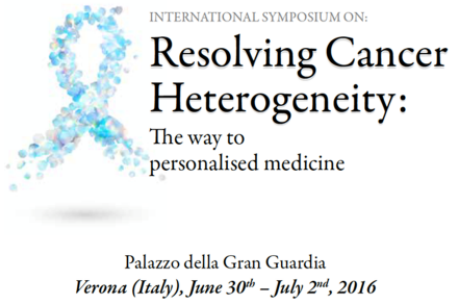
International Symposium
On
Resolving Cancer Heterogeneity:
The Way
to
Personalised Medicine
Verona (Italy), June 30 July 02, 2016
Highlights

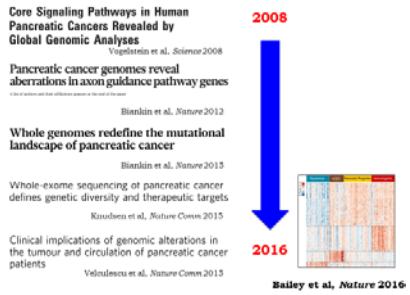
Introduction



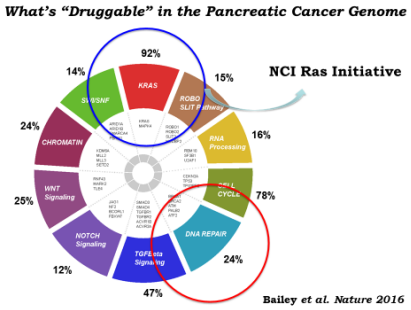
Prof. Scarpa, the Chairman of the Symposium, opened the congress by highlighting the scientific level of the meeting and presented the main oncology centres of the city of Verona: the Medical Oncology and Verona Comprehensive Cancer Centre and the ARC-Net Research Centre. The speaker concluded his talk by introducing the lecture on Pancreas Cancer and his speaker: Prof. Maitra from Huston (USA).

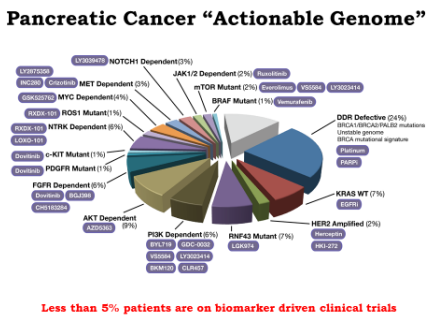
To follow the presentations of this congress, click on this link: http://www.fondazione-menarini.it/Archivio-Eventi/2016/Resolving-Cancer-Heterogeneity-The-Way-to-Personalised-Medicin/Materiale-Multimediale … and, after having logged in, enter in the multimedia area.

Emerging targets from the pancreatic cancer genome.



Prof. Maitra from Houston, (USA), in his lecture about the new targets derived from the pancreatic cancer genome, pointed out the increase of pancreatic cancer incidence: in the USA this is the 3rd cause of death by cancer. From 2008 to 2016 there have been papers published about the genomic alterations in this tumour and the discovery of some gene families that target defective DNA in pancreatic cancer. The speaker presented data about patients' response to therapy, explaining that the response was obtained only in those patients characterized by the presence of specific DNA repair mutations. In the first part of his speech Prof. Maitra highlighted the main gene mutations present in pancreatic cancer, introducing the concept of a genomic driver which develops in specific tumors and their response to therapy. In the second part of his lecture Prof. Maitra spoke about the new approach to therapy in patients with advanced pancreas cancer. No more tissue biopsies for detecting the cancer's lesions but liquid biopsies as a platform for therapeutic stratification and monitoring in pancreatic cancer patients. This new technique is able to detect the genomic alterations during the course of therapy. The speaker concluded his lecture stressing the fact that liquid biopsies are able to detect early mutations which have a potential to lead to the disease in healthy people.





Less than 5% patients are on biomarker driven clinical trials

- **What is the main function of the chromatin regulator Brg1 in pancreatic cancer?**
- **What does the loss of Arid 1a lead to?**
- **How many "actionable genome" mutations are present in Pancreatic Cancer?**
- **How many exosomes are present in Pancreatic cancer patients?**
- **What are the main detection methodologies for pancreatic cancer CTCs?**
- **How important is intra-patients monitoring of CTCs?**
- **Is it possible to map tumour genome evolution during the natural history of pancreatic cancer?**

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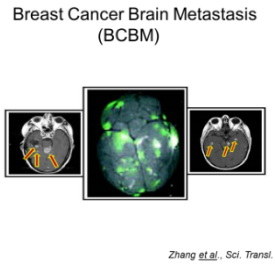
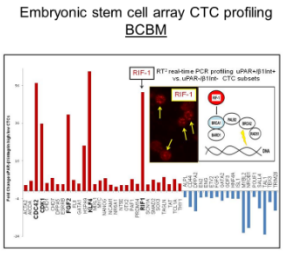
Dissecting CTC subsets: insights into the evolution of breast cancer CTCs mediating brain metastasis.

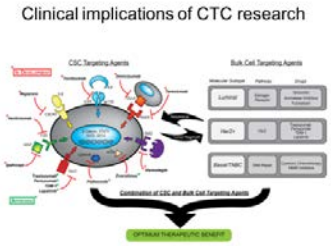


Zhang et al., Sci. Transl. Med., 2013

Prof. Marchetti from Houston (USA) talked about this very innovative methodology characterized by the dissection of circulating tumour cells that start from breast cancer. In his speech Prof. Marchetti pointed out the importance of this technique and presented data on CTCs with competence for brain metastasis that are the key point for the progression of primary breast cancer to Breast Cancer Brain Metastasis (BCBM). From a genomic point of view, the speaker highlighted the presence of the so called CTC subset, that avoids organ arrest by having pluripotent stem cell, quiescence properties and hyperactive mechanism of DNA repair. In the second part of his presentation Prof. Marchetti presented data about the use of BCBM as clinical discriminator of CTC evolution towards metastatic competence. In conclusion the speaker stressed the point that CTC can represent the future of cancer diagnostics by driving effective sequential therapies thanks to the real-time monitoring of CTC clonal heterogeneity.



Vishnoi et al., Sci. Rep., 2015



- **What is the effect of viable CTCs?**
- **What is the CTC evolution in blood?**
- **Why can CTCs be the future of cancer diagnostics?**
- **What is the way for regulation of gene expression profile by CTCs?**
- **Why is it possible to apply for "Alternating treatment regimens" by using CTC biomarkers?**

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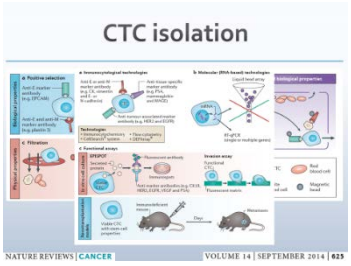
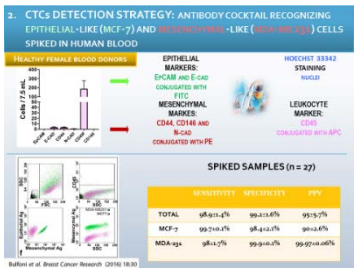
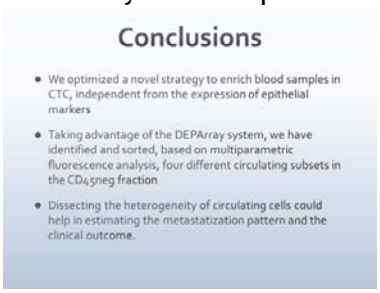
Identification of circulating tumor cells in epithelial-to-mesenchymal transition in metastatic breast cancer patients



Prof. Cesselli from Udine (I) presented very interesting data regarding this topic, highlighting the importance to detect CTCs in blood in order to identify metastatic lesions as a signature of the tumour in the blood. There are various methods used for identifying CTCs in the blood, but the speaker highlighted that until now only one method has been approved by FDA. Starting with data published in 2013 on the changes in epithelial and mesenchymal composition of circulating breast tumour cells, the speaker presented her data derived from a study aimed to optimize a protocol for identification and quantification of viable CTCs. Thanks to these data, Prof. Cesselli has identified four circulating CTCs subsets, highlighting that this is the way for a better estimation of the metastatization pattern and the clinical outcome in patients with breast cancer.





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- **What are the unmet clinical needs in metastatic tumors?**
- **What is the best method for the identification of CTCs derived from breast cancer?**
- **What are the main open questions about CTCS?**
- **What are the aims of the study presented by the speaker on CTCs identification?**
- **What are the future researches about Exome highlighted by the speaker?**

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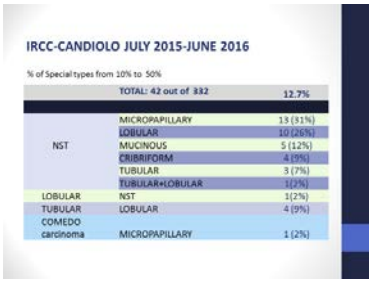
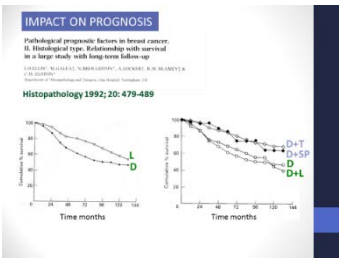
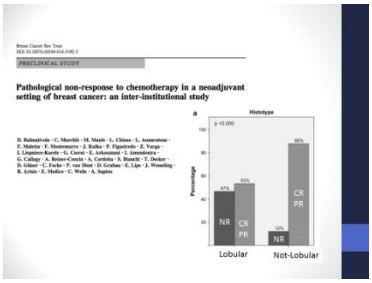
Assessing tumor heterogeneity in breast cancer



Prof. Sapino from Torino (I) addressed this topic pointing out the intratumor heterogeneity from the histological point of view. In her talk the speaker highlighted the importance of a correct classification of the tumour from an histological point of view for its very close relationship with the management and the outcome of the patients. The speaker presented data about the main histomorphological heterogeneity types of breast cancer, stressing the importance of a better examination of the tumour and a better detection of prognostic/predictive biomarkers linked to these heterogeneities. In conclusion Prof. Sapino highlighted the importance for performing more than one biopsy in order to better identify the specific heterogeneity present in the tumour and the importance that any kind of molecular study on heterogeneity can include the morphological heterogeneity in the planning of the experiments and the assessment of the results.





- **How many paper have been published about histological heterogeneity of breast cancer?**
- **What is the impact on prognosis of histological heterogeneity in breast cancer?**
- **How many different histological types can be present in the same tumour?**
- **What is the clinical significance of mixed phenotypes in breast cancer patients?**
- **How many biomarkers linked to these heterogeneities have been presented by the speakers?**

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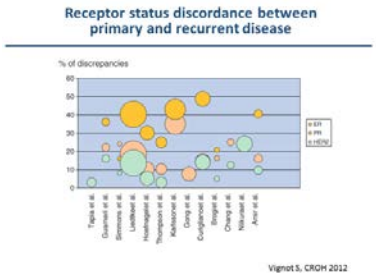
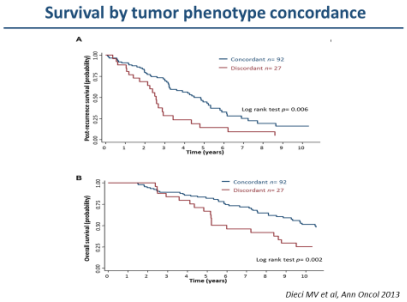
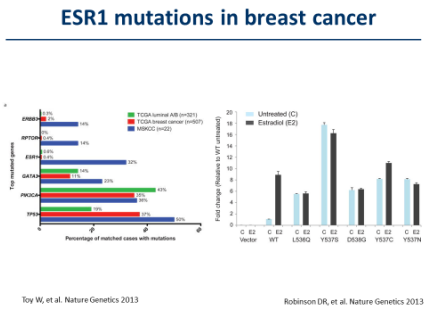
Change of molecular characteristic and breast cancer progression.



Prof. Conte from Padua (I) talked about this very important topic and its impact on disease progression. The speaker started his speech pointing out the correlation between primary tumor biology and the related therapeutic choices. But what to do when the tumor changes its characteristics over times? The main part of his presentation was spent on trying to answer this question. One of the main options in order to explain this discordance between the beginning of the tumoral lesion and its evolution, is represented by the investigation of the biological discordances such as intramural heterogeneity, genetic drift occurring during progression or even the selective pressure that treatments exert to the biology of the tumor itself. The speaker presented data demonstrating that the presence of discordance between primary and recurrent disease has a worse impact on survival: patients with discordant phenotypes have a shorter survival time than patients with concordant phenotypes. Prof. Conte spent the second part of his speech in presenting data on molecular characterization of post-neoadjuvant residual disease, the emergence of resistant disease and finally on the dynamic relationship between immune system and cancer. Finally, the speaker announced the beginning of a new clinical trial on adjuvant treatment for high-risk triple negative breast cancer patients with the anti-pd-l1 antibody Avelumab.





- **Is the receptor discordance between primary tumors and metastasis a simple technicality or a biological effect?**
- **What are the main molecular characterizations of the post-neoadjuvant residual disease?**
- **What about the ESR1 mutations in breast cancer patients?**
- **What are the main methods allowing for the detection of emerging resistant clones?**
- **Why chemotherapy can modify the relation between immune system and cancer?**
- **Why tumor progression is related to a decreased immune competence?**

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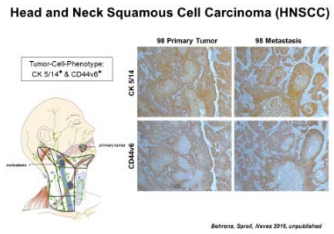
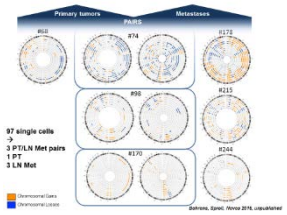
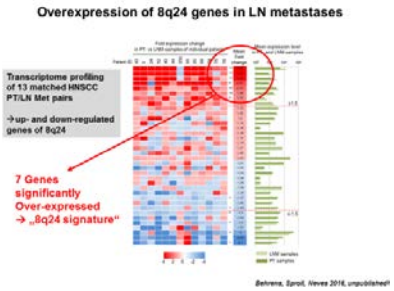
Genomic profiling of HNSCC on the single cell level indicates metastasis-relevant genes.



Prof. Stoecklein from Dusseldorf (D) went deep into this topic with his talk. He started his speech by highlighting the fact that HN Squamous Cell Carcinoma (HNSCC) is one of the more aggressive and common cancers worldwide and, even more important, the prognosis is very poor and unchanged in the last 40 years. The most frequent metastases are located in the limphonodes of the Neck and represent the single most important prognostic factor and, moreover no known genetic drivers for LN metastases have been discovered until now. The main part of his talk was spent presenting data produced by his group of researchers and their discovery of genomic profiles of HNSCC at the single cell level. By comparing the same chromosomes locations in primary tumors and metastases samples, the speaker highlighted the fact that some alterations are most frequently shared in LN metastases, and among these the one more frequent is the 8 q 24 signature. The speaker concluded his speech by highlighting that the presence of 8 q 24 signature is linked to a rapid disease progression and 8 q 24 gains are an important requirement for LN mets.





- **Do the LN metastases have a specific CAN profile?**
- **Which alterations are most frequently shared in LN mets?**
- **Which 8 q 24 -genes are overexpressed in LN mets?**
- **What is the prognostic relevance of 8 q 24 signature in LN mets patients?**

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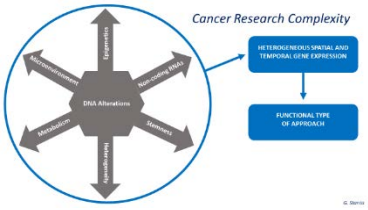
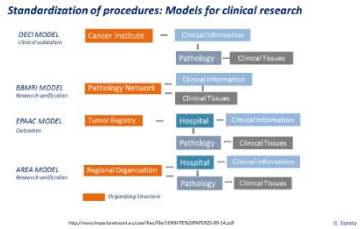
Functional and not clonal heterogeneity: practical approaches.



Prof. Stanta from Trieste (I) in his presentation on this very important topic, pointed out the complexity of clinical research in the cancer field depending by the presence of a lot of DNA alterations that lead to heterogeneity. The speaker proposed a new type of approach the so called "functional type of approach". The main part of his presentation was spent presenting clinical research strategies and the related methods to be applied in order to standardize the data produced by clinical studies in breast cancers patients. Prof. Stanta concluded his talk stressing the importance of the standardization of the procedures as an applicable model for clinical research.



- **What are the main causes of complexity for clinical research in breast cancer?**
- **What are the main steps for breast cancer care according to care processes?**
- **What are the main strategies in clinical research presented by the speaker?**
- **What are the main models for clinical research in breast cancer, presented by the speaker?**
- **What are the main important patient materials to be collected for diagnostic and clinical research purposes?**

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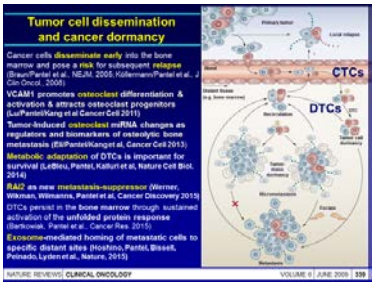
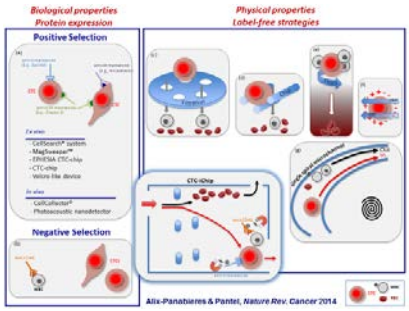
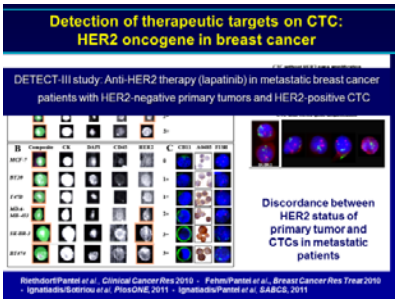
Liquid biopsy: implications for cancer therapy.



Prof. Pantel from Hamburg (D) in his talk spoke about this topic, stressing that this technique is able to detect CTCs also in an early phase of the tumor when it is possible to eradicate the lesion with the treatment. The main part of his speech was spent presenting data on screening and early detection of cancer and moreover by presenting data on estimation of the risk for metastatic relapse or metastasis progression, stratification and real time monitoring of therapies, identification of therapeutic targets and resistance mechanisms and finally on understanding the biology of metastatic development. One of the most important characteristics of this methodology is represented by its availability in all types of cancers: the solid and also the blood line ones. At the end of his speech the speaker presented the main groups of researchers working in touch in this field: the Micrometastasis Research-Network at UCCH/UKE and the Center of Experimental Medicine located in Hamburg.





- **What are the main results in CTCs detection in patients with early stage cancers?**
- **Is it possible to detect CTCs in brain cancer patients?**
- **Can early changes in CTC counts predict the efficacy of therapeutic interventions?**
- **What are the main therapeutic targets of CTC characterization?**
- **What about ctDNA early detection and the tumor-associated mutations in ageing individuals?**
- **What are the main functional studies on CTC presented by the speaker?**

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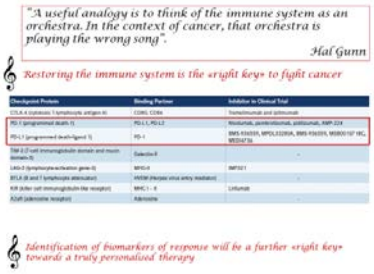
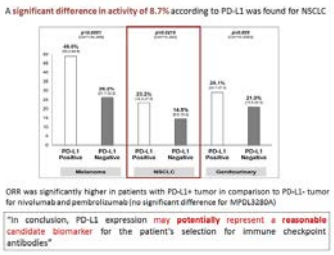
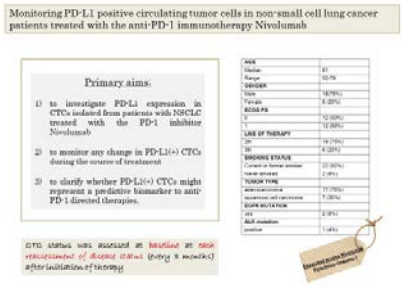
Molecular features of circulating tumor cells in lung cancer patients treated with checkpoint inhibitors: avoiding predation.



Prof. Gazzaniga from Rome (I) spoke about the molecular features of CTC in lung cancer patients treated with checkpoint inhibitors, pointing out the importance for helping the immune system to "play the right song", of restoring the immune system in patients with cancer. Another topic, strictly linked with restoring the immune system, is characterized by the identification of the right biomarkers for the patient's selection of immune checkpoint antibodies. The main part of her presentation was spent by Prof. Gazzaniga presenting interesting data on PD-L1 such as a candidate biomarker for immune response in many types of cancers. The speaker presented data produced by a study performed in patients affected by non-small cells lung cancer in order to detect PD-L1 expression in CTCs isolated by these patients. In conclusion the speaker highlighted the importance of choosing the right therapy suitable for patients at the right time.





- **What is the ideal sample for investigating the role of PD-L1 as a biomarker in cancer patients?**
- **What populations of cells are to be selected for the same task?**
- **How to counteract the variability of PD-L1 expression in tumor cells?**
- **Why is there a slow response to checkpoint inhibitors by using PD-L1 as biomarker in patient with cancer disease?**

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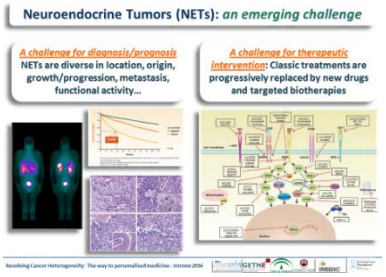
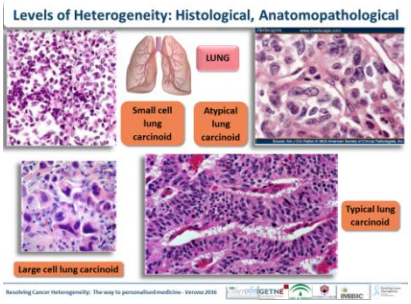
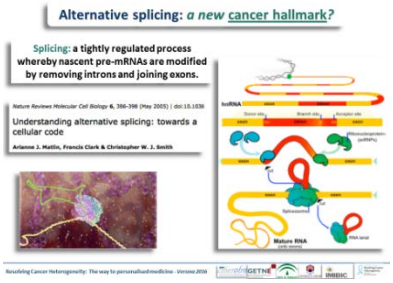
Splicing defects as a novel factor contributing to tumor development and heterogeneity.



Prof. Castaño Fuentes from Còrdoba (E) spoke about splicing defects pointing out their role in contributing to tumor development and etherogeneity. The speaker particularly highlighted the role of Neuroendocrine Tumors (NETs) as an example of an intrinsically heterogeneous type of cancer, he then went on to define what heterogeneity means, analysing additional factors that contribute to heterogeneity like miRNAs and epigenetics. The speaker pointed out the role played by heterogeneity as an intrinsic hallmark of NETs that allows to better understand tumor biology and the future development of new therapy strategies. The speaker stressed the importance of the same molecular factors that critically contribute to heterogeneity, as targets of intervention and source of new tumor biomarkers. In conclusion Prof. Fuentes pointed out that Splicing is an emerging mechanism in oncology, providing novel tools to understand NETs pathogenesis, development and response.





- **Why alternative splicing is a novel cancer hallmark?**
- **What are the additional factors leading to heterogeneity?**
- **Why are NETs a challenge for cancer hallmarks?**
- **What generates the aberrant oncogenic splicing products?**

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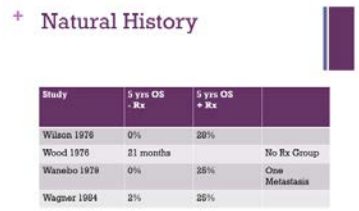
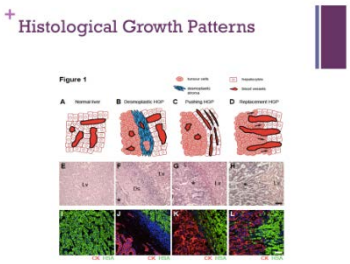
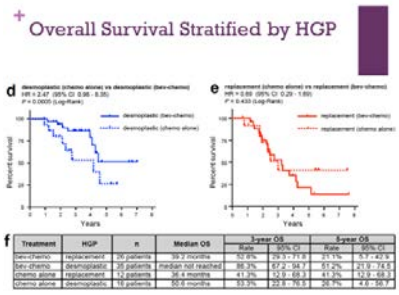
Heterogeneity in colorectal cancer metastasis and response to therapy.



Prof. Metrakos from Montreal (CDN) spoke about heterogeneity in colorectal cancer metastasis in relationship with the response to therapy, pointing out the state of the art concerning the outcome of patients, dramatic in the past but not sufficiently better in the present-day. Colon cancer liver metastasis, are the third most common cancer type, the second most lethal cancer disease after lung cancer and Liver is the most common metastatic site. The speaker highlighted the failure of every drug since 5FU in order to reply 5FU. The main part of his talk was dedicated to present data on a new patients' classification, based on three histological growth patterns (HGP): replacement, desmoplastic and pushing. In conclusion the speaker pointed out that HGP is a valid method for a correct prognosis of the patient and that HGPs can be useful in selecting patients for the right therapy. The speaker also stressed the importance of the imaging techniques for the stratification of the patients. In conclusion the speaker highlighted the necessity to identify the molecular mechanisms underlying the replacement pattern in order to develop new therapeutic strategies.





- **What is the natural history of the colon cancer liver metastases?**
- **What is the current 5-years survival for patients with liver metastases derived from colon cancer?**
- **What are the main patterns identified by the speaker in the HGP model?**
- **Can the HGP model be applied to other cancer types?**

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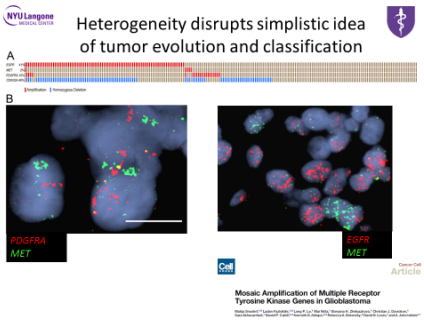
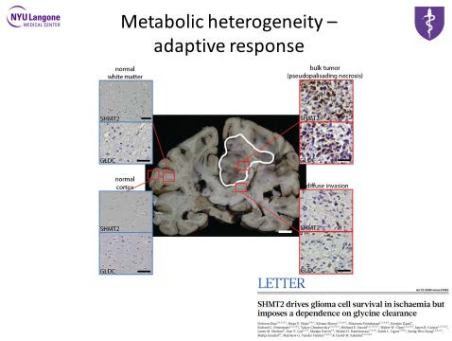
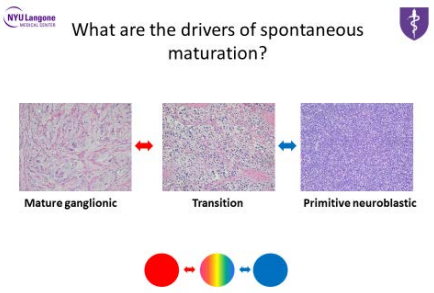
Dissecting epigenetic heterogeneity in cancer: functional implications and therapeutic opportunities.



Prof. Snuderl from New York (USA) presented some very interesting data on dissecting epigenetic heterogeneity in cancer, pointing out the role of epigenetic in design new treatment strategies. The speaker highlighted the role of heterogeneity in disrupting the simplicistic idea of tumor evolution and classification and presented more data on heterogeneity applied to brain tumors, pointing out that the response of glioma cells to hypoxia varies based on underlying genetic drivers. The main part of his talk was dedicated to demonstrating that the ability of the tumoral cells in adaptation to stress stimuli depends on epigenetic heterogeneity. This characteristic can explain the ability demonstrated by genetically relatively uniform tumor cells, to behave and look differently not only in adaptation to the stress, but also in staying dormant for years. The speaker concluded by highlighting the importance to acquire ability in turning the epigenetic switch on/off in order to provide future options for cancer therapy.





- **What is the functional purpose of heterogeneity in human brain tumors?**
- **Is it possible to utilize "natural developmental" pathways to target cancer?**
- **What are the main characteristics in epigenetic heterogeneity present in neuroblastoma?**
- **What is the main effect of the epigenetic regulation on cancer cells?**

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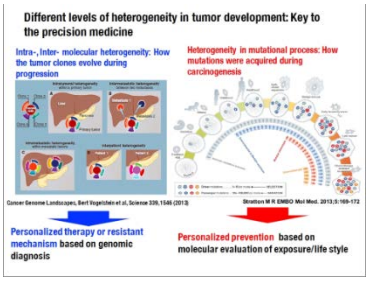
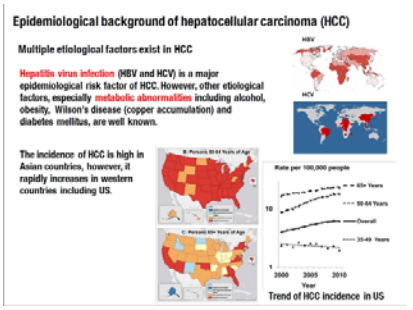
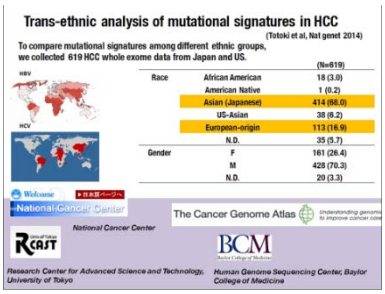
Liver cancer heterogeneity



Prof. Shibata from Tokio (J) spoke about liver cancer heterogeneity, pointing out the inter-tumor heterogeneity in mutational signatures as a key for precision medicine. In his presentation the speaker presented data on two main topics: the intra-inter- molecular heterogeneity and the heterogeneity in mutation processes leading to personalized prevention based on molecular evaluation of exposure/life style. In particular the speaker went further to explain the meaning of the mutual signatures in hepatocellular carcinoma (HCC), the trans-ethnic diversity of these mutations and finally spoke about the future exploration in mutational signatures. The speaker stressed the point that the presence of subgroups with specific mutational signature combinations, can be associated with epidemiological pattern as well as specific driver genes. The speaker concluded his talk by stating that In order to identify unknown signatures, it is important to unify international efforts for a larger cancer genome data base in order to perform new genetic evaluations of new carcinogenesis models.





- **What are the main epidemiological backgrounds of hepatocellular carcinoma?**
- **How many mutational signatures were extracted form HCC WGS data?**
- **How many trans-ethnic mutational signatures have been found in the study runned by the speaker?**
- **What is the relationship between mutation signature and tumor biology?**
- **Can the comprehension of the mutational processes be helpful for the so called "precision cancer prevention"?**

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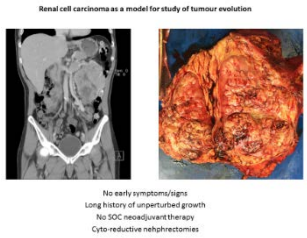
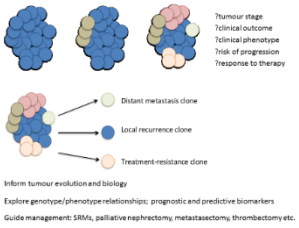
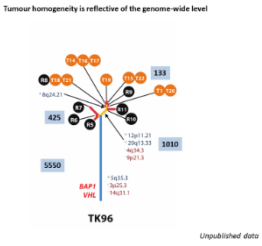
Mapping renal cancer evolution through space and time.



Prof. Turajlic from London (UK) presented data on this topic, taking in account for the particular characteristics of the Renal cell carcinoma, leading to the use of this cancer as a model for studying tumor evolution. The speaker pointed out the data about the branched evolution in patients with RCC and the correlation between epigenetic mutations and tumor stage, clinical outcome, clinical phenotype, risk of progression and response to therapy. In performing this analysis, the speaker delivered 110 gens significantly mutated in RCC. The second part of her talk was dedicated to the presentation of data concerning the relationship between primary RCC and metastasis. In conclusion the speaker highlighted the need of large-scale studies in order to work out the rules of cancer evolution.





- **What are the main characteristics of the Renal cell carcinoma from a clinical point of view?**
- **What is the relationship between epigenetic mutations and clinical outcome in RCC?**
- **What is the correlation between primary RCC and bone metastases?**
- **Why is tumor homogeneity reflective of the genome-wide level?**

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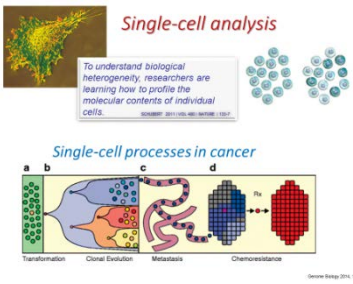
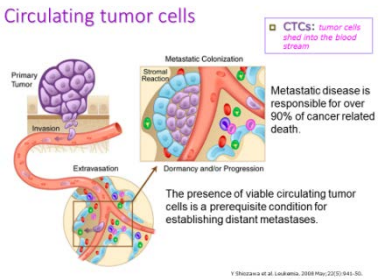
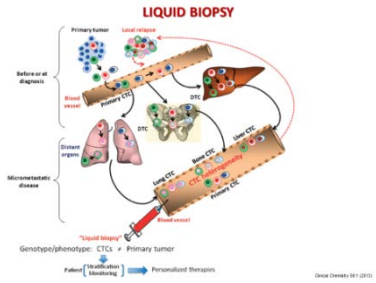
Mutational analysis of single circulating tumor cells



Prof. Pinzani from Florence (I) spoke about this topic, pointing out that in order to understand biological heterogeneity it is necessary to learn how to profile the molecular contents of individual cells. Starting from this point, the speaker presented data on CTCs and single cell analysis produced by her team of researchers, highlighting the extreme heterogeneity of the





mutational status of single CTCs in metastatic breast cancer patients. The speaker also addressed the differences in mutational status between CTCs and the corresponding primary cell tissue. In conclusion Prof. Pinzani highlighted the exponentially increasing of technological development in CTC field for a more suitable clinical application and the importance of the heterogeneity analysis as the basis for better understanding of the clonal evolution of the tumor and identifying some druggable mutations for precision medicine.

- **What are the main CTC enrichment and detection methods presented by the speaker?**
- **What are the main characteristics of CTCs?**
- **What are the main characteristics of Bulk versus single cells analysis?**
- **What are the DEP Cages?**
- **What are the main steps leading to the standardization of the CTCs analysis process?**
- **What are the main tools used in performing a liquid biopsy?**

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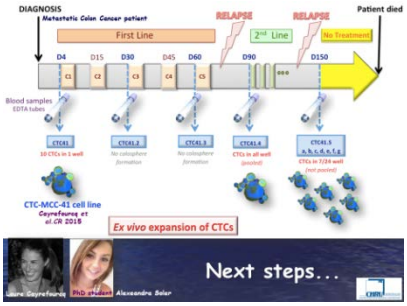
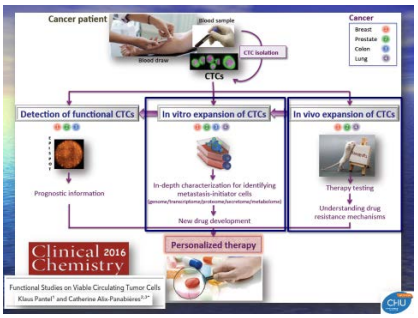
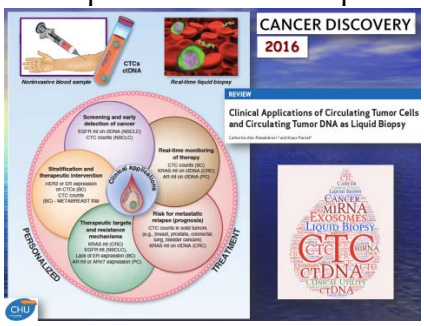
Detection, characterization and ex vivo expansion of viable circulating tumor cells.



Prof. Alix-Panabieres from Montpelliér (F) in her presentation talked about liquid biopsy and CTCs, coming from primary tumors and after, from metastases. In the first part of her presentation spoke about the history of the discovery and the setting of CTCs, resulting in the production of 1 permanent cell line called CTC-MCC-41, characterized by epithelial, mesenchymal, stem cell and oncogene properties. This discovery allowed the speaker and her team of researchers to perform functional studies on the biology of special CTCs, in vitro/in vivo drug testing and understanding drug resistance mechanisms. In the second part of her presentation the speaker presented data derived from studies conducted on tumor cells taken from patients. With this technology the speaker was able to detect PD-L1 expression on breast cancer CTCs pointing to potential new cell search use and setting new anti-PD-L1 therapies. In the last part of her presentation talked about the discovery of other circulating biomarkers, thanks to the Cancer-ID EU Konsortium 2015-2020 collaboration.





- **What are the main potentials of the molecular characterization of CTCs ?**
- **What are the main steps performed by the speaker in the discovery of CTC-MCC-41?**
- **What are the potentials showed by the antibodies targeting the PD-L1 checkpoint?**
- **Why is PD-L1 expression in breast cancer rare?**

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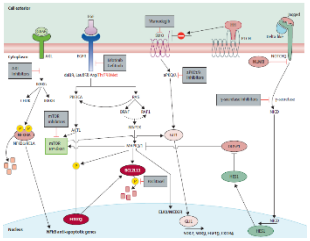
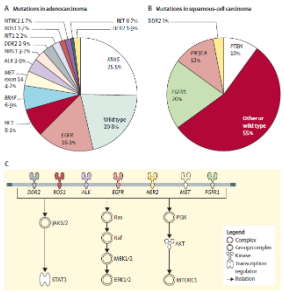
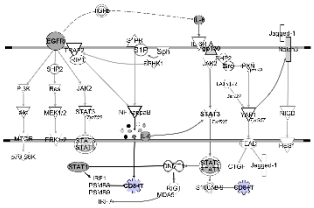
Future perspectives for treatment strategies in EGFR mutant NSCLC.



Prof. Rosell from Barcellona (E) presented data about the future perspectives for treatment strategies in cancer patients. The speaker spoke about compensatory signalling pathways resulting in acquired resistance to targeted therapies, highlighting the complexity of these pathways and the limited number of mutations derived from. More in particular Prof. Rosell talked about PC-9 cell line, and other cell line like H1975, STAT3 and SFK inhibitors. The speaker presented data produced with the research





model developed by his team of researchers, pointing out that this model involves STAT3 and YAP-NOTCH signalling pathways as a primary mechanism of resistance to single EGFR antagonist. In conclusion Prof. Rosell highlighted the no longer adequacy of the treatment performed with a single epidermal infusion of the growth factor receptor tyrosine kinase inhibitor.

- **What are the main signalling pathways involved in resistance mechanisms?**
- **What do STAT3 and YAP1 predict?**
- **What are the main characteristics of PC9 cell line?**
- **What is the role of EGFR in the signalling pathways presented bt Prof. Rosell?**

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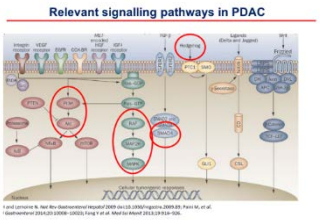
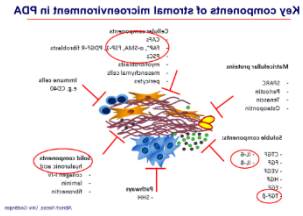
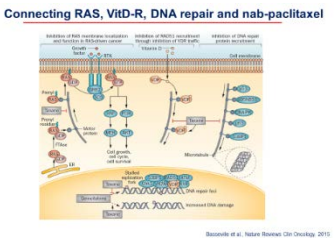
Clinical translation of biomolecular studies in pancreas cancer patients.



Prof. Tortora from Verona (I) spoke about clinical translation of biomarkers studies in pancreas cancer patients, pointing out that in the last decade a lot of pathways have been discovered, but no benefit these new pathways have driven to pancreas cancer patients. In the first part of his presentation the speaker spoke about the main characteristics of this cancer, explaining why the drugs are not able to reach the tumoral area. Than talked about stroma and its function in pancreatic cancer and inflammatory cells, cytokines, fibroblast and their role in building up dysplasia and creating the rights conditions leading to a protected tumor growth and progression. Prof. Tortora highlighted that all these events are functionally linked to each other in a complex and perfect network of signals. In conclusion the speaker pointed out the importance of genomic analysis and immunology's studies leading to unravelling these networks and shedding lights on the obscure features of this disease.





- **What are the main relevant signalling pathways in pancreatic cancer?**
- **What are the main key molecular mechanisms and potential novel vulnerabilities?**
- **What are the common mutations in pancreatic cells cancer?**
- **What are the key components of stromal environment in pancreatic cancer?**
- **What is the dual function of stroma in pancreatic cancer?**
- **Do the JAK Kinase inhibitors have a role in pancreatic cancer?**

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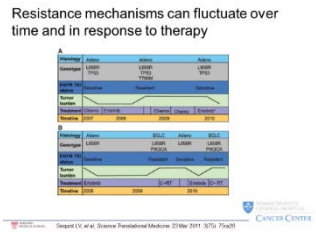
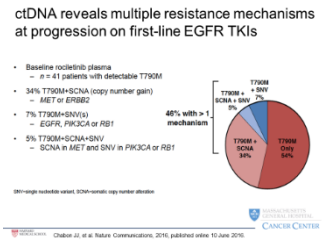
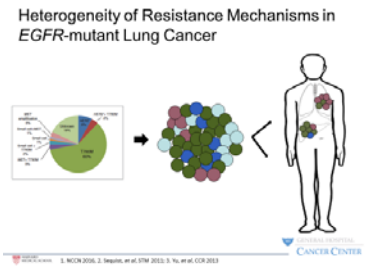
Heterogeneity of resistance mechanisms in EGFR-mutant Non Small Cells Lung Cancer.



Prof. Piotrowska from Boston (USA) spoke about heterogeneity of resistance mechanisms in EGFR-mutant NSCLC patients, pointing out that these mutations are present in about the 20% of patients with lung adenocarcinoma. The speaker talked about the history of the discovery of this mutation and the relative acquired resistance. The main part of her presentation was dedicated for explaining the mechanisms leading to acquired resistance and its relationship with heterogeneity. The speaker highlighted the necessity to discover more resistance mechanisms other than the binary "present/absence" classification of T790M. Qualitative assessments are also important for their role in therapeutic implications. The speaker stressed the necessity for implementing new methods, such as ctDNA-based testing, able to better capture the spectrum of clones present at the time of the acquired resistance. In conclusion the speaker highlighted the need for an early implementation of new combination strategies in the course of the treatment for targeting the inhibition of multiple clones and for inducing more durable remissions.





- **What are the main mechanisms of resistance present in lung adenocarcinoma patients?**
- **How many biopsies are needed for discovering the full heterogeneity of a resistant cancer?**
- **What do the presence of multiple resistance mechanisms predict about the outcome of T790M-target therapy?**
- **What is the consequence of heterogeneity mechanisms in EGFR-mutant lung cancer patients?**

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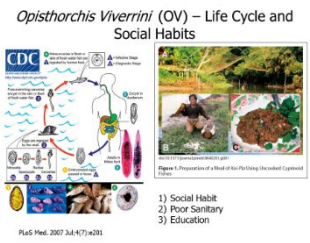
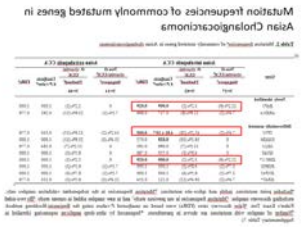
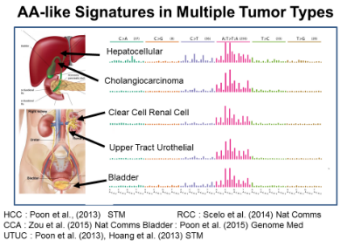
Asian Cancer Genomics and Its Clinical Implications



Prof. Bin Tean Teh from Singapore (SGP) presented data taken from literature and studies conducted by his team of researchers. At the beginning of his presentation pointed out the causes for the very high prevalence and incidence of cholangiocarcinoma (CCA) in people living in the Nord Est of Thailand, stressing the role of metacercariee, particularly Opisthorchis Viverrini (OV), in developing this type of cancer. The speaker presented data about exome sequencing of Ov associated CCA, highlighting the main mutations in chromatin enzymes and the genomic heterogeneity related to different etiological factors and their clinical implications such as clinical outcome. In the second part of his speech talked about the presence of a specific mutation, the so called "AA signature" in other types of cancer, like Renal, Urothelial and Bladder cancer. Than spoke about Breast Fibroepithelial Tumors, a particular type of tumors very different from breast carcinomas, and their subtypes: Fibroadenomas and Phylloides tumors, highlighting that the only treatment option for these tumors in surgery. Finally, the speaker presented data on a novel diagnostic tool finalized with the collaboration of a worldwide team of researches.





- **What are the life cycle of OV and the social habits surrounding its development?**
- **What are the main mutations in chromatin enzymes in cells of CCA patients?**
- **What are the main genomic heterogeneity related to the different etiological factors?**
- **What are the main characteristics of the AA signature?**
- **What are the main chracteristics of the Brast Fibroepithelial Tumors?**

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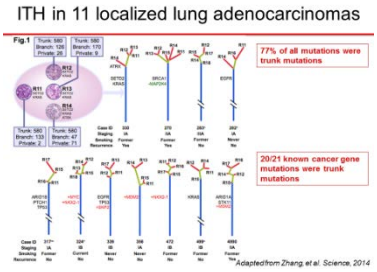
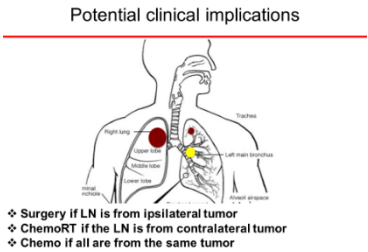
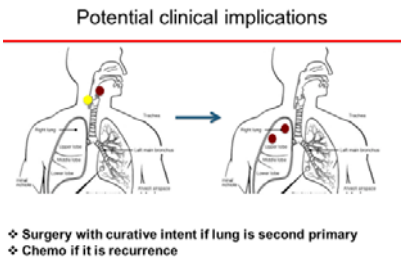
The potential impact of intra-tumor heterogeneity on biopsy and molecular profiling in lung cancer



Prof. Zhang from Houston (USA) in his very interesting talk spoke about inter-tumor and intra-tumor heterogeneity by presenting data on 6 real patients and the decisions taken for their diagnosis and treatment. The speaker highlighted that the inter-tumor heterogeneity can analysed from 2 different points of view: difference between primary tumors and distant metastases and difference between multiple synchronous primary tumors. Thanks to the clinical data of these 6 patients the speaker was able to give very comprehensive answers to the aroused questions. In conclusion the speaker highlighted that genomic profiling may provide additional information to the clinicopathological assessment in distinguishing multifocal primary lung cancers from intrapulmonary metastases, giving the opportunity to distinguish disease recurrence versus second primary cancers.





- **What are the main clinical implications in patients with lung cancer?**
- **How different are different synchronous tumors within the same patient?**
- **How different are metastases from primary tumors?**
- **How complex is the disease within a single tumor of lung?**
- **How different are cancers of the same histopathological type in different patients?**

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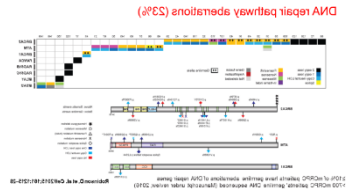
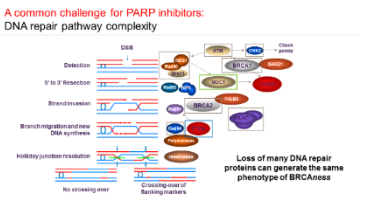
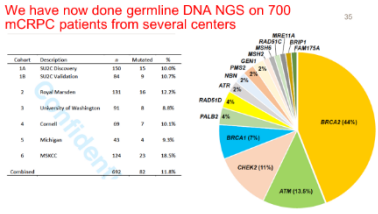
Molecular predictive biomarkers for target agents in prostate cancer.



Prof. De Bono from London (UK) spoke about genomics of prostate cancer, highlighting that in patients suffering from advanced prostate cancer there are more than 23% of cases characterized by the presence of DNA repair pathway aberrations. The speaker presented data on a particular subclass of prostate cancer with DNA repair defects, vulnerable to synthetic lethal therapeutic strategies utilising PARP inhibitors. Some trials were performed on this topic, with the aim to identify predictive biomarkers suitable for PARP inhibitor antitumor activity in CRPC patients. The speaker presented and deeply discussed these data highlighting that the treatment of metastatic prostatic cancer is changing rapidly thanks to these studies. In conclusion Prof. De Bono pointed out that molecular stratification for CRPC was able to identify very important therapeutic implications through a synthetic lethal strategy.





- **What about Prostate cancer genomics?**
- **What is the target of the so called "Synthetic lethal strategies"?**
- **What are the main characteristics of DNA repair defects in mCRPC patients?**
- **What is the response to olaparib in sporadic mCRPC patients?**
- **What are the main conclusions of the TO-PARP trial?**

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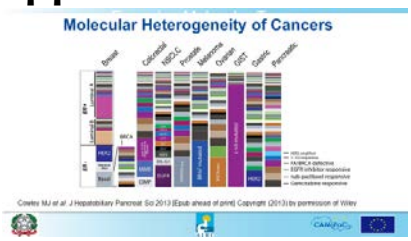
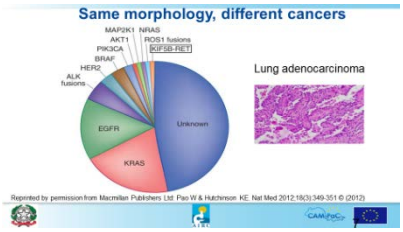
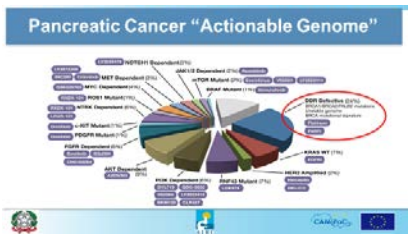
Next generation histopathological diagnosis for precision medicine in solid cancers "from genomics to clinical application"



Prof. Scarpa from Verona (I) spoke about this topic by presenting interesting data on histopathology of liver carcinoma and pancreatic cancer linked to the main molecular heterogeneity present in these diseases. The speaker highlighted the importance to identify the correct methods and also the right tissues to be used in diagnosis from a quantitative and qualitative point of view. One very important issue is linked to a better selection of patients to be included in the clinical studies in order to obtain better answers from a research and a clinical application point of view. The main part of his talk was spent in presenting data derived from the histopathological analysis of tissue's specimens taken by pancreas cancer lesions. The speaker particularly, highlighted the importance to select the correct tissue between cells, stroma and inflammatory agents in order to perform the correct diagnosis and to choose the correct therapeutic strategies.





- **What do the speaker mean when addresses the concept of Cancer as a tissue?**
- **What are the main cancer diagnosis tasks?**
- **Why is it necessary a better selection of patients for a clinical and sequencing trials from the speaker point view?**
- **What are the main characteristics of the qualitative and the quantitative diagnosis strategies?**

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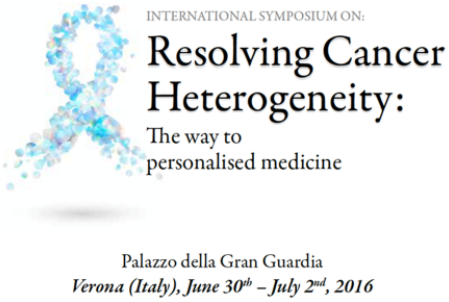

These are only some of the topics addressed in the congress's sections

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