The Pezcoller Foundation

Journal

Summary

News from the
Pezcoller Foundation Word

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Picture on front page:
James P. Allison, *Pezcoller Foundation Award winner in 2015, Nobel Laureate in Medicine in 2018*

November 2018 Editorial

We can open this issue with a very exciting news: the important increase of the number of the Pezcoller Foundation's awardees winning also the Nobel Prize.
J. Allison becomes Nobel laureate in 2018 after Paul Nurse (Pezcoller 1995 - Nobel 2001), Mario Capecchi (Pezcoller 2003 – Nobel 2007), Elizabeth Blackburn (Pezcoller 2001 – Nobel 2009). He was the winner of the Pezcoller Foundation-AACR International Award for Cancer Research in 2015 with the following motivation: a world-renowned cancer immunologist who has made seminal discoveries in basic immunology; these discoveries established a new paradigm in basic cancer immunologic research that has also led to the development of a new class of immunologic anticancer therapeutics. Allison's discovery and elucidation of the cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) T cell signaling pathway and the development of the inhibitor of this pathway, ipilimumab (Yervoy) has been approved by the FDA for the treatment of malignant melanoma in March 2011.
We congratulate again our new Nobel winner and at the same time we are deeply confident that the number of our prestigious candidates will soon be increased.
On May 19th, the 2018 Pezcoller Foundation – AACR International Award for Extraordinary Achievement in Cancer Research was solemnly awarded in Trento to Tony Rex Hunter for his important discovery of tyrosine kinases (1975) which has led to proven success in the usage of cancer drugs that target disease-causing tyrosine kinases. Hunter, who had given three outstanding lectures in Chicago at the AACR Annual Meeting, at the University of Padova and at the University of Trento, received the award in the Teatro Sociale from the President of the Pezcoller Foundation Galligioni. He spoke about his life, about his constant scientific curiosity and, with appreciable fairplay, of some unpredictable circumstances at the origin of his discovery.
Another important event has been the agreement between Pezcoller Foundation and MUSE, the important museum of science designed by Enzo Piano in Trento. This agreement has been focused in a conference held by the winner of the Pezcoller Foundation-EACR Cancer Researcher Award. Aiming to celebrate academic excellence and achievements in the field of cancer for young European researchers. President Galligioni had awarded Jan

Gios Bernardi, President Emeritus remembers the founder of the Foundation during the Award Ceremony.

Korbel in Amsterdam in July 2018. He has been selected among 20 candidates for his achievements as interdisciplinary scientist working at the interface of human genetics and computational biology. Korbel, in spite of his young age, has become a leading figure in the cancer genomics field.
The lecture delivered by Jan Korbel on Convergence Science was held In the Main Lobby of the MUSE and attracted a good number of participants for its interesting subject.
In June 2018 the 30th Pezcoller Symposium "Overcoming The Innate Resistance of Cancer to Therapy" took place in Trento and was opened by Harold Varmus, Nobel Laureate in 1989, who gave the Enrico Mihich Lecture. The critical review of this Symposium by Massimo Loda and Michelangelo Fiorentino will be reported in the next pages.
We also remember that the Pezcoller Foundation, with the organizational support of SIC (Società Italiana di Cancerologia), granted two biennial fellowships for the coming years 2019-2020. The two fellowships, in memory of Ferruccio-Elena Bernardi and Alice Triangi were awarded to Candida Vitale of the Division of Hematology of the University of Torino and Lorenzo Stramucci of the National Cancer Institute "Regina Elena" of Roma.
During the 60th SIC Congress in Milano the two previous awardees of the same Fellowships, Annalisa Lonetti and Mattia Boeri, presented the results of their researches.
The focus and goals of the 31st Pezcoller Symposium are on the last page. This Symposium will be held in Trento on June 17-18, 2019 titled " Cancer as a Corrupted Tissue"

Gios Bernardi MD
Editor

2018 Pezcoller Foundation–AACR International Award for Extraordinary Achievement in Cancer Research

Professor Hunter has held two scientific lectures in Italy: one at the University of Padova and the other at the University of Trento.

Award Ceremony Speech at the Teatro Sociale of Trento on May 19, 2018

……..”The formative step in my career was when I took a two-year break from my college fellowship to join Walter Eckhart’s lab at the Salk Institute in La Jolla as a Research Associate in 1971. My first wife, Pippa Marrack, a graduate student in Alan Munro’s lab, had arranged to do a postdoc with Dick Dutton, an immunologist in the Department of Biology at UCSD across the street from the Salk, and Alan, who had done a one year sabbatical at the then brand new

Salk Institute in 1966, had suggested that I join Walter's lab. Walter was using polyoma virus, a small DNA tumor virus that causes cancer in rodents, as a cancer model in the hope it might give insights into how normal cells become cancer cells. Once I arrived at the Salk, I began to inveatigate how polyoma virus replicates its DNA genome with another postdoc on the lab. By the end of my two years, Pippa and I had split up, and I returned to Cambridge alone for the final year of my fellowship, while she stayed in the US (she also became an FRS!). Once back in Cambridge in 1973, I started working on protein synthesis again and began applying for faculty jobs. Both the Department of Biochemistry and the Imperial Cancer Research Fund (ICRF) in London turned me down (even though I had published three Nature papers and two JMB papers, among others), but luckily the Salk Institute, which was only 7 years old at the time, had just begun to appoint its first group of Assistant Professors. I had been offered one of these positions (without any interview!) before I left, and in the end with no job in the UK in sight I returned to California, where I started as an Assistant Professor in 1975, and started working on tumor viruses again. I have been at the Salk Institute ever since, and don't for one minute regret leaving the UK!

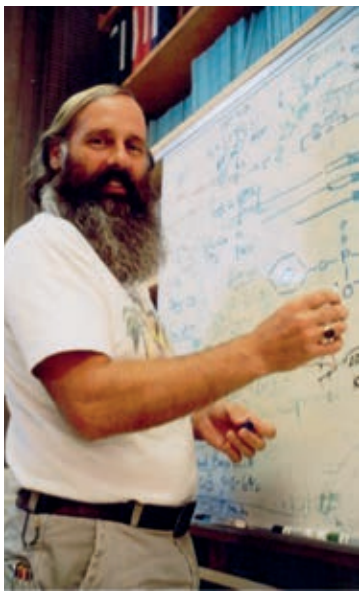
When I rejoined the Salk in 1975, I became a member of the newly formed Tumor Virology Laboratory (TVL), which included Rudolf Jaenisch, Inder Verma, Hung Fan and Bart Sefton, as the other newly appointed Assistant Professors, all working on different RNA and DNA tumor viruses. The TVL was an amazing and vibrant scientific environment, and there were a lot collaborations, because each of us only had a few people in the lab. It was natural for me to continue to work on polyoma virus, and I began using in vitro translation methods that I had learned when back in Cambridge to try to identify the virally encoded transforming proteins, called tumor or T antigens that convert normal cells into cancer cells. Together, with Walter Eckhart, and Ted Friedmann at UCSD, who had just completed the nucleotide sequence of the small polyoma virus genome, we found that polyoma virus uses alternative splicing of a single viral RNA to make three overlapping T antigens - large, middle and small T antigens. The most important for transforming normal cells into tumor cells turned out to be middle T.

President Galligioni congratulates Tony Hunter after his speech at the Teatro Sociale of Trento

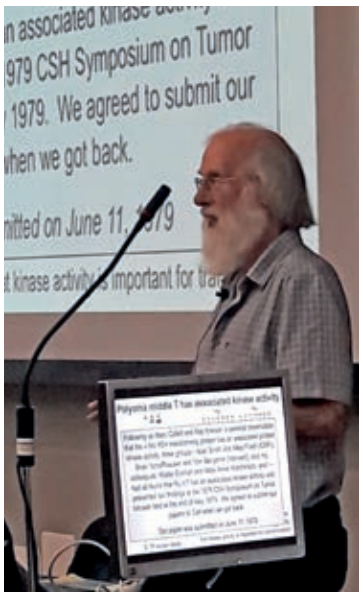
Karen Beemon joined the lab in 1976 as my first postdoc from the University of California, Berkeley, where she had recently completed her Ph.D. on the structure of the genomic RNA of Rous sarcoma virus (RSV), another animal tumor virus. Karen brought her RSV stocks with her when she came, and this proved to be a lucky happenstance. Karen and I set out to try and identify the transforming protein of RSV by in vitro translation of virion genomic RNA in a reticulocyte lysate protein synthesis system. We succeeded in identifying truncated forms of the src gene product, but we were pipped at the post in the discovery of the v-Src protein by Joan Brugge and Ray Erikson in Denver. Nevertheless, my laboratory was now firmly established in the RSV field and over the next two years, largely in collaboration with Bart Sefton, another new Assistant Professor in the TVL, we characterized the v-Src protein.

In 1978, Marc Collett and Ray Erikson made the seminal discovery that v-Src had protein kinase activity, which adds phosphate to proteins. This finding implied that malignant transformation of cells by RSV involves aberrant protein phosphorylation. This was such a provocative discovery that almost immediately every group in the world working with viral transforming proteins tested their own protein to see whether it had protein kinase activity. We were no exception, and examined whether any of the polyoma virus T antigens had protein kinase activity. Early in 1979, Walter Eckhart and I found that the polyoma middle T became phosphorylated in the immune complex protein kinase assay that had been used to show that v-Src had protein kinase activity. This suggested that middle T might also be a protein kinase (although we now know that this is not an intrinsic activity of middle T but rather due to its association with the cellular Src kinase). It was in the course of determining which amino acid residue was phosphorylated in middle T that I made the unexpected finding that the phosphate incorporated in middle T is linked not to the conventional serine or threonine, but rather to tyrosine. As some of you know, this discovery was entirely serendipitous, and resulted from me being too lazy to make up fresh electrophoresis buffer for separation of phosphoamino acids, and using and old buffer instead. In the critical experiment where I analyzed which amino acid was phosphorylated in middle T, an unexpected radioactive spot appeared, and my biochemical training led me to guess that this might be phosphorylated tyrosine, which turned out to be the case - as they say chance favors the prepared mind.
Our discovery that polyoma middle T is associated with a tyrosine kinase activity was quickly followed by our finding that the RSV v-Src protein is also a tyrosine kinase – this discovery was also made quite by accident – I was using v-Src as a control that should have phosphorylated threonine, but to my amazement it also phosphorylated tyrosine. In a very productive collaboration with Bart Sefton, we quickly showed that there is phosphotyrosine in proteins in all mammalian cells, that v-Src itself is phosphorylated on tyrosine in cells, and that RSV-transformed cells have greatly elevated levels of phosphotyrosine in protein. Shortly afterwards, Owen Witte and David Baltimore found that the Abl transforming protein of Abelson murine leukemia virus also has tyrosine kinase activity. This was quickly followed by reports from other groups that several additional viral transforming proteins had a similar tyrosine kinase activity, and that the cellular EGF receptor is also a tyrosine kinase. Within the next few years, human oncogenes that encode tyrosine kinases were discovered, which like v-Src, are constitutively active.

We now know that about half of all the 90 human tyrosine kinases play a role in cancer. Ultimately this led to the development of a new class of cancer drugs, called TKIs, that inhibit oncogenic tyrosine kinases. The first TKI drug approved for human cancer therapy was Gleevec, an inhibitor of the BCR-ABL tyrosine kinase that causes chronic myelogenous leukemia.



Gleevec proved to be a wonder drug, and many of the treated CML patients who went into remission in 2001 are still taking Gleevec. This striking success has led pharma to develop many additional TKIs that block other oncogenic tyrosine kinases for the treatment of specific cancers – as of last month 32 TKIs have been approved for cancer therapy. This is a remarkable outcome of discoveries made with two simple tumor viruses, and a strong justification of continuing funding for basic research



The 1979 discovery of tyrosine phosphorylation was the turning point in my career, and has had a major influence on what I have done for the past nearly 40 years. As a result, I became interested not only in the role of tyrosine phosphorylation in regulating cell function and triggering cell transformation, but also in protein phosphorylation in general. We have gone on to study many types of protein kinase and their downstream targets. We have cloned new tyrosine kinases and phosphotyrosine phosphatases and characterized their functions, and we have expended a lot of effort in identifying substrates for oncogenic and growth factor receptor tyrosine kinases, mapping tyrosines that are phosphorylated in target proteins, and trying to elucidate what these tyrosine phosphorylation events do. Through Jon Pines, a postdoc who came to me from Tim Hunt's group, we made an entrée into the cell cycle, cloning the first human cyclins in 1989. Ironically, this led us straight back into the field of protein phosphorylation when it was discovered that the cyclins are activating subunits of the key regulators of the cell cycle, the cyclin-dependent kinases. Our most recent work is on yet another type of protein kinase that phosphorylates histidine in proteins, and we have just obtained the first evidence that this may also play a role in cancer.

It seems like a long time since I discovered tyrosine phosphorylation 40 years ago, but an amazing amount has been learned since then about the importance of this process, and the payoff in understanding and treating human disease has been remarkable and gratifying. Let me end by thanking the Pezcoller Foundation again.

2018 Pezcoller Foundation-EACR Cancer Researcher Award

Since 2012, the Pezcoller Foundation and the European Association for Cancer Research have collaborated in the organisation of the biennial Pezcoller Foundation – EACR Cancer Researcher Award, which celebrates academic excellence and achievements in the field of cancer research, for cancer researchers who have demonstrated academic excellence and achievements in the field of cancer research and who meet the criteria of :

- Having no more than 15 years post-doctoral experience (or equivalent degree)
- Being currently employed in a European institution
- Having a record of at least five years employment in Europe

The winner gives the prestigious Pezcoller Foundation – EACR Cancer Researcher Award Lecture at the Biennial EACR Congress and receives a €10,000 honorarium.
For the 2018 award, 21 European scientists have been evaluated by the international selection committee. They came from different countries and were all working in European Institutions (4 Spain, 1 Netherland, 6 UK, 2 Belgium, 2 Ireland, 3 Italian, 3 German)
The winner of the 2018 award is Jan Korbel, Group Leader and Senior Scientist, Genome Biology Unit, European Molecular Biology Laboratory (EMBL) Heidelberg, Germany, with the following motivation:
Korbel is an interdisciplinary scientist working at the interface of human genetics and computational biology and, in spite of his young age, he is among of the leading scientists investigating a key class of genetic variations i.e. Structural Variation (SV) and their consequences in germinal and somatic cells. Dr. Korbel has had leading roles with the 1000 Genomes Project

Anton Berns, President EACR, Jan Korbel winner, Enzo Galligioni, President Pezcoller Foundation

(1000GP) and is co-leading the Pan-Cancer Analysis of Whole Genomes (PCAWG) project. Dr. Korbel's exceptional accomplishments have resulted in numerous high impact publications (including 16 in Nature, 2 in Cell, 2 in Science, in addition to those in Nature Genetics, Nature Biotechnology and Cancer Cell).
Jan Korbel was officially awarded by the Pezcoller President E. Galligioni and the EACR President A. Barnes in a plenary session at EACR, the 25° Biennial Congress of the European Association for Cancer Research, on July 3, 2018 , in Amsterdam, where Jan Korbel gave the Pezcoller Foundation – EACR Cancer Researcher Award Lecture: *From Genomic Variation to Molecular Mechanism*.

On November 6, 2018 a press conference was held at MUSE to underline the new cooperation between Pezcoller Foundation and MUSE. The Two Presidents , Enzo Galligioni and Michele Lanzingher together with Patrizia Famà, Supervisor of the Scientific Communication Sector and Exhibition Program Manager at MUSE, spoke of this new occasion given by the contextual exhibition on Human Genome (*see picture*). MUSE is one of the most important Science Museums, recently built on the 2013 project of Renzo Piano. The agreement is particularly important for the notable international importance recognized to both institutions.

Precisely within this framework was the lecture by Jan Korbel, maximum Convergence Science specialist. Convergence Science could be defined the third scientific revolution in the biomedical field of the last 50-60 years, after Molecular Biology and Genomics. It comes from the need for integration of individual scientific disciplines, such as engineering, physics, computer science, chemistry, mathematics and life sciences, which they merge, "converge" into a new unitary science.

The agreement between Pezcoller Foundation and MUSE

Jan Korbel at MUSE in November 2018

30th Pezcoller Symposium

Overcoming the innate resistance of cancer to therapy

The 30th Pezcoller Symposium entitled " Overcoming the Innate Resistance of Cancer Therapy" was held in Trento in June 2018 and was opened with the Enrico Mihich lecture by Harold Varmus, 1986 Nobel Laureate.

We are glad to be able to report a summary of the meeting made by Massimo Loda and Michelangelo Fiorentino.

The outstanding meeting held in Trento on June 25-26th 2018 marked the 30th anniversary of the annual Pezcoller Symposium. The meeting was focused on the innate resistance of cancer cells to therapy and the strategies that can be employed to overcome such resistance. Models as well as human data were utilized to understand the mechanistic underpinnings of resistance. Different approaches were proposed including generation of tumor models derived from embryonal stem cells, establishment of patient-derived xenografts (PDX) or organoids (PDO). Of particular interest was the concept of "mouse clinics" devoted to the study of individual patient tumor avatars in which drug resistance can be tested in a personalized manner.
A brief overview of the salient findings that were presented is outlined below.
The Dr. Harold Varmus gave the opening lecture and focused on lung cancer. The development of non-small cell lung cancer (NSCLC) models confirmed that the relatively common finding of mutual exclusivity of mutations in lung cancer and melanoma holds true in mouse models. In fact, genetically engineered lung cancer cells do not even tolerate simultaneous mutations of KRAS and EGFR, even though these occur in human cancer, albeit rarely. Similarly, melanoma cells cannot survive the concomitant mutation of NRAS and BRAF. Dr. Varmus showed that using human embryonal stem cells they were able to generate pulmonary neuroendocrine cells and to transform them into small cell lung cancer (SCLC) cells through the dual inhibition of the RB and NOTCH oncogenes.
Dr Anton Berns showed that induction of Nuclear Factor I B (NFIB) and knock-out of E-Cadherin (CDH1) confer chromosomal instability and invasive potential in vitro. Importantly, NFIB positive tumors appear to be more sensitive to cisplatin. Dr. Berns also showed that in vivo models of pleural mesothelioma have been established through the suppression of NF2 and BRCA Associated Protein 1 (BAP1). BAP1 causes an epigenetic switch mediated by EZH2 and therefore BAP1 deficient mesotheliomas are more sensitive to PARP and EZH2 inhibitors. In animal models of mesothelioma the morphological appearance of the tumor depends on the gene that is enforced, possibly allowing the pathologist to predict sensitive versus resistant tumors with traditional light

microscopy approaches.
While tyrosine kinase inhibitors are effective in non-small-cell lung cancers (NSCLCs) with epidermal growth factor receptor (EGFR) mutations, relapse typically occurs within 1 year of continuous treatment, along with a histologic change from NSCLC to small-cell lung cancer (SCLC) in a subset of the resistant cancers. The molecular changes associated with this transformation remain undefined. Dr. Poirier analyzed tumor samples and cell lines derived from resistant EGFR mutant patients and showed that the retinoblastoma (RB) gene is lost in 100% of SCLC cases, but rarely in those that remain NSCLC. Further, increased neuroendocrine marker- and decreased EGFR- expression as well as greater sensitivity to inhibition of BCL2 family members are observed in resistant SCLC transformed cancers compared with resistant NSCLCs.
Pancreatic ductal cancer (PDAC) is characterized by innate drug resistance and general poor prognosis in unresectable patients. Dr. Tuveson showed that PDO profiling revealed two clusters of PDAC, classic and basal, with transcriptional differences and exceptional response to PARP or PI3K inhibitors. The data Dr. Tuveson presented established PDO profiling as a means to test molecular signatures on clinical samples and guide therapy.
Dr. Bardelli showed that in animal models of colorectal cancer the blockade of the MAPK and WNT pathways prevents resistance to agents targeting HER2 and APC, respectively. Colon cancers displaying microsatellite instability result in the generation of neo-antigens, which in turn stimulate an immune anti-tumor response. Knock-out of mismatch repair genes such as MLH1 in patient-derived cancer cells will activate neo-antigen production and induce cancer cell rejection. The development of MLH1 inhibitors might therefore be an adjunct to checkpoint inhibitors, even while inducing a "conditional Lynch syndrome". The net effect of this approach is thought to result in a benefit for cancer patients.
Dr. Fisher focused on aspects of melanoma biology that may affect resistance to targeted therapy. Ultraviolet exposure can induce DNA damage, synthesis of vitamin D, and affect melanoma development. Keratinocytes containing damaged DNA secrete both α-melanocyte-stimulating hormone (α-MSH), which stimulates pigment production by melanocytes, and β-endorphin, which can trigger addiction-like responses to UV exposure. The pigmentation response to UV exposure driven by melanocytic microphthalmia-associated transcription factor (MITF), protects against DNA damage and melanomagenesis, while the opioid response may be an evolutionary adaptation for promoting sun-seeking behavior to prevent vitamin D deficiency. Repression of the SIK1-CRTC pathway in animal models is able to restore pigmentation and this mechanism could be utilized for protection and prevention. In addition, UV exposure induces β-endorphin and it is possible to experimentally modulate animal behavior using Vitamin D and UV. Interestingly, forced induction of BRAF mutations in an experimental models of red-hair mice induces melanoma formation irrespectively of UV exposure. Finally, resistance to anti BRAF targeted therapy in melanoma is mediated by high AXL and low MITF, as a result of epigenetic changes induced by LSD1. Thus, LSD1 inhibitors may be utilized in BRAF-resistant melanoma.
Dr. Kaelin discovered the pathway by which cells sense and adapt to changes in oxygen availability. The von Hippel-Lindau (VHL) tumor suppressor is inactivated in the majority of clear cell renal cell carcinomas (ccRCCs), leading to inappropriate stabilization of hypoxia-inducible factor-2α (HIF-2α). Unfortunately, mutations in HIF2a (S304M) confer resistance to anti HIF2a inhibitors. Similarly, CDK4/6 inhibitors are able to kill VHL -/- cells in experimental models. D. Josey from Peloton Therapeutics developed PT2385, a first-in-class HIF-2α antagonist. He showed that this compound has a good

safety profile and is active in patients with heavily pretreated ccRCC, potentially overcoming resistance.

Dr. Sawyers, defined lineage plasticity as the ability of cancer cells to change their identity either by dedifferentiation back to a progenitor cell or by transdifferentiation towards another differentiated cell type. Such plasticity can be stimulated by oncogenic signals or it can be induced in organoids by cell reprogramming. In organoid models of castration resistant prostate cancer, AR inhibition accelerates lineage plasticity with a transition to AR-negative, neuroendocrine phenotype. RB1 loss, in these models, gives rise to small cell carcinomas even in the absence of androgen blockade. He also provided data to support that an adjunct mechanism of resistance was represented by mutations in the DNA binding domain of FOXA1. These are enriched in CRPC and confer a proliferation advantage to prostate cancer organoids.

While progression from normal prostatic epithelium to invasive cancer is driven by molecular alterations, tumor cells and cells in the cancer microenvironment contribute to both tumorigenesis and tumor progression. Dr. Loda generated gene expression profiles of laser capture microdissected stroma surrounding low- and high-grade prostate tumors. He showed that a stromal gene signature reflecting bone remodeling and immune-related pathways was upregulated in high compared to low Gleason grade cases. In validation data, the signature discriminated cases that developed metastasis from those that did not. These data suggest that targeting the microenvironment may prevent metastatic progression and/or resistance.

The genetic alteration that underlies hairy cell leukemia (HCL) is the V600E BRAF mutation. Drs. Falini and Tiacci showed that resistance to anti BRAF agents such as Vemurafenib can be overcome by adding Rituximab to the therapeutic regimen, reaching almost 100% complete responses. Resistance to Vemurafenib occurs through phospho-ERK activation. Thus, patients with relapse may benefit from MEK inhibitors such as Dacometinib.

In Acute Myeloid Leukemia (AML) one fourth of patients harbors mutations in the IDH1/2 genes leading to 2-hydroxyglutarate (2-HG) increase and leukemogenenesis but inhibition of IDH1/2 in these patients does not cure the disease. Resistance occurs either by increase of one-carbon metabolism or by inhibition of LSD1 demethylase. Dr. Pandolfi, utilizing PDX and PDO in the "mouse clinic", showed that therapy with all trans-retinoic acid (ATRA) in Acute Promyelocytic Leukemia (APL), targets the PIN1 isomerase, a negative regulator of ATRA signaling, overcoming resistance.

There is only handful of animal models of hormone-sensitive breast cancer because of poor engraftment. Dr. Brisken showed that an alternative route to subcutaneous injections is the direct engraftment through the nipple into breast ducts. Intraductal injection of MCF7 hormone-sensitive cells (MCF7-MIND model) re-capitulates human tumors, even with the occurrence of microcalcifications and the development of metastases. These PDXs can be used for drug testing. Resistance is thought to occur through epithelial-mesenchymal transition or by the appearance of a basaloid, p63 positive phenotype.

The presence of cancer cells with stem cell features gives rise to heterogeneity in medulloblastoma. Sox2 positive medulloblastoma stem cells are quiescent and ultimately drive primary tumor growth. Dr. Dirks showed that these cells are therapy-resistant and become enriched following chemotherapy and Smoothened inhibition, creating a reservoir for tumor regrowth. These cells propagate a subgroup of medulloblastoma driven by sonic hedgehog mimicking a neurogenic program. In a transposon-driven, functional genomic mouse model of medulloblastoma treated with therapeutic regimens that mirrored those used in patients, dominant clone at recurrence arose through clonal selection

of a pre-existing minor clone present at diagnosis.
Diffuse gliomas are not curable because of the evolutionary changes of tumor cells during therapy through either new mutations or cell-matrix interactions. Since plasma cfDNA is always negative in glioma patients resistant to therapy a possible alternative strategy to detect resistant mutations is the collection of DNA from cerebro-spinal fluid (CSF). Dr. Mellinghoff showed that tumor mutational burden is detectable in CSF DNA and might be predictive for response to immunotherapy. A second, equally important mechanism of resistance is mediated by EGFR and PDGFRA and their associated RTK signaling.
Dr. Livingston, the driving force behind this meeting, closed with remarks describing yet another outstanding scientific retreat focused on major topics emerging from some of the best basic science laboratories in the world. He emphasized that importance of such discoveries in overcoming resistance to therapy in cancer.

More than 200 young Italian and European researchers attended the meeting. Among the presented posters (42) the best three have been selected and awarded the Begnudelli Scholaships: V. Audrito from Department of Medical Sciences and Department of Molecular Biotechnologies of University of Torino; Giuseppina Barutello, from Department of Medical Sciences and Department of Molecular Biotechnologies of University of Torino; A. Bruni from Radiation Oncology Unit, University Hospital "Policlinico of Modena".

Pezcoller Foundation-SIC (Società Italiana di Cancerologia) Fellowships

President Galligioni congratulates the winners of the scholarships Candida Vitale and Lorenzo Stramucci.

In September 2018 during the 60th Annual Meeting of the Italian Cancer Society in Milan, Annalisa Lonetti and Mattia Boeri, recognized winners of the two 2016 Pezcoller scholarships, presented the results of their two-year work.
In the same congress the Pezcoller Foundation presented the two new 2019-2020 scholarships: the "Ferruccio and Elena Bernardi" to Candida Vitale of the University of Torino and the "Alice Triangi" to Lorenzo Stramucci of the Regina Elena Cancer National Institute of Roma; chosen among 32 candidates for their best research projects.

31th Pezcoller Symposium

CANCER AS CORRUPTED TISSUE

Trento, Italy, June 17-19, 2019

Co-Organizers: Alberto Bardelli, Cathrin Brisken, David Livingston, Massimo Loda, Stefano Piccolo, Maria Rescigno

Focus and Goals: Cancers are, in essence, products of organ and tissue development gone wrong. In fact, many critical cellular and organ-based operations from genome integrity, the behavior of one's own microbiome, oxygen utilization and cell metabolism, orderly tissue and organ anatomy, disciplined cell behavior, and the immune response may become disordered in the interest of tumor development. In this year's Symposium, the focus will be on the newest insights into the processes that give rise to cancer tissue and its persistence. Also included will be recent findings that have the potential to influence clinical cancer therapeutics in novel ways.

PRELIMINARY PROGRAM

MONDAY JUNE 17, 2019

Enzo Galligioni - Welcome

David Livingston - Focus & Goals

Sean Morrison - The Enrico Mihich Lecture
Discussion

Session 1, The Microbiome and Cancer
Chair: Maria Rescigno

Rosmina Goldszmid
Discussion

Jennifer Wargo
Discussion

Session 2, Cancer and Metabolism
Chair: Massimo Loda

Bill Sellers
Discussion

Matt Vander Heiden
Discussion

Session 3, Cancer Metastasis
Chair: Stefano Piccolo

Christoph Klein
Discussion

Mikela Egeblad
Discussion

Poster Session

TUESDAY, JUNE 18, 2019

Session 4, Tissue and Organ Formation
Chair: Cathrin Brisken

Cedric Blanpain
Discussion

Stefano Picolo
Discussion

Nicholas Rajewsky
Discussion

Session 5, Genome Order and Disorder
Chair: FabrizioD'Adda di Fagagna

Roger Greenberg
Discussion

Daniel Durocher
Discussion

Simon Boulton
Discussion

Fabrizio D'Adda di Fagagna
Discussion

Session 6 Cancer and Immunology
Chair: Alberto Bardelli

Andrea Ablasser
Discussion

Cathy Wu
Discussion

Poster Discussion and Poster Presentation (led by Massimo Loda)

David Livingston
Concluding Remarks

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