The Future of Genetics in Medicine and beyond
Turin (Italy), June 22-23, 2017
Highlights

Introduction

Prof. Amoroso, chairman of the symposium, opened the congress, by highlighting the role played by Genomics in Regenerative and Precision Medicine. "Genomics can be considered the most advanced field of Genetics, for the ability to identify individual differences that can explain a significant part of the state of health and disease" the speaker pointed out. The main topics discussed in this symposium were about genomics, epigenomics, personalized medicine, pharmacogenomics, new molecules, target therapy, genome editing and finally about gene therapy. The congress has been attended by many of the top researchers of this field coming from Italy, other European and extra-European countries, together with many young physicians attending the University of Turin.

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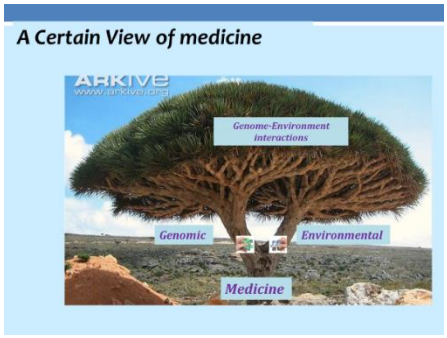
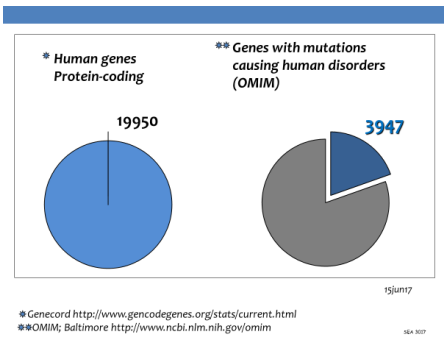
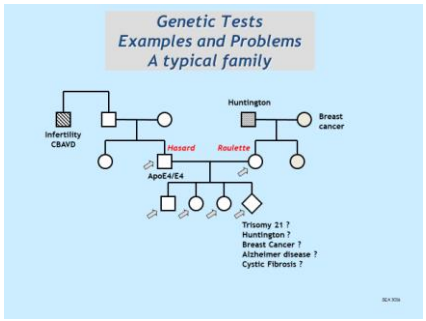
The future of genetic medicine: medical and ethical considerations



The future of genetic medicine: medical and ethical considerations, was the topic discussed by Prof. Antonarakis in his lecture. The speaker, coming from Geneve (CH), went deeper in his talk and presented very interesting data on genome variability till to phenotype. More in particular, Prof. Antonarakis spoke about genome inheritance, germline, normal somatic and cancer cell somatic mutation rate. Thanks to these mutations, we are very different one to each other, the speaker pointed out. In the main part of his lecture, Prof. Antonarakis presented very interesting data on genomic medicine as personalized or also precision medicine, more in particular he spoke about prediction, diagnosis, prognosis and treatment. The speaker presented also data on the main diseases due to genetic variations like achondroplasia, breast cancer, Alzheimer disease and on genomic analysis for diagnosis. In the second part of his lecture, Prof. Antonarakis spoke about the diagnostic level of the genomic medicine and about the genomic elements like, protein coding, long and small non-coding RNA and pseudogenes. Finally, the speaker presented very interesting data on the genomic clinic dedicated to the diagnosis of mendelian disorders, identification of somatic causative mutations in cancer and to the genetic counselling of genomic test. Prof. Antonarakis talked also about the Genetic clinic experience on 529 cases characterized by 35% of pathogenic variant found, 13% of variants of unknown significance and on 52% of nothing found. In the last part of his talk, the speaker presented very interesting data on genomic homozygosity, the related diseases and the available treatments and spoke about myGenome a project able to identify a specific genome sequencing of any people submitting to this examination.





- What is the goal of genetic medicine, from the speaker point of view?
- How many are the DNA sequence variants, based on the data presented by the speaker?
- How many mutations have any new born, based on the data presented by the speaker?
- What's about genomic and environmental medicine based on the data presented by the speaker?
- What's about the past and the future of genomic medicine from the speaker point of view?
- How many time do we practice genomic medicine in our medical activity, from the speaker point of view?
- What's about the myGenome project from the speaker point of view?
- What are the main problems linked with the myGenome analysis

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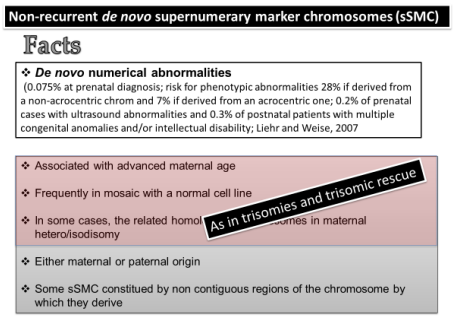
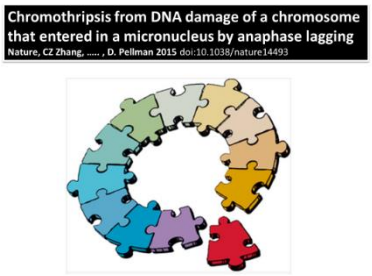
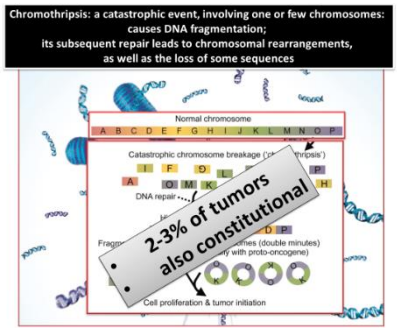
Genomic Medicine



Prof. Zuffardi from Pavia (IT), spoke about Genomic Medicine. The speaker talked about trisomies and their legacy. Going deeper in her lecture, Prof. Zuffardi presented very interesting data on the maternal age related to its effect in trisomies and on aneuploidy. In the main part of her talk, Prof. Zuffardi spoke about the relationship between trisomy and the mother age and presented very interesting data on the so called "Trisomic rescue" leading to mosaicism with both a normal and a trisomic cell line, either confined to the placenta or present in the embryo as well. The speaker presented also very interesting data on the non-recurrent de novo supernumerary marker chromosomes, that are associated with advanced maternal age, frequently in mosaic with a normal cell line. Finally, Prof. Zuffardi spoke about chromothripsis characterized by a DNA damage of a chromosome entered in a micronucleus by anaphase legging and presented very interesting data given by a genomic study running in her center on 8 cases analysed through the whole exome sequencing. In conclusion, the speaker pointed out that de novo supernumerary marker chromosomes are the remnants of the supernumerary chromosome present in the trisomic zygote and that chromotripsis has already been suggest being at the basis of ring cancer chromosomes.





- What are the main characteristics of the Trisomy rescue, based on the data presented by the speaker?
- What are the main effects of chromothripsis based on the data presented by the speaker?
- Is chromotripsis at the basis of de novo supernumerary marker chromosomes, based on the data presented by the speaker?
- Why the prenatal genetic counselling for de novo supernumerary marker chromosomes is challenging from the speaker point of view?
- What's about the results of the genomic study presented by the speaker?

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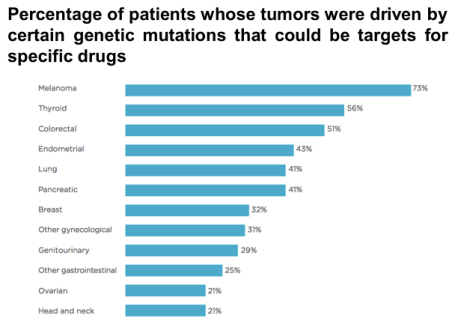
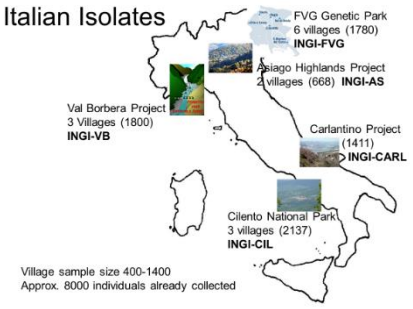
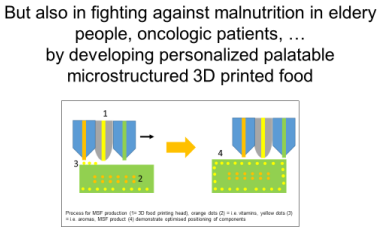
Personalised Medicine



Personalised Medicine, was the topic Prof. Gasparini spoke about in his lecture. The speaker coming from Trieste (IT), started his talk, by presenting very interesting data on pharmacogenetics. Going deeper in his lecture, Prof. Gasparini spoke about the inefficiency of drugs adminstered to the wrong patients, intended as non-responder patients. In the main part of his lecture, the speaker presented very interesting data on his research on genetic isolates populations living in many specific areas of Italy. Prof. Gasparini talked also about pharmacogenetics in these isolated populations and presented very interesting data on the breast cancer treatment. In the last part of his lecture the speaker presented very interesting data on the relationship between genes, lifestyle, taste and nutrition, given by data collected in people living in the so called "silk road", in babies in the waning time, in red wine drinkers, in people affecting by obesity, smokers and athletes. In conclusion, Prof. Gasparini pointed out that personalized medicine offers significant benefits, especially for chronic and complex diseases.





- What are the main advantages of the genetic isolates, based on the data presented by the speaker?
- How many genetic isolated people have been studied by the speaker and his coll?
- What's about the toxicity data found in the FVG cohort, based on the data presented by the speaker?
- What's about the genetic variations leading to different infants' feeding behaviour at weaning, based on the data presented by the speaker?
- What is the gene variation typical of people drinking red wine, based on the data presented by the speaker?
- What's about the genetic variations present in smokers and in people loving physical activity, based on the data presented by the speaker?

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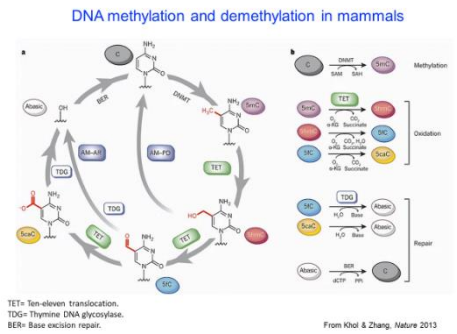
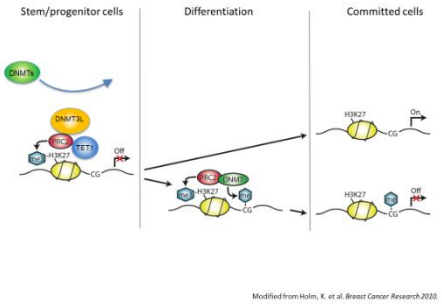
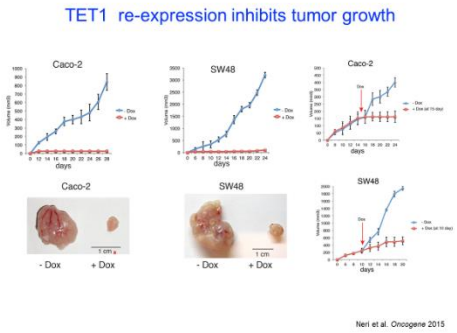
Epigenetics and Epigenomics



Epigenetics and Epigenomics, was the topic discussed by Prof. Oliviero. The speaker, coming from Turin (IT), spoke about the new generation sequencing. Going deeper in his lecture, Prof. Oliviero presented very interesting data on epigenetics and more in particular on DNA methylation, hydroxy methylation, histone modifications, chromatin remodelers and higher order chromatin structure. In the main part of his lecture, the speaker talked about DNA methylation, by presenting very interesting data on the main modifications at the chromatin and enzymes levels and about DNA demethylation thanks to serious oxidative reaction. Prof. Oliviero presented also very interesting data given by a genomic study running in his center on the so called "Polycomb complex" able to block the methylation process at the stem/progenitor cell level.



In the second part of his presentation, the speaker talked about another experiment running at his center on the possibility to promote active demethylation on the methylated gene levels and demonstrated that is TET1 the molecule responsible for this downmethylation. Prof. Oliviero presented also very interesting and impressive data on the effects of TET1 on tumor growth and on the enzymatic mechanisms responsible for intragenic DNA methylation and on its biological role in preserving cells against cancer modifications.



- How does the DNA of the zygote to give rise to the different cells of the body from the speaker point of view?
- What is the main distribution of the DNA methylation based on the data presented by the speaker?
- What have we learned in the last years on the DNA methylation, based on the data presented by the speaker?
- What is the meaning of methylation in the cells from the speaker point of view?
- How stable is the DNA methylation, based on the data presented by the speaker?
- Who is responsible for intragenic DNA methylation?
- What is the functional role of gene body DNA methylation?

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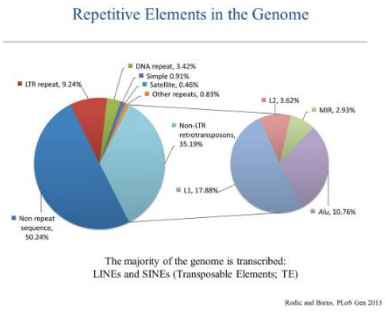
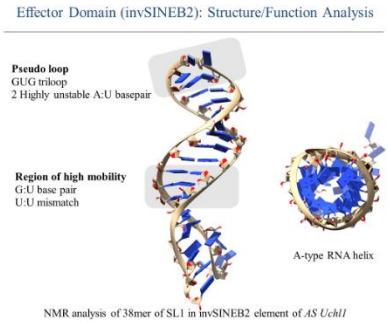
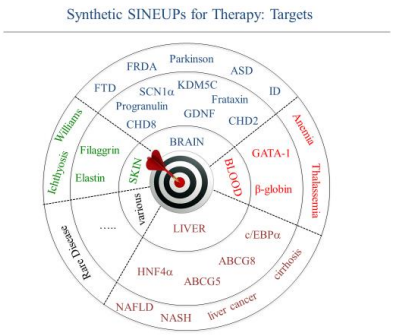
The new world of RNAs



The new world of RNAs, was the topic discussed by Prof. Gustincich. The speaker, coming from Genoa (IT), talked about the transcriptional landscape of the mammalian genome and about the repetitive elements present in the genome. Going deeper in his lecture, Prof. Gustincich presented very interesting data on the antisense transcription, the mammalian transcriptome and the related neurodegenerative diseases. In the main part of his lecture the speaker talked about the antisense IncRNAs in Parkinson disease starting from studies running on animal models. Prof. Gustincich presented also very interesting data on the identification of the Effector domain-binding protein, its functions and activity. In the second part of his presentation, the speaker talked about the identification of natural human and about the role played by the synthetic SINEUPs from the molecular biology, protein production and the therapeutic point of view. Finally, Prof. Gustincich presented other very interesting data on two therapeutic applications, the first one on the use of synthetic SINEUPs for the haploinsufficiency treatment and the second one microphtalmia with skin lesions. In conclusion, the speaker pointed out that the 80% of human INCRNAs are TEs-containing and, more important, 405 of nucleotides present in IncRNAs are TEs.





- What is the definition of Sense/antisense transcription, based on the data presented by the speaker?
- What is the role played by the antisense IncRNAs in neurodegenerative diseases?
- What are the main mouse loci involved in the antisense IncRNAs leading to Parkinson disease?
- What's about the new functional class of natural antisense IncRNAs presented by the speaker?
- What is the Effector Domain structure and function, based on the data presented by the speaker?
- Is the effector domain (invSINEB2) sequence an internal ribosomal entry site?
- What's about the IRES activity meaning from the speaker point of view?
- What are the main target of the synthetic SINEUPs for therapy, based on the data presented by the speaker?

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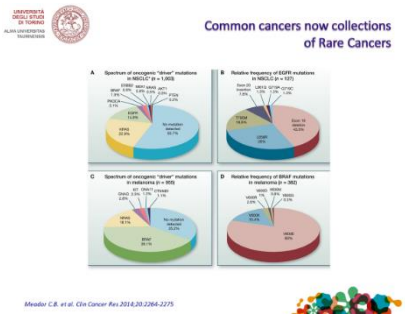
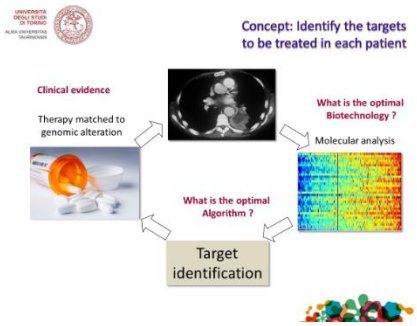
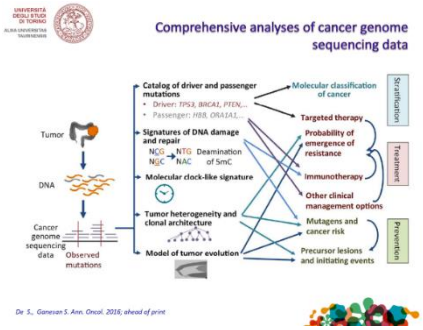
How genomic approaches will change the diagnosis of tumours



How genomic approaches will change the diagnosis of tumours, was the topic of Prof. Scagliotti presentation. The speaker, coming from Turin (IT), talked about the coming of targeted therapies and the role of the immune system in cancer. Going deeper in his lecture, Prof. Scagliotti presented very interesting data on the main molecular phenotyping, tumor-directed. In the main part of his lecture, the speaker talked about tumor and molecular heterogeneity applied to new clinical trial designs like the basket and the umbrella studies. Prof. Scagliotti, more in particular, presented very i interesting data on the rationale of these two types of studies and about liquid biopsy as a new test for a better estimation of the dynamic changes of cancer during time. In the last part of his lecture, the speaker talked about immunotherapy and its new frontier, characterized by the neo-epitope load in lung cancer. Finally, Prof. Scagliotti presented a very interesting precision medicine research strategy, based on the detection of the evolution of the mutational processes typical of the dynamic nature of cancer. In conclusion, the speaker pointed out that for an effective drug development in the genomic era it is of high importance the use of genomic tools for refining patient selection, by using the extreme responders.





- What are the main patterns of somatic genome alterations in adenocarcinoma and squamous cell carcinoma of the lung cancer, based on the data presented by the speaker?
- What are the main mutations of the non-smokers lung cancer patients, based on the data presented by the speaker?
- What are the key points of the basket and the umbrella studies, based on the data presented by the speaker?
- What are the key points of cancer immunotherapy, based on the data presented by the speaker?

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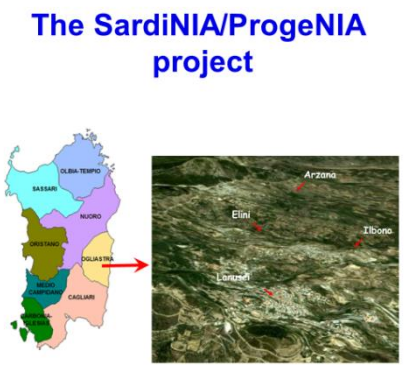
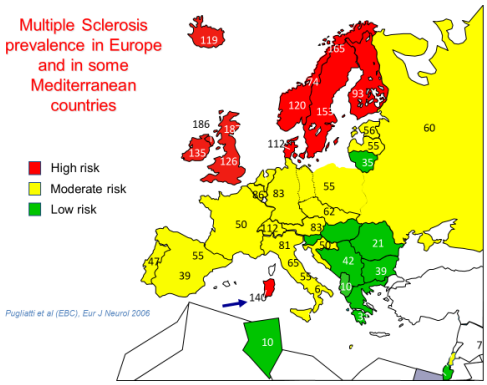
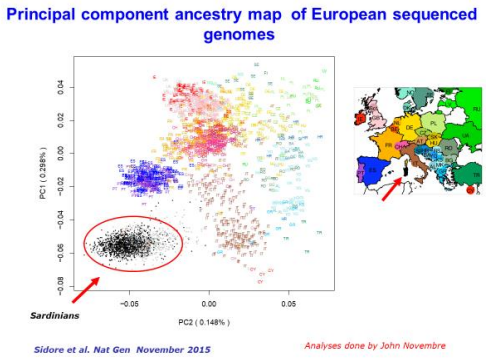
Genomic analyses for susceptibility to complex diseases



Prof. Cucca coming from Cagliari (IT) spoke about Genomic analyses for susceptibility to complex diseases and presented very interesting data on monogenic vs multifactorial traits. Going deeper in his lecture, Prof. Cucca talked about traits divided into discrete and quantitative and presented very interesting data on the GWAS revolution and on the tests to be performed. In the main part of his lecture, the speaker talked about multifactorial diseases and more in particular on the Sardinian project on Multiple Sclerosis – type 1 diabetes patients and on the general population cohort study. Prof. Cucca, presented very interesting data on the main characteristics of this project like the deep extraction of the genetic information based on the DNA and RNA sequencing project. In the second part of his lecture, the speaker talked about another project taking part of the main Sardinia project, that is the immunity/autoimmunity study, aiming to use genetics as a tool to discover the biology of specific autoimmune diseases and genetic associations for revealing drug targetable pathways. Finally, the speaker presented very interesting data on the immune cell project analysis based on fractionation of immune cell subtypes by FACS, and highlighted that the same DNA variants associated with the quantitative traits discovered, are also associated with immune-related diseases.





- What's about the Sardinia/ProgeNIA project, presented by the speaker?
- What are the key points of the DNA sequencing project, presented by the speaker?
- What's about the RNA sequencing project and its experimental design and data set, presented by the speaker?
- How many proteins of the immunity/autoimmunity project are druggable based on the data presented by the speaker?
- Why findings obtained in Sardinia should be relevant for the rest of humanity, from the speaker point of view?

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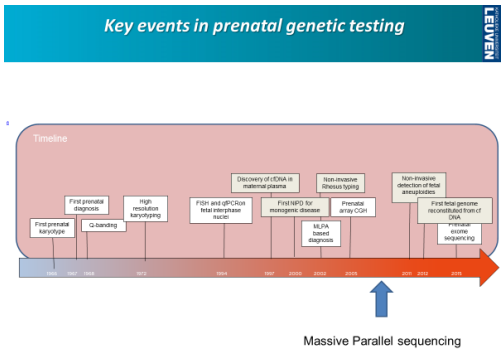
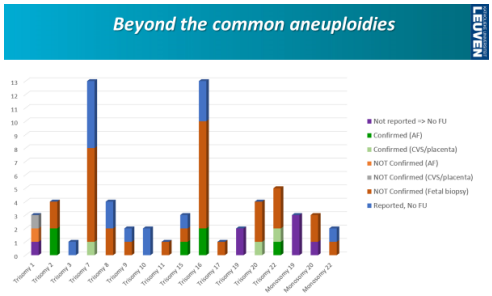
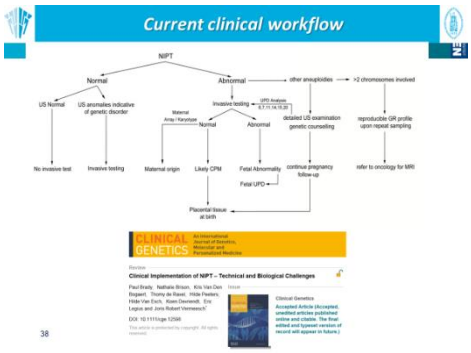
NIPT: non-invasive prenatal testing on fetal DNA circulating in maternal blood



Prof. Vermeesch from Leuven (BE), spoke about NIPT: non-invasive prenatal testing on fetal DNA circulating in maternal blood and presented very interesting data starting from the key events in preimplantation genetic testing. Going deeper in his lecture, Prof. Vermeech talked about prenatal diagnosis and NIPT. In the main part of his talk, the speaker presented very interesting data on the application of the massive sequence technology for the fetal aneuploidies detection following maternal blood samples. More in particular Prof. Vermeech talked about the main parameters for the chromosome detection, like the Z-score, the SD-score and others, enabling to remove the false positive due to maternal CNVs. The speaker presented also very interesting data on the rate of success in the assessment of aneuploidies through the NIPT application. In the second part of his lecture, Prof. Vermeech talked about the fetal and the maternal segmental imbalances and presented very interesting data on the clinically relevant maternal incidental findings detected with NIPT. In conclusion, the speaker pointed out that the NIPT application can improve the pregnancy management and can be a challenge for genetic counselling.



Determination of aneuploidies can avoid UPD and fetal aneuploidy mosaicisms. Moreover, it helps explain IUGR due to abnormal placental karyotype



- What is the right pregnant time for the NIPT application, based on the data presented by the speaker?
- What's about the applied methodology for NIPT at the Leuven Center?
- What's about the diagnostic experience from 2013 to 2017, presented by the speaker?
- How many aneuploidies can be detected thanks to the NIPT application, based on the data presented by the speaker?
- What's about the potentiality of the repeat sampling for the detection of reproducible aberrant GR profiles, based on the data presented by the speaker?

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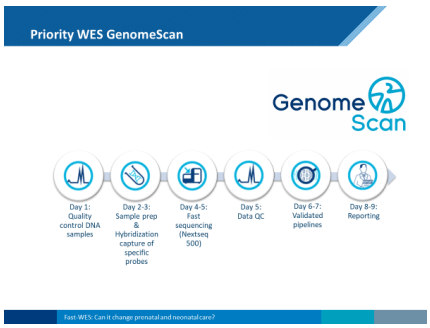
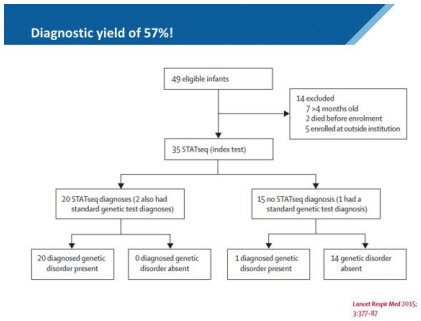
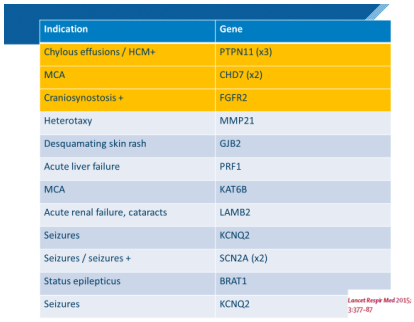
Fast-track WES: can it change prenatal and neonatal care?



"Fast-track WES: can it change prenatal and neonatal care?", was the topic discussed by Prof. Santen from Leiden (NL), more in particular the speaker presented very interesting data starting from this question: what is the most important factor holding back wider application of WES/WGS? And his answer was: the time. Going deeper in his lecture, Prof. Santen talked about the technical fast-WES feasibility and cost. In the main part of his lecture, the speaker presented very interesting data on fast-WES application in neonatal and prenatal time. Speaking about neonatal WES application, Prof. Santen presented very interesting data given by his clinical activity at the Leid University medical Center on its positive experiences, but also on its limits and discussed all the related issues and talked about the overall outcome and all the genetic diagnoses performed thanks to the application of this technique. In the second part of his lecture, Prof. Santen presented very interesting clinical cases on the fat-WES prenatal application. In conclusion, the speaker pointed out that fast-track WES will change medicine, but it seems to be more beneficial in the prenatal application than in the neonatal one.





Indication	Gene
Chylous effusions / HCM+	PTPN11 (x3)
MCA	CHD7 (x2)
Craniosynostosis +	FGFR2
Heterotaxy	MMP21
Desquamating skin rash	GJB2
Acute liver failure	PRF1
MCA	KAT6B
Acute renal failure, cataracts	LAMB2
Seizures	KCNQ2
Seizures / seizures +	SCN2A (x2)
Status epilepticus	BRAT1
Seizures	KCNQ2

Lancet Respir Med 2015; 3:377-87

- What is the most important factor holding back wider application of WES/WGS?, based on the data presented by the speaker?
- How much additional value does fast-WES have in the NICU population, based on the data presented by the speaker?
- Is fast-WES completely useless?
- What are the main genetic spot-diagnoses, based on the data presented by the speaker?
- What's about the three prenatal clinical cases presented by the speaker?

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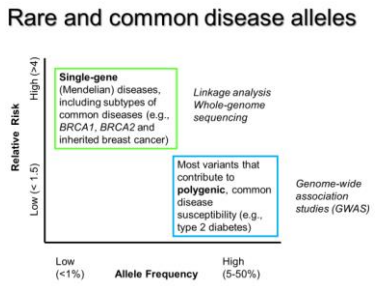
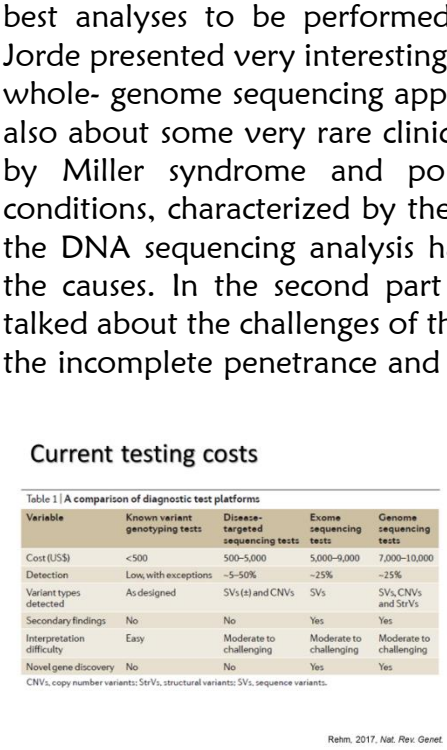
Genomics screening for genetic diseases



Prof. Jorde from Salt Lake City (USA), spoke about genomics screening for genetic diseases. More in particular, the speaker talked about the context in which genomic screening can be used and about the challenges facing genomic analysis, testing and scrrening. In the main part of his lecture, Prof. Jorde presented very interesting data on prenatal screening and diagnosis and on newborn screening. Going deeper in his lecture, the speaker spoke about the differences between the single-gene diseases and the polygenic diseases and about the best analyses to be performed. More in particular Prof. Jorde presented very interesting data on the GWAS and the whole- genome sequencing application. The speaker talked also about some very rare clinical cases of families affected by Miller syndrome and pointed out that in similar conditions, characterized by the presence of very few data the DNA sequencing analysis has the potential to identify the causes. In the second part of his lecture, Prof. Jorde talked about the challenges of this diagnostic technique, like the incomplete penetrance and sensitivity, the detection of variants of unknown significance, cost and reimbursement and education of the health care professional and presented very interesting data on a polygenic risk score, composed by the effects of multiple low-penetrance variants. Finally, the speaker pointed out that a very high rate of physicians has a very poor knowledge of genetic. In conclusion, Prof. Jorde, pointed out that whole-exome and whole-genome sequencing are now affordable and commonplace, but interpretation remains the major challenge.



- What's about the correlation between genetics and life style from the speaker point of view?
- When is it better to perform a whole-genome sequencing analysis, based on the data presented by the speaker?
- What are the main diseases to be diagnosed thanks to the GWAS application?
- What's about the cost of the GWAS, based on the data presented by the speaker?
- How many variants has any person, based on the data presented by the speaker?
- What's about the incidental findings detected thanks to the genomic testing and screening application?
- What are the main differences between the single-gene and the complex disease in DNA coding and non-coding, based on the data presented by the speaker?

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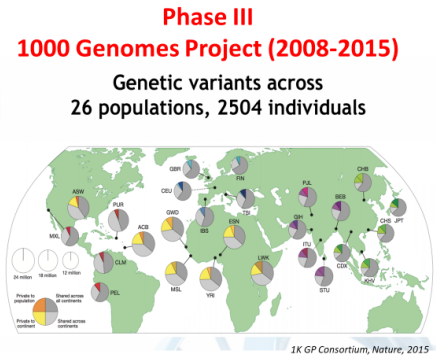
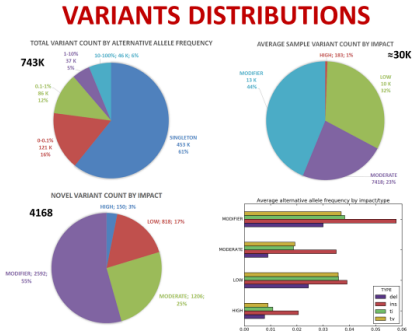
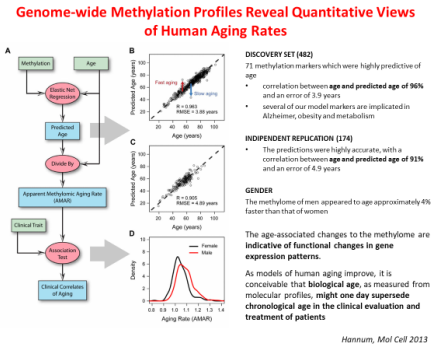
Genomic and epigenomic variability in complex diseases



Genomic and epigenomic variability in complex diseases, was the topic discussed by Prof. Matullo from Turin (IT), more in particular the speaker talked about the 1000 genomes project, characterized by the detection of genetic variants across 26 population around the world, collecting 2504 individuals. In the main part of his lecture, Prof. Matullo presented very interesting data on the Italian population involved in this genomic study and highlighted that this population is characterized by a very high variation level compared to the other european populations. The speaker talked also about the EPIC study, a European project involving also Italy and presented very interesting data on the CVD sub-study, characterized by the detection of 15 new risk loci for CAD. Speaking about cancer, Prof. Matullo presented a lot of data on the genetics of mesothelioma and its polygenic risk. Speaking about genomics and precision prevention, the speaker highlighted that the polygenic risk score is useful for the risk reduction determination in CHD patients. In the second part of his lecture, Prof. Matullo presented very interesting data on epigenomics and more in particular on the DNA methylation profile detected in different cell types and on the correlation between DNA methylation and biological aging, by highlighting that, thanks to this technology it is possible to identify people with accelerating aging due to specific dietary and life style profiles. In conclusion, Prof. Matullo pointed out that genomics and epigenomics are useful for understanding the disease mechanisms, primary and secondary prevention and for tailoring therapies.





- What is main characteristic of the Italian population involved in the 1000 genome project, based on the data presented by the speaker?
- What's about the variants distribution from the speaker point of view?
- What's about the role of the polygenic risk in determining the absolute risk reduction for CHD, based on the data presented by the speaker?
- What is the correlation between DNA methylation changes in peripheral blood samples and the lung cancer risk, based on the data presented by the speaker?
- What's about the correlation between DNA methylation and the risk of mesothelioma?

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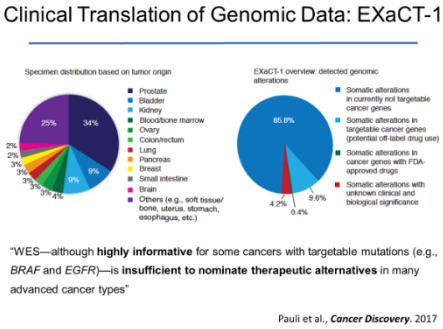
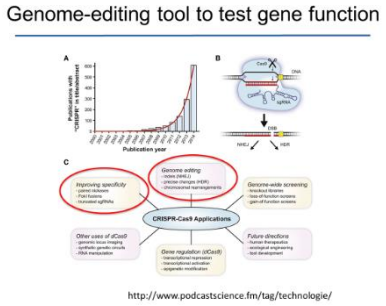
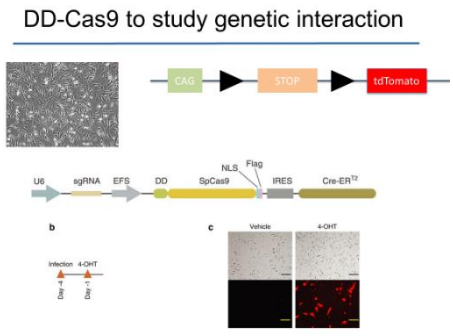
Personalised cancer therapy



Prof. Corbo from Verona (IT), presented very interesting data on Personalised cancer therapy. More in particular the speaker talked about precision oncology, challenges, possible approaches to the problem and about the results. Going deeper in his lecture, Prof. Corbo presented very interesting data, starting from the reality of precision oncology. The speaker highlighted that despite the amount of information discovered with the genetic studies, most of them showed correlation but not causation and, more important, poor clinical translation. Prof. Corbo, presented other very interesting data, showing that many diseases have complex genetic interactions and spoke about the limited feasibility of the integrated precision medicine platform for all cancer patients. In the main part of his lecture, the speaker presented very interesting data on pancreatic cancer and new possible approaches like to grow up models of disease for testing hypotheses like the human organoids and to develop tools to test the gene function. More in particular Prof. Corbo talked about the main characteristics of the Crispr/Cas 9 system, by highlighting that the Cas9 stabilization is possible. In the second part of his lecture, the speaker presented very interesting data on subtypes of pancreatic cancer not yet personalized due to many mutations, like the KRAS, that are the most important ones. Prof. Corbo spoke also about the identification of subtype-specific mechanisms of resistance. In conclusion, Prof. Corbo pointed out that there is the need to functionalize the genome in order to gain benefits from genomics analysis especially for those cancers yet quite unknown like the pancreatic cancer is.





- What's about the correlation between the amount of genetic mutations discovered and their clinical translation?
- How to functionalize the genome for cancer diagnosis and treatment, based on the data presented by the speaker?
- What's about the main problems of the pancreatic cancer from the speaker point of view?
- What's about the organoids model of pancreatic cancer presented by the speaker?
- What is the central function of CRISPR-Cas9 gene based on the data presented by the speaker?
- What are the main subtype-specific pancreatic cancer adaptive mechanisms, presented by the speaker?

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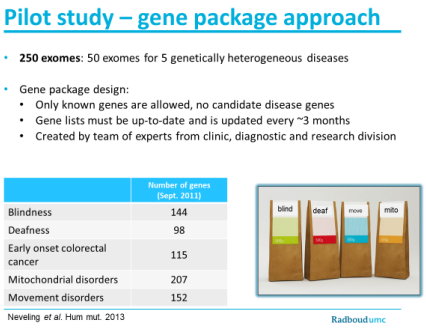
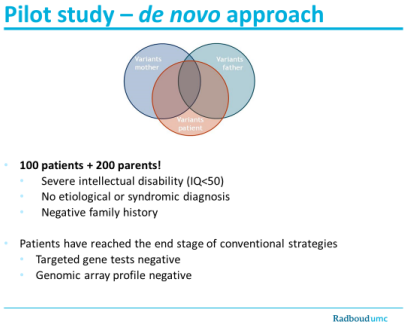
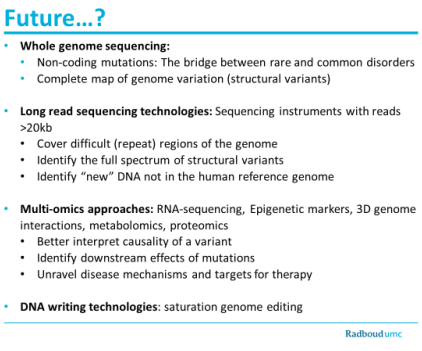
How the genomics era will change the diagnosis and treatment of the neurological diseases



"How the genomics era will change the diagnosis and treatment of the neurological diseases". The speaker, coming from Nijmegen (NL), presented very interesting data on the clinical exome sequencing. Going deeper in his lecture, Prof. Gilissen talked about a pilot study characterized by the evaluation of 250 exomes, composed by 50 exomes for 5 genetically heterogeneous diseases. In the main part of his lecture, the speaker presented very interesting data on the routinely clinical use of WES in his clinical center and on the disease panel evolution. Based on these data, Prof. Gilissen pointed out that NGS is improving the diagnosis yield for genetically heterogeneous disorders and that genetics is becoming more prominent in disease diagnosis and treatment. In the second part of his lecture, the speaker presented very interesting data on the de novo mutations in neurological diseases like autism or schizophrenia, given by a pilot study applying the de novo approach. Prof. Gilissen talked also about whole genome sequencing and the possibility to identify de novo mutations. Finally, the speaker talked about the possibility to open the genome analyses for all and presented very interesting data on the RUMC cohort of ID trios, a study running on 820 patient-parent trios for intellectual disability at RUMC. In conclusion, Prof. Gilissen pointed out that in the future, the whole genome sequencing will produce the complete map of the genome variation.





- How can we identify the genetic causes of the sporadic neurological diseases presented by the speaker?
- Why are these reproductively lethal disorders so frequent in our population?
- Is it possible to identify de novo mutations through the whole gene sequencing application, based on the data presented by the speaker?
- What is the future of the whole genome sequencing from the speaker point of view?

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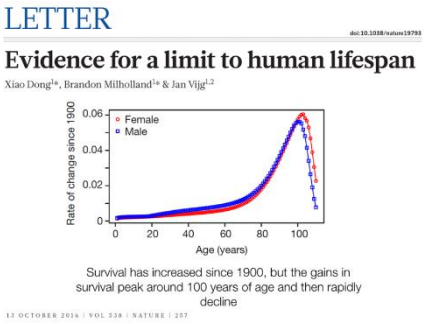
How the genomics era will change the diagnosis and treatment of heart diseases

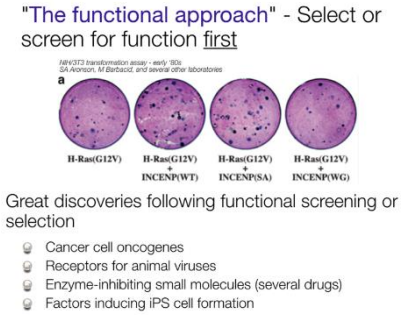

LETTER

Evidence for a limit to human lifespan

Xiao Dong[1]*, Brandon Milholland[1]* & Jan Vijg[1,2]

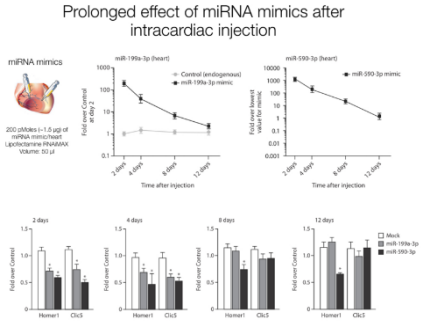
Survival has increased since 1900, but the gains in survival peak around 100 years of age and then rapidly decline

The main topic of Prof. Giacca presentation, was "How the genomics era will change the diagnosis and treatment of heart diseases". The speaker, coming from Trieste (IT), presented very interesting data on aging and its relationship with genetics. Going deeper in his lecture, Prof. Giacca talked about the main common degenerative conditions due to unrecoverable loss of post mitotic cells linked with the aging processes. In the main part of his lecture, the speaker presented very interesting data on Biotherapeutics to be used for the treatment of degenerative disorders and on the methods to be applied for their discovery. More in particular Prof. Giacca spoke about the so called "functional approach" and highlighted that great discoveries were made following functional screening or selection. The speaker presented very interesting data given by the application of the adeno-associated virus vectors (AAV) able to in vivo transduce post-mitotic cells against a myocardial infarction lesion in a selective manner. In the second part of his presentation, the speaker talked about cardiac regeneration and all the experiments performed on this topic and presented very interesting data on the effects of miRNAs on the hearth regeneration in large animals like pigs and mice.


"The functional approach" - Select or screen for function first

Great discoveries following functional screening or selection

- Cancer cell oncogenes
- Receptors for animal viruses
- Enzyme-inhibiting small molecules (several drugs)
- Factors inducing iPS cell formation


Prolonged effect of miRNA mimics after intracardiac injection

- How long shall we live, based on the data presented by the speaker?
- What are the main theories about aging, based on the data presented by the speaker?
- What are the main common degenerative conditions due to unrecoverable loss of post mitotic cells linked with the aging processes, presented by the speaker?
- How can we identify effective biotherapeutics for tissue degeneration, based on the data presented by the speaker?
- How to in vivo select genes able to counteract tissue degeneration?
- Is really the adult hearth a post-mitotic organ, based on the data presented by the speaker?
- What's about the effect in large animals, based on the data presented by the speaker?
- What's about the long-term effect, based on the data presented by the speaker?

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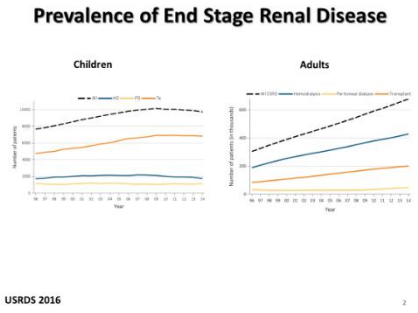
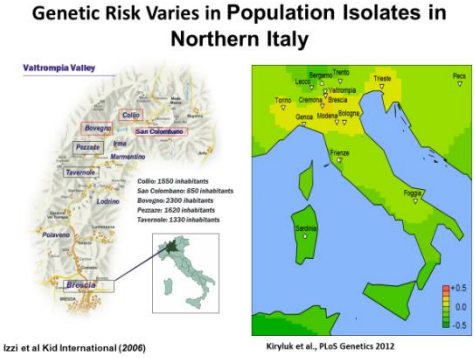
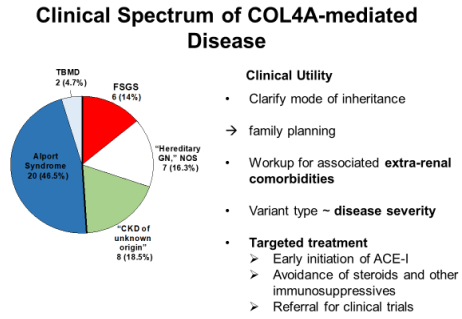
How the genomics era will change the diagnosis and treatment of kidney diseases



Prof. Gharavi from New York (USA), spoke about "how the genomics era will change the diagnosis and treatment of kidney diseases" and presented very interesting data starting from the prevalence of the end stage renal disease. Going deeper in his lecture, Prof. Gharavi talked about the causes of ESRN in children and adults and about the main questions raised by patients on this disease. In the main part of his lecture, the speaker presented very interesting data on the IgA nephropathy, its main characteristics, the involved genes and the geospatial risk model in 85 world populations. Speaking about Italy, Prof. Gharavi presented very interesting data on the association between IgAN genetic risk and well identified environmental factors. In the second part of his lecture, the speaker presented very interesting data on a clinical case of a 20 y.o. patient affected by kidney disease and impaired neurocognitive functions, with the 17q12 deletion. Starting from this case, the speaker went deeper and presented very interesting data on the relationship between the genomic disorders and the neurocognitive dysfunction in CKD patients. Finally, Prof. Gharavi talked about the exome sequencing and presented 2 clinical cases where the exome sequence was of high importance for diagnosis and for identifying the right treatment. In conclusion, the speaker pointed out that the exome sequencing can identify genetic disorders in 10% of adults with CKD.





- What are the main characteristics of the IgA nephropathy, based on the data presented by the speaker?
- What are the main environmental factors affecting the genetic risk for IgA nephropathy in Italy, based on the data presented by the speaker?
- What's about the exome sequencing utility in diagnosis, based on the data presented by the speaker?
- What are the main characteristics of the Alport syndrome, based on the data presented by the speaker?

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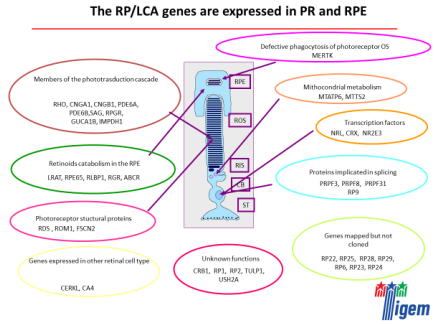
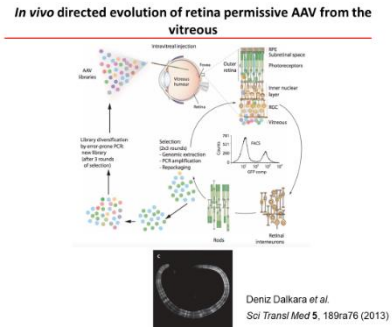
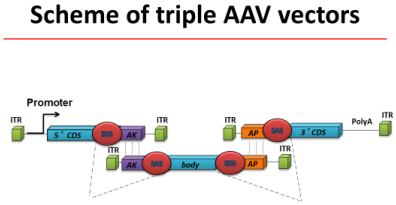
Medical application of gene therapy: the example of the diseases of the eye



Medical application of gene therapy: the example of the diseases of the eye, was the topic discussed by Prof. Auricchio from Naples (IT), more in particular the speaker presented very interesting data on untreatable inherited retinal diseases. Going deeper in his lecture Prof. Auricchio talked about the eye as a target for gene therapies. In the main part of his lecture, the speaker talked about the surgical delivery of viral vectors to the retina and presented very interesting data on adeno-associated viral vectors for in vivo gene transfer. In the second part of his talk, the speaker presented very interesting data on the gene therapy clinical trials for retinal diseases. More in particular Prof. Auricchio talked about the challenges linked with this gene therapy and presented very interesting data on the way to avoid subretinal delivery in very damaged retinas, on the treatment of dominant conditions like the dominant RHO mutations, on the treatment of advanced retinal degeneration like the optogenetic therapy and finally on the delivery of large genes. In conclusion, Prof. Auricchio pointed out that gene therapy is safe and effective in humans and dual and triple vectors expand AAV transfer capacity in the retina.





- How many people are blinded due to inherited retinal degeneration, based on the data presented by the speaker?
- What are the main surgical delivery of viral vectors to the retina, based on the data presented by the speaker?
- What's about the main three classes of viral vectors for retinal gene therapy, presented by the speaker?
- What are the main advantages and disadvantages of the AAV vector for in vivo gene transfer, based on the data presented by the speaker?
- What's about the scheme of triple AAV vectors, based on the data presented by the speaker?

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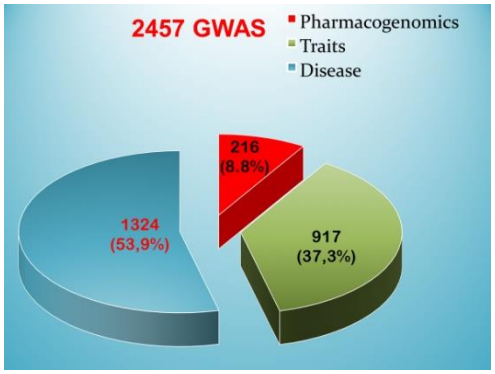
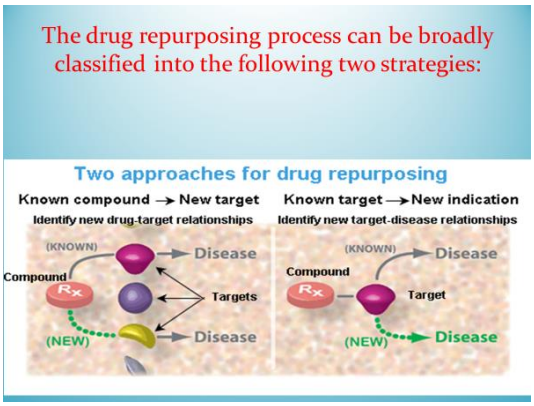
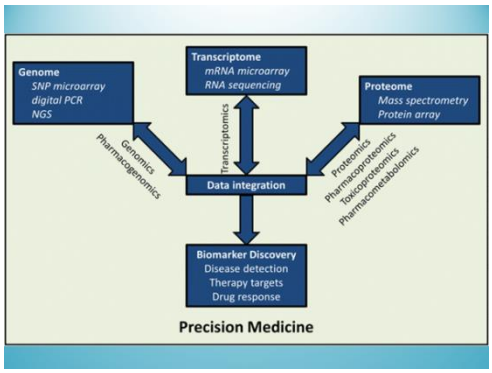
Introduction to Pharmacogenomics



Prof. Giardina from Rome (ITA), spoke about Introduction to Pharmacogenomics. More in particular, the speaker talked about the genetic contribution to the differentiation in the individual response to drugs, many examples of specific medications and associated pharmacogenomic consideration, the epigenetic regulation of pharmacogenomics and finally about the use of genomics for drugs reposition. Going deeper in his lecture, Prof. Giardina presented very interesting data on the pharmacogenomic biomarkers in relationship with GWAS studies. In the main part of his lecture, the speaker talked about the genetic testing required and recommended and about the actionable and the informative pharmacogenomic. More in particular Prof. Giardina pointed out that only 47 genes with germline variants have a PGx effect and presented very interesting data on the Abacavir hypersensitivity reaction. In the second part of his talk, Prof. Giardina spoke about genomic biomarkers as a tool for measuring the expression, the function and the regulation of a gene. The speaker presented a lot of data as relevant examples of epigenetic biomarkers of drug responses. In the last part of his lecture, Prof. Giardina presented very interesting data on drug repositioning, based on two main strategies: known compound for new target and known target for new drug indications. In conclusion, the speaker pointed out that a worldwide "network of networks" is expected to be the only platform able to capture the dynamic nature of the biological systems.





- What's about the epigenetics mechanisms related to the gene expression, based on the data presented by the speaker?
- How many are the well-known drugs for genetic diseases, based on the data presented by the speaker?
- How many are the drug databases for drug discovery presented by the speaker?
- What are the main pharmacogenomic biomarkers presented by the speaker?

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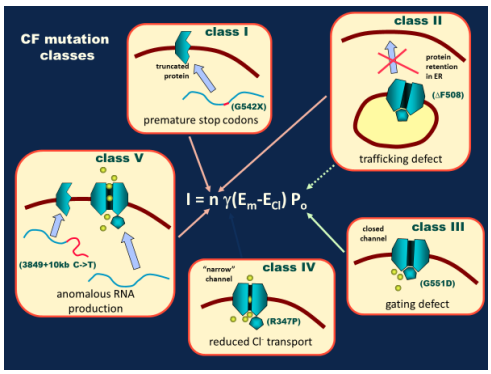
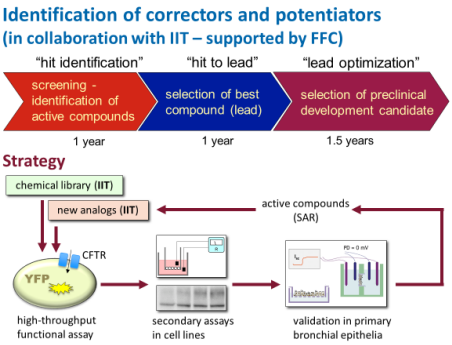
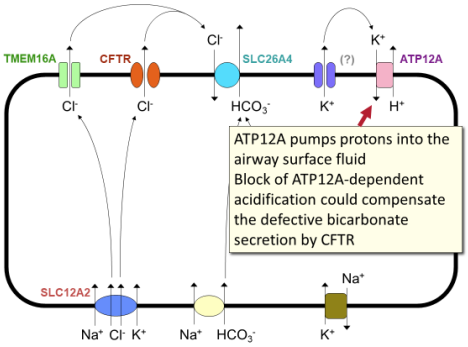
The search for new molecules for the treatment of genetic diseases. The special case of cystic fibrosis



The search for new molecules for the treatment of genetic diseases. The special case of cystic fibrosis, was the topic discussed by Prof. Galietta from Naples (IT), more in particular the speaker talked about the mutant proteins and about the alternative targets. Going deeper in his lecture, Prof. Galietta presented very interesting data on cystic fibrosis characterized by a defect in the airways epithelial cells, that changes the properties of apical fluid. In the main part of his lecture the speaker talked about the CRTR protein and the protein mutation classes and about the identification of drugs that rescue mutant CFTR. More in particular Prof. Galietta presented a lot of data on all the phases for the compounds delivery and optimization. Finally, the speaker talked about the preclinical development, characterized by the screening of 15.000 compounds in order to select only one pre-clinical candidate and about alternative targets to circumvent the CFTR functional defect. Prof. Galietta presented very interesting data on ATP12A that is a non-gastric form of the proton pump, that pumps protons into the airway surface fluid. In conclusion, the speaker presented all the sponsors taking part to this very important project aiming to the development of a very effective new treatment of the Cystic Fibrosis syndrome.





- **What are the main CF protein mutations presented by the speaker?**
- **What are the main druggabilities of mutant CFTR, based on the data presented by the speaker?**
- **What is the alternative target for cystic fibrosis, presented by the speaker?**
- **What's about the ATP12A proton pump based on the data presented by the speaker?**

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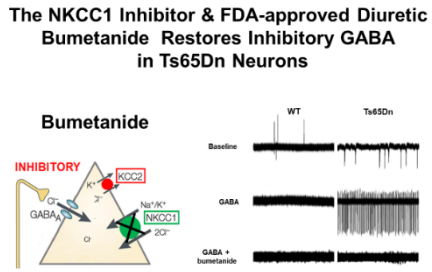
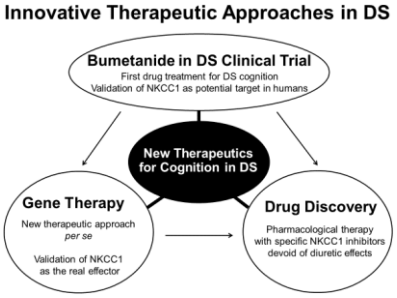
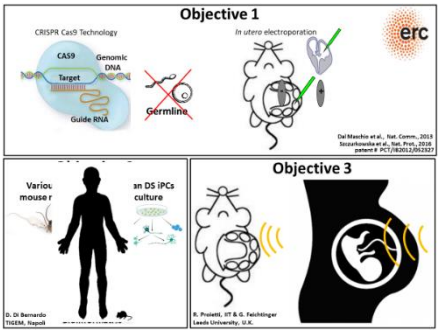
How neurogenomics will drive new therapeutic approaches



Prof. Cancedda from Genoa (IT), presented very interesting data on "how neurogenomics will drive new therapeutic approaches". More in particular the speaker talked about the neurodevelopmental disorders characterized by different ethiologies but sharing a variety of symptoms. Going deeper in her lecture, the speaker presented very interesting data on the glutamate-GABA balance altered in these diseases. In the main part of her talk, Prof. Cancedda talked about the NKCC1 inhibitor activity on neurons affected by neurodevelopmental diseases. More in particular the speaker presented very interesting data on the effect of bumetanide on learning and memory processes and on the open issues for the first treatment of the Down syndrome. The speaker talked about the effect of bumetanide and of new NKCC1 inhibitors. In the last part of her talk Prof. Cancedda presented very interesting data on the main clinical trials running in ptients affected by neurodevelopmental disorders, treated with bumetanide and on new projects aiming to the development of ideal treatments through the application of the genome editing technique.





- What are the main symptoms, shared by the neurodevelopmental disorders based on the data presented by the speaker?
- What are the main neurodevelopmental diseases presented by the speaker?
- What's about the Bumetanide mechanism of action, based on the data presented by the speaker?
- What are the main open issues for the first Down Syndrome treatment, based on the data presented by the speaker?
- What's about the novel selective NKCC1 Inhibitors, based on the data presented by the speaker?

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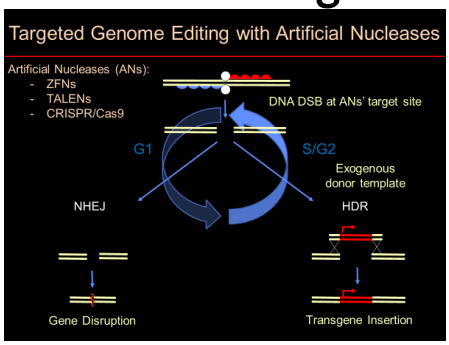
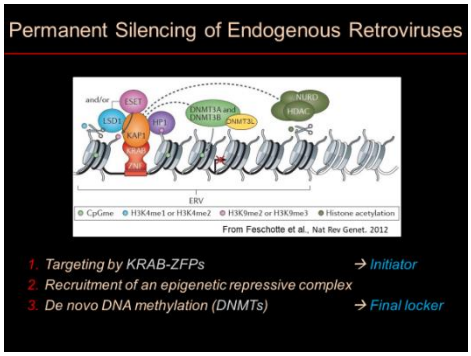
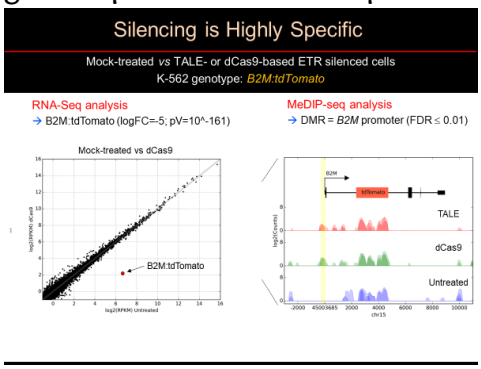
Genome editing for human diseases



Prof. Lombardo from Milan (IT), spoke about Genome editing for human diseases and presented very interesting data starting from the basic principles of gene therapy. Going deeper in his lecture Prof. Lombardo spoke about CRISP, that is an artificial nuclease able to repair the break and presented very interesting data on the targeted gene correction with artificial nucleases. In the main part of his lecture, Prof. Lombardo talked about another technique, that is the exploit of the gene editing for confirming novel biological properties to the cells. More in particular the speaker presented very interesting data on the generation of universally transplantable donor cells. In the second part of his presentation, Prof. Lombardo, talked about the therapeutic gene silencing, the scope of gene therapy in relation to the gene expression and about the main methodologies useful for silencing the gene expression. More in particular the speaker presented very interesting data on the main experiments performed by his team of researchers on the gene silencing, its association with the epigenetic repression and its resistance to many reactivation stimuli. Finally, Prof. Lombardo talked about the ongoing studies and the future research perspectives characterized by the acquisition of new developmental models and insight mechanisms of the Epi-silencing processes, leading to new therapeutic application for diseases like β thalassemia and sickle cell disease.





- What are the main principles of the gene therapy presented by the speaker?
- What are the main topics of the targeted gene correction with ANs, based on the data presented by the speaker?
- What is the scope of the gene therapy on the gene expression, based on the data presented by the speaker?
- What are the main silence gene expression methods presented by the speaker?
- What's about the correlation between gene silencing and DNA methylation, based on the data presented by the speaker?

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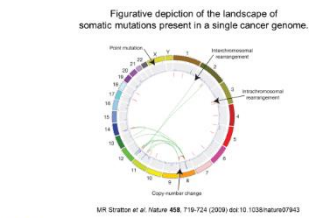
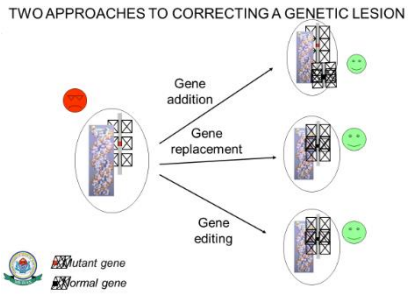
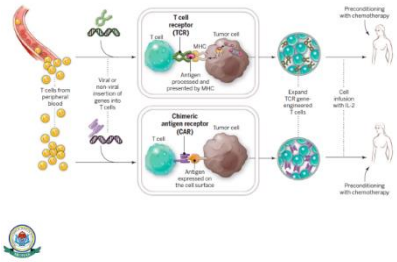
How far can genome editing and related technologies really help medicine in the near future?



"How far can genome editing and related technologies really help medicine in the near future?", was the topic discussed by Prof. Luzzatto from Dar-es-Salaam (TZ), more in particular the speaker presented very interesting data on the sickle cell anaemia burden in the world. Going deeper in his lecture, Prof. Luzzato talked about genomics vs genetics applied to the sickle cell anemia. In the main part of his lecture, the speaker presented very interesting data on the molecular oncology and on the approaches able to corrects a genetic lesion, characterized by gene addition, gene replacement and gene editing. Prof. Luzzatto spoke also about the neoantigens application in cancer immunotherapy. Finally, the speaker presented very interesting data on the public health/ethic agenda on sickle cell anemia and talked about a genome-editing strategy for the treatment of β-hemoglobinopathies characterized by a mutation associated with benign genetic conditions.





- What's about molecular oncology from the speaker point of view?
- How can a vector function from the speaker point of view?
- What's about the organoids definition based on the data presented by the speaker?
- What's about the CRISP/Cas9 β-globin gene targeting in human hemopoietic stem cells, based on the data presented by the speaker?

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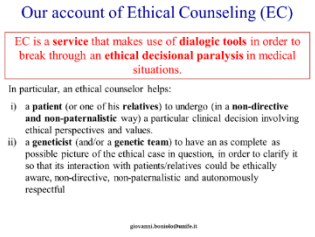
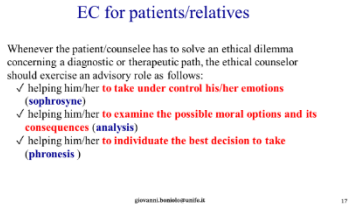
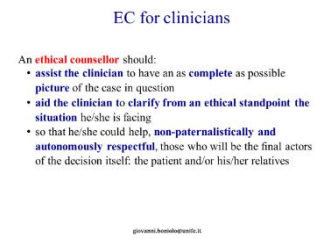
Ethical and philosophical issues on genome modification in humans



Prof. Boniolo from Ferrara (IT), spoke about Ethical and philosophical issues on genome modification in humans and presented very interesting data starting from the list of the major problems in medical genetics from the ethical point of view. Going deeper in his lecture, Prof. Bodiolo talked about the ethical implications of the epistemological comprehension of what probabilistic causality is. In the main part of his lecture, the speaker presented very important data on the ethical best practice and talked about his account of Ethical Counselling (EC), that is a service that makes use of dialog tools in order to break through and ethical decisional paralysis in medical situations. More in particular Prof. Boniolo spoke about the role of EC with patients/relatives and with doctors and presented very interesting data on the two different methodologies to be applied with parents and clinicians. Finally, the speaker presented very interesting data on EC around the world and highlighted the importance of this service also for any Italian patient. In conclusion, Prof. Boniolo pointed out that patients and their existential problems come first, but there is no point in discussing the ethical implications of genetics, without implementing a real ethical counselling service.





- Is knowledge always beneficial, based on the data presented by the speaker?
- Why is the ethical counselling important from the speaker point of view?
- What is the role of EC for patients and relatives, based on the data presented by the speaker?
- What's about the EC role for clinicians, based on the data presented by the speaker?
- What are the main characteristics of EC, based on the data presented by the speaker?

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

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