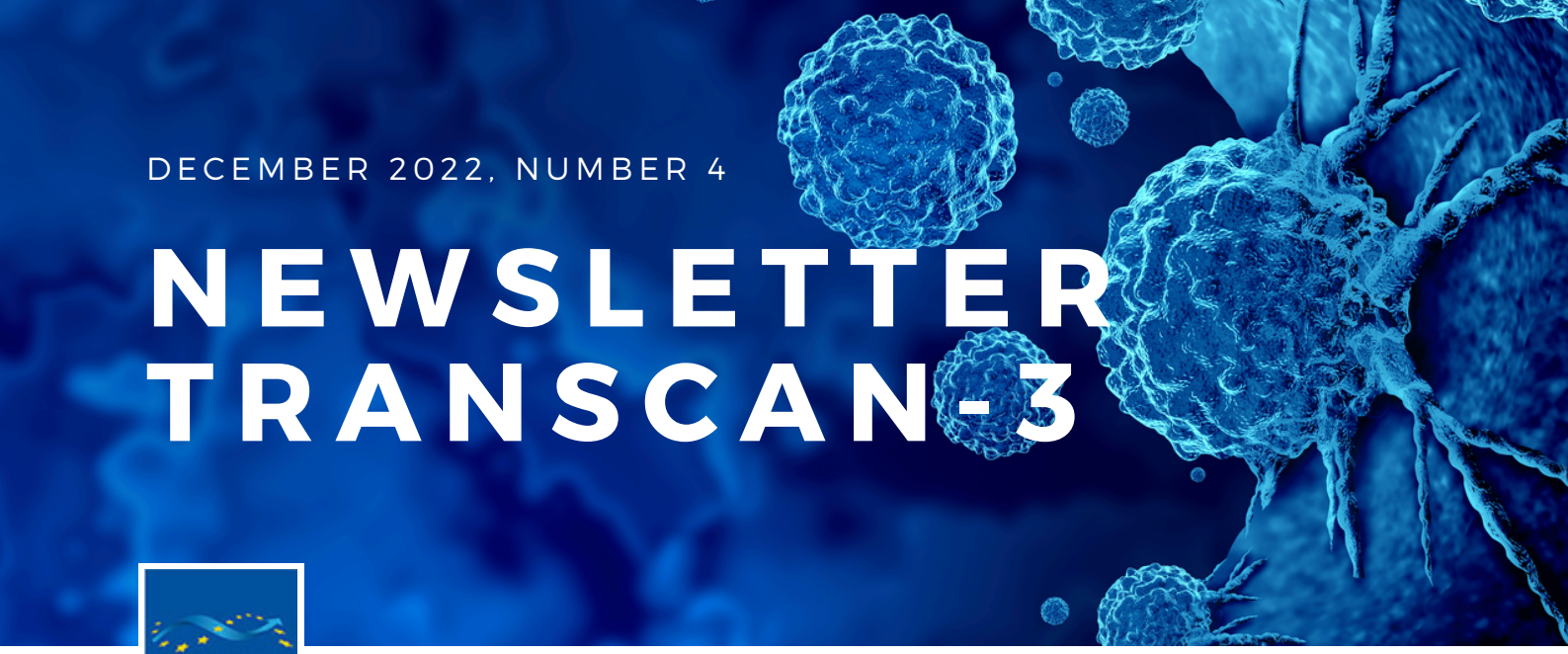

DECEMBER 2022, NUMBER 4

NEWSLETTER TRANSCAN-3

On behalf of the TRANSCAN-3 consortium, we are happy to send you the **4th newsletter**.
The TRANSCAN consortium is committed to support the career development of young researchers, either Ph.D. students or postdoctoral researchers. This new issue describes how TRANSCAN funded projects are an opportunity for two early career researchers: **Dr. Pinar Pir**, a young Principal Investigator partner in the iParaCyts project (co-funded call 2021) and **Dr. Sheng-Fang Su**, a young researcher that participated in the BeFIT project, (co-funded call 2014). Read the interviews here.
In addition, in spring 2022, TRANSCAN-3 launched the second Joint Transnational Call for proposals (**JTC 2022**) focused on "**Novel translational approaches to tackle the challenges of hard-to-treat cancers from early diagnosis to therapy**". Recently, the Call Steering Committee has selected 40 pre-proposals that are now required to submit full proposals by **15th December 2022, at 12:00 CET**. More information can be found here.
Most relevant **upcoming events and initiatives** promoted by TRANSCAN-3 partners are also listed in the newsletter.

Stay posted and don't miss any TRANSCAN-3 news and the project results, have a look at our official channels:

Enjoy reading!

An interview with young Principal Investigator, Dr. Pinar Pir*, partner in the iParaCyts project

"Evaluating the therapeutic potential of immunosuppressive paracrine cytokines in the tumor microenvironment of metastatic lesions", project funded under the co-funded Joint Transnational Call 2021 of TRANSCAN-3.

***Pinar Pir, Principal Investigator of the Pirism Lab,Department of Bioengineering, Gebze Technical University, Turkey**

Our consortium proposes the integrated study of immunosuppressive cytokines expressed in liver metastatic lesions. While most of the studies in immuno-oncology are focused on primary tumors, the majority of patients treated with immunotherapies suffer from disseminated metastatic disease and, in many instances, liver metastasis. Liver metastases are common, confer dismal prognosis, constitute a clear unmet medical need, and are strongly associated with resistance to immunotherapy. We will study 5 highly relevant cytokines (TGFβ, TNFα, IL8, LIF and GDF15) in liver metastasis. The reasons for this choice are: (a) Evidence for integrated regulation of this cytokine network; (b) the expertise of the members of the consortium; (c) inhibitory compounds against these targets are undergoing early clinical development in our institutions and serial biopsies from liver metastases are and will become available. We hypothesize based on preliminary data that these 5 paracrine cytokines are crucial to promote tumor escape from the immune system in liver metastases, with potential redundancies when considering them as therapeutic targets. Our aims are: (a) Epidemiology of the cytokines in human liver metastases. (b) Effect of the inhibition of the cytokines on tumor growth and the cancer immune response. (c) Study of the tumor immune landscape in patients treated with inhibitors of these cytokines in the context of clinical trials. Our studies will focus on patient-derived samples as well as syngeneic animal models of liver metastasis. Importantly, pre- and on-treatment biopsies from liver lesions in early phase clinical trials testing inhibitory compounds will be studied.

Our project will evaluate the 5 immunosuppressive cytokines as therapeutic targets inisolation or in potential synergistic treatment combinations, identify predictive biomarkers of response to the blockade of the cytokines, and discover novel therapeutic targets for the treatment of liver metastasis.

Project Coordinator:

- Joan Seoane, Fundación Hospital Universitario Vall d'Hebron – Fundación Privada Institut d'Investigació Oncològica de Vall d'Hebron (VHIO), Spain

Project Partners:

- Ignacio Melero, Fundación Instituto de Investigación Sanitaria de Navarra, Spain
- Bruno Ségui, Cancer Research Center of Toulouse -INSERM (Institut National de la santé et de la recherche médicale), France
- Jörg Wischhusen, University Hospital Wuerzburg, Germany
- Gianluigi Giannelli, Ente Ospedaliero Specializzato in Gastroenterologia "Saverio de Bellis", Italy
- Pinar Pir, Gebze Technical University, Turkey

1

How did you know about JTC 2021 TRANSCAN-3 call?

Although I was aware of the TRANSCAN-3 calls via announcement emails from TUBITAK (Editor's note: TUBITAK is the funding agency from Turkey, partner of TRANSCAN-3), I did not have collaborators to initiate a consortium myself, hence I never attempted to apply for these calls. A former colleague, Dr. Vera Pancaldi was already involved in the first stage of a project proposal to TRANSCAN-3 together with Prof. Bruno Ségui, and she noticed that a team working purely on bioinformatics could contribute to both project design and to the data analysis throughout the project. She introduced me to Prof. Ségui, we exchanged few emails about my potential contribution to the project, and eventually, I joined the consortium after meeting Prof. Joan Seoane and other consortium members.

2

What is the added value of the participation of an emerging group in TRANSCAN-3 projects?

As a computational biology group in a technical university, Gebze Technical University (GTU), we do not have access to Next Generation Sequencing (NGS) facilities or clinical samples. Without collaboration with hospitals and experimental groups, we cannot have access to any unpublished data, and therefore our work is confined to applying novel analysis methods to published data shared in the databases.

In Turkey, the use of NGS technologies is still expensive compared to other countries and local funding is limited to about 50K euros per project, hence even if we collaborate with hospitals and experimental groups, the volume of the data produced in our projects have a limited impact in the field. Taking part in a TRANSCAN-3 project will help us overcome most of these difficulties, the consortium will have a larger total budget towards our goal, we will have access to novel clinical data, and contribute to novel discoveries in the field. These opportunities will motivate the whole team and the outputs of this project will have a positive impact on their future careers.

As an emerging group, we have little experience in taking part in international projects. Although I worked in international projects as a postdoc previously, taking part in such a project as a Principal Investigator (PI) will allow me to gain expertise in leading a sub-team within a larger consortium. My group will also gain expertise in working with international researchers. Further, the outputs of this project will help us get wider recognition for our work and perhaps lead to future collaborations.

3

How do you think international consortia can help emerging groups to develop their careers?

The benefits of emerging groups can be in many ways. One would be the opportunity to take part in a project with a potentially big impact in the field, rather than working on smaller projects that will lead to smaller contributions. The students/postdocs in emerging groups usually have limited access to funds for training, but a consortium can provide them with opportunities to get training from other members of the consortium.

Finally, both the PI and the other group members can find the opportunity to extend their scientific network which may lead to future collaborations, even after decades. One example would be the collaboration between Dr. Pancaldi and myself, which goes back to the times when both of us were postdocs. We met in the EpiGeneSys Consortium in 2012, and although we never worked in the same institution, we always kept in touch, met up at conferences, and collaborated in organising joint workshops or applying to calls such as TRANSCAN-3. I believe that, taking part in such consortia will help my group members to build similar long-lasting and fruitful scientific networks.

4

How do you envision TRANSCAN projects' success in the patients' treatment?

TRANSCAN projects will allow consortium members to jointly collect samples from many types of cancer and produce data on these samples. The output of the projects will shed light on active molecular mechanisms of these cancer types, and lead to the proposal of drug targets and drug candidates to be tested. Eventually, the data will be publicly available, and other researchers will access to these data and apply their novel methods on the data to extract additional biological information. All in all, the whole field will be learning more on mechanisms of cancer and have novel drug candidates to be taken into clinical trials. Therefore, I believe that the new data and knowledge produced in TRANSCAN projects will lead to improved and perhaps personalized treatment options for patients in the near future.

5

How did you get interested in looking for solutions in cancer research?

I worked on yeast, bacteria and stem cells as a PhD student and a postdoctoral researcher in computational biology. In 2016, I was invited to take part in a collaborative project by Prof. Devrim Gözüaçık and Prof. Tunahan Çakır based in Turkey where the effect of cellular dormancy on the emergence of metastasis was to be studied in cell lines and mouse models. While working on the project, I was fascinated by the mechanisms involved in dormancy and I realized how important it is to understand these mechanisms and to prevent metastasis to be able to save lives. Since then, the majority of my projects focuses on better understanding cancer and its microenvironment. Sadly, many people I know are suffering from cancer and few of them passed away shortly after they were diagnosed with metastasis, including Dr. Andrew Sims, who was a colleague and collaborator since we were postdocs in Manchester, he worked on cancer himself. His loss motivated me even further to focus on cancer research.

This TRANSCAN-3 project will bring my work closer to translational medicine and perhaps will help save lives in the future. It feels like a new chapter in my career, for the first time I will be directly involved in the analysis of clinical samples together with experienced clinicians who already made a difference in the field.

6

Do you think the collaboration among different countries in this type of consortia will accelerate the transfer of results to the patient?

I do believe that these international collaborations will accelerate the transfer of results to the clinic as expertise from groups located in different countries can be synergistically integrated to produce more comprehensive outputs rather than confining the efforts to groups located in one institution or country. Outputs of a project with partners from multiple countries will be more effectively disseminated and followed up by more researchers or perhaps R&D companies, who will take the finding to the next stage of drug development.

7

How do you think TRANSCAN-3 can reach a higher number of emerging groups?

Joining a consortium is usually mediated by previous contacts, where mutual trust is already established. Hence the emerging groups would need such contacts to be able to join consortia built by more experienced researchers. If the PI of the emerging group has previously worked in a research group with many collaborations, having such contacts is perhaps much easier. But in some cases, the PI maybe changed their field of research recently or worked in groups with no collaborations; in these cases, they would have no existing contacts to help them find a consortium to join. I believe COST (European Cooperation in Science and Technology) actions provide good opportunities to meet new collaborators in the same field. Also, consortia such as EpiGeneSys does not provide any funding to most participants but provide the networking environment in a relatively informal setting. I personally find it difficult to meet people in conferences with hundreds of participants, but it is much easier to make contacts if there are only 30-50 participants. I think events with a focus on a specific field such as cancer research should be both encouraged and funded by funding bodies so that young PIs and group members can build their scientific networks effectively. It is crucial that travel grants for young researchers are available for attending such events. I am aware that online platforms are also very effective on building such networks without any financial burden. For instance, some of my students meet with new people on LinkedIn and start collaborating online on a project of their interest. But I still find face-to-face interactions and informal social settings more fruitful in building long-lasting collaborations. Perhaps, I am too old to be a 'young researcher' after all.

An interview with an early-career researcher, Dr. Sheng-Fang Su*, involved in the BeFIT project

"Patient-derived models for intratumor functional heterogeneity and its implications for personalized medicine", co-funded under the Joint Transnational Call 2014 of TRANSCAN-2.

***Dr. Sheng-Fang Su. Project-Appointed Assistant Professor, Graduate Institute of Oncology, National Taiwan University College of Medicine; YongLin Scholar, NTU YongLin Institute of Health, TAIWAN.**

Our "BeFIT" (Belgium + France + Italy + Taiwan) Team focuses on the study of the inter- and intra-patient heterogeneity, which represents the major driving force for drug-resistance, tumor recurrence, and metastasis. We hypothesize that the phenotypical heterogeneities of tumor and stromal cells may contribute to the adaptation of tumor growth under dynamic and stressful conditions of the tumor microenvironment (TME) via changing its malignant and survival potential, especially under therapeutic and growth stresses. To investigate the evolution of the inter-/intra-tumoral heterogeneity and benefit pre-clinical drug screening, we have established the primary cancer stem cells (CSC)/cancer-associated fibroblasts (CAF) co-culture system and patient-derived xenograft (PDX) models to mimic the TME both **in vitro** and **in vivo**. Here, we have identified several important key regulators of cancer plasticity and stemness, drug resistance, and immune checkpoints that are significantly modulated in tumor heterogeneity and evolution under the stress conditionings and could be a benefit to develop novel strategy for the anti-cancer precision medicine.

Project Coordinator:

- Pan-Chyr Yang, National Taiwan University College of Medicine, Taiwan

Project Partners:

- Cédric Blanpain, Interdisciplinary Research Institute (IRIBHM) Université Libre de Bruxelles, Belgium
- Patrick Mehlen, Cancer Research Center of Lyon, Centre Léon Bérard, University of Lyon, France
- Sandro De Falco, Institute of Genetics and Biophysics "A. Buzzati Traverso", Department of Biomedical Sciences, CNR, Italy

1

How do you think this project has advanced our knowledge about the disease (in concrete, about therapeutic resistance in cancer, a JTC 2014 topic)?

As a young scientist whose study focuses on translational research in tumor biology, I endeavor to integrate the genomic/epigenomic platforms on the patients-derived models, aiming to overcome the unmet needs in anti-cancer treatment. To our knowledge, tumor grows in and co-evolutions with the tumor microenvironment (TME) with a dynamic and heterogeneous property. The complexity of crosstalk between cancer cells/cancer stem cells (CSC) and the stromal niche leads to the difficulty in curing cancer. Our goal of studying the intratumor heterogeneity to explore the mechanisms/roles of cancer cell plasticity and cancer stemness on drug resistance and tumor recurrence well fit the aim of JTC 2014 TRANSCAN-2 at "Translational research on human tumor heterogeneity to overcome recurrence and resistance to therapy". By our ambitious teamwork using patient-derived models to mimic TME both **in vitro** and **in vivo**, this project could improve the understanding of the cue of intra-tumorous heterogeneity and help develop the personalized treatment for cancer patients.

2

What TRANSCAN-2 funding has meant to you to carry out / to be part of the project?

With the support of TRASCAN-2, I had the opportunity to work together with the BeFIT teammates, to share the enthusiasm towards science, which is fulfilling and beyond the funding.

3

How has the transnational collaborative aspect of the project contributed to project success?

“Be fit” our goal - the transnational collaboration of BeFIT team brings scientists and clinicians across countries together to study tumor biology, from bench work to the clinic, from basic mechanism approach and modeling to pharmaceutical applications.
It has sparked the chemistry interaction of brain-storming and open-minded thinking towards science. It is amazing what such transnational collaboration has given to us.

4

Additional comments.

To form a tacit and successful team to stimulate scientific collaboration is by no means easy. I would thus recommend a long-term programmatical project organization and a stable funding support that allow this transnational collaboration could continue in the future.

Full proposal stage of Joint Transnational Call 2022 of TRANSCAN-3

The JTC 2022 Call Secretariat has announced the outcome of the first JTC 2022 evaluation meeting that took place in Naples on October 26th and 27th, 2022. Based on the final ranking list that was established by the Scientific Evaluation Committee, 40 pre-proposals have been selected for the second stage and they are now required to complete the full proposal by 15th December 2022 at 12:00 CET.

Based on the successful experience in the JTC 2021, TRANSCAN-3 consortium decided to implement a widening process to increase the involvement of underrepresented countries also in the JTC 2022 (see Call Text, Section 10):

"After pre-proposal evaluation, the Call Steering Committee will decide on the final list of underrepresented countries for this step, which will be published in the TRANSCAN-3 website. To support the process, coordinators of successful pre-proposals will be informed about the possibility to benefit from inclusion of one team from an underrepresented country in their consortium and will receive the list of the funding organisations that adhere to the process. Coordinators willing to incorporate a new partner in their consortium will get in contact with the national contact person of the funding organisation concerned in order to:

1. Share a summary of their project to disseminate it to the most suitable research groups in the concerned country/region
2. Receive contacts and details of expertise of research groups that are interested in participating."

Therefore, pre-proposals can be enriched with the participation of new partners that will contribute to boosting the geographical impact of TRANSCAN-3 cancer research.

International initiatives supported by TRANSCAN-3 partners

ATTRACT

Five European anti-cancer funds (FC AECC, Spain; Anticancer Fund, Belgium; Fondation ARC, France; Kom op tegen Kanker, Belgium; and KWF Dutch Cancer Society, the Netherlands) are joining forces to stimulate international research on rare cancer drug development.

The focus of this joint international call, the ATTRACT Call, is on **late-phase(2/3)** collaborative, international clinical trials that aim to develop a better drug treatment for **rare cancers**. We encourage **researchers and clinicians** from **different countries** to join forces, share knowledge, and collaborate. Improving treatment for rare cancers as well as bringing drug development to the next developmental stage are two of the current target goals. Applicants from the **Netherlands, Belgium, France** and **Spain** are invited to submit collaborative proposals and are welcome to involve inclusion centers from other countries as well.

The call has an indicative budget of up to 12 million Euros and opens on **22nd November 2022**. The pre- and full proposals must be submitted through the electronic submission system no later than the exact application deadline of **31st January 2023** for the pre-proposal and **28th June 2023** for the full application.

For further information about the application, visit the following link: https://www.kwf.nl/en/attract.

The 2023 FC AECC Calls (Spain)

The Scientific Foundation of the Spanish Association Against Cancer (FC AECC) has launched the 2023 Calls. The objective is to support scientific talent and to fund excellent cancer research projects developed in Spain.

The Foundation aims at financing basic, translational, and clinical research through a variety of fellowships that cover PhD, Postdoctoral or MD/PhD salaries or grants for specific projects.

Information about the calls and deadlines can be found here: https://www.contraelcancer.es/es/area-investigador/ayudas.

The VISION project (Slovakia)

The Biomedical Research Center of the Slovak Academy of Sciences (BMC SAS) is coordinating the EU-funded VISION project, together with researchers of the TRANSCAN-2 NeXT project (JTC 2017), to promote strategies and initiatives to strengthen scientific excellence and innovation capacity for early diagnosis of gastrointestinal cancers. The following lecture has been organized by the VISION project:

- **February 8, 2023, invited lecture**

Radiomics and radiogenomics in cancer (**Dr. Carolina de la Pinta**, Radiation Oncologist, Ramon y Cajal University Hospital (IRYCIS), Madrid, Spain).

Information about the events and the registration form can be found here: http://vision.sav.sk/lectures.html.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 964264.