

DECEMBER 2021, NUMBER 2

NEWSLETTER TRANSCAN-3



As the end of the year 2021 is approaching and a new year is anticipated, we are happy to send you the **TRANSCAN-3 2nd Newsletter**. This issue of the newsletter opens with an interview with Prof. Walter Ricciardi, Chair of the EU Cancer Mission Board, who provided insights on the EU Cancer Mission and the current and future synergies with TRANSCAN-3. Do not miss his vision on how TRANSCAN-3 contributes to advances in translational cancer research, in alignment with the priorities of the EU Cancer Mission, for the benefit of patients, society and healthcare systems.

In addition, we are pleased to share with you the **achievements made by two projects funded under TRANSCAN-2 (EU co-funded call, JTC2014)**, which exemplify how advanced knowledge on tumor heterogeneity and molecular mechanisms linked to therapeutic resistance may be translated into clinical practice for the benefit of cancer patients.

Do not miss any of the fascinating **success stories** included in this newsletter and the perspective of early-career researchers involved in these projects:

- Overcoming Neuroblastoma Tumour HETerogeneity, Resistance and RecurrAnCe - ONTHETRRAC
- Clinical utility of tumour heterogeneity in triple negative breast cancer and high-grade serous ovarian carcinoma for prediction of therapy response - TH4RESPONS

Enjoy reading the newsletter!

A special interview with Prof. Ricciardi



1

How does TRANSCAN-3 contribute to advances in translational cancer research for the benefit of patients?

The Funding Agencies, which are part of the TRANSCAN-3 Consortium, have provided, and are still providing, important investments to increase the knowledge on this burdening disease, bringing advanced diagnostics and therapeutic solutions to patients while contributing to raise the awareness among the European policy makers on the importance of investing in cancer research.

2

How are TRANSCAN-3 goals aligned with the priorities of the EU Cancer Mission

The [EU Cancer Mission](#) has already approved a series of overarching objectives, including 'Understanding Cancer', 'Preventing what is Preventable', 'Optimizing Diagnostics and Treatments', 'Supporting Quality of Life' and 'Ensuring Equitable Access', to be sought by reinforcing and maximizing the already existing activities and avoiding dispersion of what is currently being carried out. TRANSCAN-3 has fully demonstrated to be in line with these goals and keeps providing scientific ground to all of them.

With respect to the future evolution of TRANSCAN-3 through a European Partnership, synergies can be leveraged: nowadays, within the European Commission's Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases (SGPP) there is a working-group on cancer that is periodically discussing these aspects. The TRANSCAN-3 Consortium should engage with the Member States and delineate the importance of such partnership at a European level, while highlighting the complementarity with the other running activities.

3

What should European citizens expect from the EU Cancer Mission?

European citizens will benefit from several expected tangible results: besides the investments on cancer research, this Mission is focused on advancing the diagnostics and treatments of cancer, while reducing inequalities in healthcare. Another priority is the valorization of health data: in this perspective, the EU Cancer Mission is fully committed to reduce health data fragmentation within regions and Member States and ease a smart use of this data to create value for patients and citizens.

4

What should European researchers expect from the EU Cancer Mission?

The Mission has launched a Coordination and Support Action (CSA) called UNCAN.eu, with the objective to use existing, relevant research infrastructures and invest in the development of models and technologies to interrogate the interactions of poorly understood cancers and their host. This will translate into more resources for advancing European researchers' work and careers.

In parallel with the implementation of UNCAN.eu, the Member States and the regions have created national mirror groups in order to locally replicate what is being generated and, therefore, amplify the outcome of the UNCAN.eu. More topics are to follow in the Mission work programme reflecting the other objectives (see above).

5

Where do you see potential synergies between TRANSCAN-3 and the EU Cancer Mission?

The UNCAN.eu CSA is already an actual initiative where we expect collaboration between TRANSCAN-3 and the Mission. Other initiatives where TRANSCAN-3 brings a valuable contribution are [Europe's Beating Cancer Plan](#), [European Health Data Space](#) and [EU4Health plan](#).



TRANSCAN-2 SUCCESS STORIES

Projects funded under the EC co-funded Joint Transnational Call 2014 (JTC 2014)

“Translational research on human tumour heterogeneity to overcome recurrence and resistance to therapy”

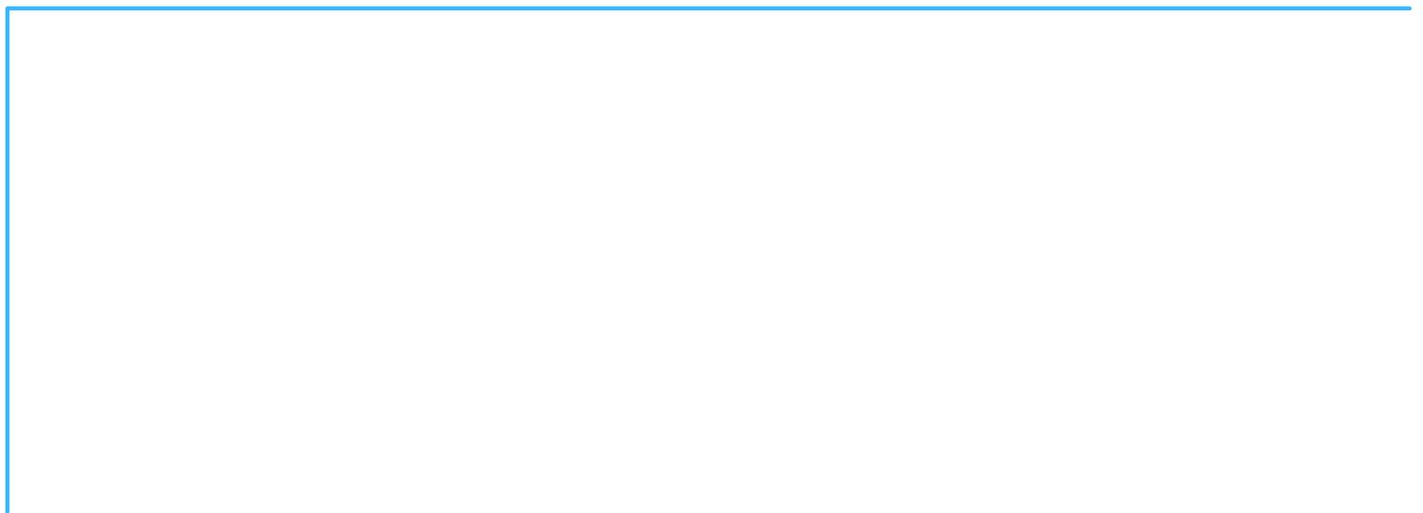
In January 2015, TRANSCAN-2 launched the first call for proposals with the aim to support innovative and ambitious collaborative projects providing a better understanding of tumor heterogeneity to improve the efficacy of cancer treatments and overcome therapeutic failure and drug resistance.

A total of **16 transnational** projects, from 85 research groups, were selected for funding with a total investment of 17.3 million Euros. More information is available [here](#).

The following two success stories are examples of how some of these projects advanced knowledge on tumor heterogeneity and molecular mechanisms linked to therapeutic resistance, which may be translated into clinical practice for the benefit of cancer patients.

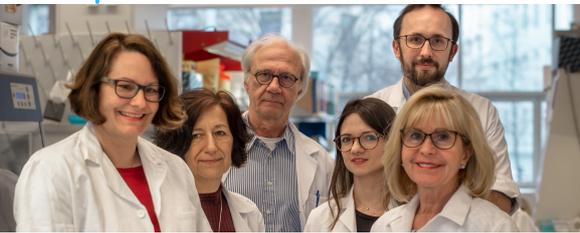
The story of each project includes a short interview with one of the young scientists who were involved in these vast projects, giving their perspective on the scientific contribution and collaborative aspects of the project and the TRANSCAN-3 funding opportunity. Furthermore, the sustainability of the investment and the research outcomes is presented by the fact that both projects continued and resulted in additional collaborative research, which was chosen to be further funded in other joint transnational calls.

Taking together the results, outcomes and sustainability of these research projects funded by TRANSCAN-2 and the EU, one can recognise the value of funding multinational collaborative translational cancer research and the impact of TRANSCAN-2 on the cancer field.



SUCCESS STORY 1

Overcoming Neuroblastoma Tumour HETerogeneity, Resistance and RecurrAnCe- ONTHETRRAC



Sabine Taschner-Mandl, Drs. Inge e Peter Ambros, Polyxeni Bozatzl, Fikret Rifatbgovic, Ruth Ladenstein - CCRI, Austria



Gudrun Schleiermacher, Inst. Curie, France



Frank Westermann, DKFZ, Germany



Angelica Eggert, Charité, Germany



Frank Speleman, Ghent Univ., Belgium

ONTHETRRAC has uncovered new aspects of tumor heterogeneity in the childhood cancer neuroblastoma, that are important for accurate diagnosis, prognosis and for overcoming treatment resistance. This collaborative transnational project, supervised by Drs. Inge and Peter Ambros and Dr. Sabine Taschner-Mandl, CCRI, St. Anna Children's Cancer Research Institute, Vienna, together with research partners from the Charité Berlin, the Institut Curie in Paris, the University of Ghent and the German Cancer Research Center in Heidelberg allowed insights into the role of tumor cells and molecular markers in biopsies (solid and liquid), and provided clinical diagnostic tools and recommendations that are now implemented in the new European high-risk neuroblastoma trial protocol.

Neuroblastoma remains a deadly disease for 60% of high-risk patients. Existing molecular classifiers/drug targets stem from single biopsies of bulky tumors, but this simplified view of neuroblastoma homogeneity is inappropriate. Intra-tumor heterogeneity must be taken into account for predictive biomarker identification. ONTHETRRAC has assembled an international expert team in neuroblastoma molecular genetics and clinical research. The ONTHETRRAC team has invested cutting-edge omics and liquid biopsy technologies to develop strategies overcoming intra-tumor heterogeneity-based sampling inaccuracy and support in-depth analysis of clonal evolution of therapeutic targets and predictive biomarkers. The research team has demonstrated genomic and proteomic heterogeneity between patients, within tumors and between tumor and relapse. Heterogeneous molecular markers and key oncogenic drivers of neuroblastoma, such as amplification of the MYCN gene, ALK alterations and mechanisms that enable the maintenance of telomeres, the activation of telomerase as well as alternative lengthening of telomeres (ALT) were found to be of prognostic relevance. ONTHETRRAC also provides clinically relevant recommendations on how to monitor disease course on the sub(clonal) level by circulating tumor DNA analysis in liquid biopsy of blood and bone marrow samples, taking spatial and temporal intra-tumoral heterogeneity into account.

The resulting diagnostics and monitoring guidelines now guide new targeted therapeutic interventions, e.g., ALK inhibitor treatment, in the next European high-risk and relapse neuroblastoma trial protocols to target the most aggressive and resistant tumor clones and to detect relapse early.

MEET DR. GERBER, AN EARLY-CAREER RESEARCHER INVOLVED IN THE ONTHETRRAC PROJECT

Teresa Gerber carried out her PhD thesis-related work at CCRI, St. Anna Children's Cancer Research Institute, and successfully completed her PhD in 2020.

She recently published a [paper](#) on the assessment of blood sample handling conditions for liquid biopsy analyses.



How do you think this project has advanced the knowledge about the disease?

Liquid biopsies are the analysis of molecular markers circulating in body fluids, such as peripheral blood. For example, DNA fragments released by tumor cells can be analyzed to gain genomic information from the tumor. Further, liquid biopsies can be used to track genomic markers at certain points to monitor the disease course.

In our study we provide blood sample handling guidelines for the harmonization of pre-analytical processes to ensure high sample qualities. These guidelines are highly relevant, because in multi-center studies, blood samples are sent between institutions within Europe to perform different analyses.

I have then focused on the investigation of how circulating genetic markers in blood and bone marrow change over time and how they compare to those found in the primary tumor.

Because of ONTHETRRAC we now know that analyzing only one tiny biopsy taken at the time point of diagnosis is not sufficient, because neuroblastoma is a highly heterogeneous disease. We also learned which genetic markers and/or therapeutic targets we need to capture with our diagnostic assays. And we found that liquid biopsy analyses can help to identify more aggressive, treatment-resistant subclones, track them and use this information for detecting relapse at an early time point.

How did TRANSCAN-2 funding assist you in carrying out this project?

TRANSCAN-2 funding has enabled me to carry out my PhD at St. Anna Children's Cancer Research Institute, embedded in the ONTHETRRAC consortium, a network of excellent European researchers. The funds also allowed me to participate in Consortium meetings and international conferences, e.g., the 'Advances in Neuroblastoma Research' congress, where I presented my work and engaged in scientific discussions. This was important for my training as PhD student, but also for my current career in clinical research.

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

Pediatric cancers affect more than 100,000 patients a year in Europe, yet they are rare (some ultra-rare) diseases. Therefore, one reason why transnational collaboration is so important is because it enables us to collect a sufficient number of samples to draw statistically meaningful conclusions, for example about the prognostic relevance of even sub-clonal mutations. Thereby, we already established harmonized standards and implementation at the European level. Another reason why transnational collaboration is relevant is that it enables the combination and efficient exchange of very specialized expertise. This is a prerequisite for high-quality research.

Any additional comments you would like to add?

I find it particularly encouraging that several members of the Consortium (Charité, CCRI and Curie) together with other European partners will build on the network and findings obtained within ONTHETRRAC, in the scope of the project LIQUIDHOPE, which received funding under the TRANSCAN-2 initiative.

SUCCESS STORY 2

Clinical utility of tumour heterogeneity in triple negative breast cancer and high-grade serous ovarian carcinoma for prediction of therapy response – TH4RESPONS



Manfred Dietel
Charité – Universitätsmedizin
Berlin, Germany



Giuseppe Viale
European Institute of Oncology,
Italy



Eliane Taube
Charité – Universitätsmedizin
Berlin, Germany



Violeta Serra
Valld'Hebron Institute of
Oncology, Spain



Alexandra Leary
Gustave Roussy Cancer Center,
France



Nanna Monjé
Charité – Universitätsmedizin
Berlin, Germany

Triple negative breast cancer (TNBC) and high-grade serous ovarian carcinoma (HGSOC) share many molecular and morphological similarities. The aim of the collaborative transnational TH4RESPONS project, coordinated by Dr. Dietel (Germany) together with research partners from Spain, Italy and France, was to analyse both tumour entities according to molecular and proteomic heterogeneity focusing on primary and recurrent tumour samples and the clinical impact.

To analyze this question, we formed an interdisciplinary consortium with clinical, pre-clinical, pathological, and bioinformatics expertise and a large experience in translational research in ovarian and breast cancer. During the course of the TH4RESPONS project the exchange of sample cohorts and technologies has been discussed and implemented. A strong and continuous cooperation and an extensive scientific exchange between partners has facilitated collaboration and generated interesting results. The work was divided up into work-packages which have procured 12 peer reviewed articles and 11 presentations at conferences dedicated to experts. Analyzed scientific problems include immune infiltration, homologous recombination / RAD51, inter-tumor and intra-tumor heterogeneity in ovarian and breast cancer. An unforeseen obstacle of course presented with Corona pandemic. After a short phase of deceleration, the TH4RESPONS project recuperated with tenacity and adaption to new requirements.

A strong network has been established with cross-validation, transfer of material and various technologies based on high-ranking scientific argumentation, which continues beyond the project and fosters continuation in new projects. As an example, an ERA PerMed grant has been obtained for the continuation of the RAD51 clinical validations (ERAPERMED2019-215).

PERSPECTIVE OF THE EARLY-CAREER RESEARCHER NANNA MONJÉ

Nanna Monjé is carrying out her medical doctoral thesis about differential genetic and immunohistochemical expression in primary and recurrent ovarian cancer tissues as well as prognostic implication at the Institute of Pathology, Charité University Hospital Berlin. Cooperation AG Taube / AG Sers.



How do you think this project has advanced our knowledge about the disease in concrete, about therapeutic resistance in cancer?

While the TRANSCAN-2 project has investigated therapeutic resistance in different types of cancer, the main goal of my project was to analyze the temporal tumor heterogeneity in primary and relapsed high-grade serous ovarian carcinoma (HGSOC) to further elucidate the mechanisms of recurrence and poor survival in this tumor entity. We found a prognostic marker set associated with heterogeneity and tumor recurrence, which might have clinical relevance in the future. The proteins in our set can be assigned to different pathways like extracellular-matrix-organization or cancer-metabolism, showing the high complexity and variability

of mechanisms involved in the tumor heterogeneity of HGSOC. Our project further reiterates the importance of translational tumor research for these tumors. Still many open questions exist, which lay the foundation for further research in this field especially in transmission to clinical studies. Collaboration between different scientific disciplines should be continued to improve the outcome of the patients, which is of utmost urgency given the still low survival rates.

What has TRANSCAN-2 funding meant to you?

When I became part of the project in 2019, I had just finished the first three years of my medical studies and was very interested in translational tumor research. Therefore, I applied for a position as a medical doctoral student at the Institute for Pathology at Charité Medical University in Berlin. Even if I could not immediately understand the project in its full scope, it seemed like an intriguing opportunity to directly apply my prior medical knowledge and deepen my scientific experience. In retrospect, doing the project not only impacted me personally and scientifically, but it increased my understanding of high-grade serous ovarian cancer. As a young medical student TRANSCAN-2 funding gave me the chance to concentrate on research and pursue my scientific interests. More than that I was able to benefit from important preliminary work that had already been done at the beginning of my research year, so that I could start my project based on preparations by the transnational interdisciplinary consortium. As a working group, it gave us the opportunity to purchase necessary resources, such as sequencing material, highly experimental antibodies for immunohistochemistry and professional medical technical assistance.

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

In addition to the translational orientation of the project, the transnational collaboration was one of the most helpful aspects for the success of the project. As an early-career researcher, it is of great importance for your own progress to be able to learn from more experienced scientists. Thanks to our European partners, I not only had this opportunity within the framework of my colleagues at our institute in Berlin but was also able to benefit from a transnational exchange of ideas. In the context of my subproject, the physical exchange possibilities were unfortunately somewhat limited, mainly because of the coronavirus pandemic. However, our European partners in France and Spain worked closely on the same tumor entity. We also had a high methodological overlap with the Italian consortium partners. Therefore, stimulating scientific meetings paved the way for our local work and shaped my personal understanding of good scientific cooperation.

International initiatives supported by TRANSCAN-3 partners

Do not miss any of the initiatives and activities carried out by
TRANSCAN-3 partners to support researchers and cancer research in
Europe and beyond!

Fondation ARC for Cancer Research (France)

Created in 1970, the **Fondation ARC Léopold Griffuel Award** from the Fondation ARC is one of the most important prizes in the field of cancer research in Europe. With a total value of 300,000 EUR divided into two categories (Award for Basic Research & Award for Translational and Clinical Research), it rewards every year internationally renowned researchers whose work has led to a major breakthrough in cancer research.



The **49th Fondation ARC Léopold Griffuel Prize** honored three prestigious international researchers for their scientific achievements. Michael Taylor and Stefan Pfister received the basic research award for their contribution to the molecular understanding of pediatric tumors and their clinical management. In translational and clinical research, Hiroyuki Mano won the award for his work in identifying a new form of lung cancer (ALK-rearrangement) and for his contribution to the development of an effective treatment. Due to the health crisis, the awards were virtually given and the video with English subtitles is available [here](#).

The **50th Fondation ARC Léopold Griffuel Award** will be awarded at an official ceremony on **April 5th, 2022, in Paris**.

Since its creation, 58 researchers from 14 different countries and from the most prestigious international research institutions have received the awards.

For further information, visit the following [website](#).

MSCA Seal of Excellence : Fondazione Regionale per la Ricerca Biomedica (FRRB), Lombardy (Italy)

Fondazione Regionale per la Ricerca Biomedica (FRRB) is funding biomedical research projects under the **Call "FRRB MSCA Seal of Excellence"**. The call was aimed at funding research projects presented in response to the European programme Marie Skłodowska-Curie Actions (MSCA) Individual Fellowships, specifically European Fellowships (IF-EF) which have been awarded the Seal of Excellence in the call MSCA-IF-2019.



The Seal of Excellence is a quality label awarded to project proposals submitted to the EU's Research and Innovation funding programme Horizon Europe and the previous Horizon 2020, which were judged to deserve funding but did not get it due to budget limits. The Seal of Excellence recognises the value of the proposals and helps other funding bodies, such as FRRB, take advantage of the Horizon 2020 evaluation process.

In 2021, the FRRB has launched the second edition of the call to fund “Seal of Excellence” projects in response to the call MSCA-IF-2020. Among the approved projects, there are two cancer research projects: one focused on the use of radiotherapy for head and neck cancer and prostate cancer, and the second one focused on the identification of new targets for the treatment of ovarian cancer. The final list of funded projects can be found [here](#).

For more information about this programme and the second edition, please visit the following [website](#).

The World Cancer Research Day: The Scientific Foundation of the Spanish Association Against Cancer (FCAECC), (Spain)



The World Cancer Research Day (WCRD), promoted by the Spanish Association Against Cancer (AECC) together with other cancer international organizations, is celebrated every year on September 24th to emphasise the high value of cancer research to improve treatment and outcomes for cancer patients.



To commemorate the **WCRD 2021**, last September 22nd the event **CANCER RESEARCH WORKS: IMPROVING CANCER PATIENTS' SURVIVAL WORLDWIDE** took place, where six internationally renowned experts in the field of oncology and cancer research discussed priorities and strategies to enable research results to improve survival and quality of life of cancer patients.

The event was held under the auspices of Queen Letizia of Spain, Honorary President of the Spanish Association Against Cancer (AECC) and the FCAECC and moderated by Dr. Julie R. Gralow (Chief Medical Officer and Executive Vice President of the American Society of Clinical Oncology (ASCO)). The panelist was composed of:

- Dr. David Tuveson, President of the American Association for Cancer Research (AACR)
- Dr. Clarissa Mathias, President of the Brazilian Society of Clinical Oncology (SBOC)
- Dr. Anil D'Cruz, President of the Union for International Cancer Control (UICC)
- Dr. Joan Seoane, Secretary General of the European Association for Cancer Research (EACR) and Director of Translational Research at the Vall d'Hebron Institute of Oncology (VHIO)
- Dr. Abubakar Bello, President of the African Organization for Research and Training in Cancer (AORTIC)
- Dr. Hong Gwan Seo, President of the National Cancer Center of Korea (NCCK). Dr. Seo was unable to join the live event, but he provided a video on the actions taken by South Korea since establishing its national cancer control plan 26 years ago to improve cancer control and survival rates from 43% to 70.4%.

During the discussion, participants shared their experiences about current challenges in cancer research and looked at strategies to promote clinical results and reduce the huge disparities that exist in cancer survival rates between regions across the globe.

You can find the recording of the event [here](#) and information about the WCRD initiative on the WCRD [website](#).

The VISION project (Slovakia)

The EU-funded VISION project is devoted to strengthening scientific excellence and innovation capacity for early diagnosis of gastrointestinal cancers. Slovakia ranks third for the incidence of colorectal cancer and is the sixth highest in the incidence of pancreatic cancer.



Strategic partnerships between Slovakia and European experts, allowing the transfer of knowledge and research ideas, sharing of know-how, expertise and best practices, together with the implementation of cutting-edge technologies, will contribute to the enhancement of high-quality translational cancer research in Slovakia, particularly gastrointestinal cancer. Furthermore, the VISION project aims to accelerate the personal and professional development of early-stage researchers and medical doctors, to increase the quality of education at universities, mainly medical and natural science faculties as well as to increase public awareness of cancer and the importance of prevention. Researchers from the **TRANSCAN-2 NeXT project (JTC2017)** are involved and contribute to overcoming existing gaps in oncology research and to support the involvement of early-stage researchers through the networking of **Biomedical Research Center of the Slovak Academy of Sciences (BMC SAS)** activities at the international and national levels.

Information about upcoming events and trainings can be found here: [invited lectures](#) & [trainings](#).

SAVE THE DATES! Upcoming cancer research events

Seed and Soil: In Vivo Models of Metastasis 25–26 January 2022

This is the 3rd joint European Association for Cancer Research (EACR) and Metastasis Research Society (MRS) Conference on Seed and Soil: In Vivo Models of Metastasis. This conference will focus on current knowledge on tumor, stromal, and metabolism-centred mechanisms promoting metastasis formation and how to translate scientific discoveries on metastasis into patient benefit. The target audience ranges from master's students to established PIs who have a keen interest in gaining knowledge about molecular mechanisms behind metastasis formation. More information [here](#).

IECC 2022. Tumor Microenvironment Heterogeneity in Cancer Progression: Challenge or Opportunity 14–16 February 2022

The 2nd International Electronic Conference on Cancers (IECC 2022) will focus on the translation of basic science understanding of the tumor microenvironment and its dysregulation in cancer to its therapeutic exploitation. It will bring together experts in basic, translational and clinical research to discuss the current research and the opportunities and obstacles that lie ahead in the field. More information [here](#).

EMBO Workshop. The many faces of cancer evolution 20–22 May 2022

This EMBO Workshop will bring together an interdisciplinary community of scientists with the goal of facilitating discussion and collaborations around genetic and non-genetic mechanisms of cancer evolution. The primary objective is to expand the current genetic-centric view with a mechanistic perspective centred around transcriptional and epigenetic alterations. More information [here](#).

