2012

A YEAR IN REVIEW

IFOM
FIRC INSTITUTE OF MOLECULAR ONCOLOGY

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Director's message

Global alliances towards personalized medicine

by Marco Foiani

For decades humanity tried to cure cancer with drug therapies without fully understanding the real causes underlying the onset and the development of the disease. The success of these approaches has been greatly limited by this lack of knowledge and today many cancer patients still die after a relapse of their illness.

The promise of research organizations like IFOM, which are involved in the exploration and understanding of such basic molecular mechanisms at the root of the disease, is therefore critical. These efforts are now showing the first results as we begin to understand why in some patients some therapies are working better than others. Moreover, an entire new predictive and personalized medicine landscape is being shaped with the aim of assessing in advance the risk of development of diseases on a genetic basis in the population.

This is a massive collective effort that the scientific community is pursuing all over the world. In this framework, IFOM is well aware that partnering with world-class institutions with complementary skills and resources is essential to reach the critical mass necessary to deliver results. IFOM has therefore taken up avenues that would maximize its own efforts, by synergizing with other institutions with the same aims. Besides the long-standing collaboration with the European Institute of Oncology (IEO) in Milan, we have therefore opened Joint Research Labs in India and Singapore (IFOM Asia) where the aims, the approach, the costs and the funding are shared.

*Thanks to our partnerships with IEO in 2000, A*STAR in 2011 in Singapore, NCBS and InStem in 2012 in Bangalore (India) we have been able to join forces and create synergies that are being of benefit to all the institutions involved, and to science in particular.*

We plan to further extend the IFOM Asia program by increasing our investments in Singapore and Bangalore, and to expand it to Japan. To this aim, plans have been put in action to increase the investment in Bangalore and details are being solved with the National University of Singapore. In addition, a partnership with the Kyoto University Medical School has started with an agreement for the exchange of scientific staff.

The return of these investments is not only that of expanding our scientific staff with highly qualified colleagues, but also a major increase in the number of highly selected young talents from Asia who come to study in our institute in Milan.

IFOM Network, Joint Research Labs, IFOM Asia

Director's message

The author:

Marco Foiani
Scientific Director

Prof. Foiani has a Ph.D. in Molecular Biology from the University of Milan (Italy).

Since 2002, Prof. Foiani, who is also Head of the Genome Integrity Laboratory at IFOM since its establishment, is Full Professor in Molecular Biology at the University of Milan.

His research interest focuses on the regulatory mechanisms that control genome integrity. Particularly, his work has contributed to elucidate the cellular mechanisms causing genome instability in cancer cells and chromosome abnormalities in certain human syndromes leading to cancer predisposition. Prof. Foiani has more than 80 papers published in international scientific journals.

Since 2008 Prof. Marco Foiani is the Scientific Director of IFOM.

Prof. Foiani was honored with internationally recognized memberships and awards, such as: the European Molecular Biology Organization membership; the Academia Europaea membership; the New York Academy of Sciences membership; the Italian Society of Genetics (AGI) membership; the Italian Society of Biophisics and Molecular Biology (SIBBM) membership; the Award from the Italian Society for Biophysics and Molecular Biology (SIBBM); the Biotec Award promoted by Amgen and Dompé; the "Chiara D'Onofrio" Prize from the Italian Federation of Life Sciences.

He was the founder in 2009 of the European Nanomedicine Foundation (CEN) and vice-president up to 2011.

He is also member of the Scientific Advisory Board of AIRC, the Italian Cancer Research Association, member of the editorial board of Cell and editor and reviewer for top impact factor scientific journals.

An institute in a dynamic stage

A view from the Scientific Advisory Board

by Tomas Lindahl

Research units and laboratories often have external Scientific Advisory Boards, which may vary considerably with regards to size, activity and relative importance. The present IFOM SAB only has five members, but they regularly provide constructive advice and attend the yearly two-day SAB meeting in Milan.

One or two SAB members also take part in committees for promotion of IFOM group leaders to tenured posts. This is done together with an external scientist with special expertise, and with the Scientific Director (Marco Foiani) and the Deputy Director (Francesco Blasi) of IFOM.

The members of the SAB have in general been recruited from Europe, to allow for regular short visits to Milan without significant jet lag.

IFOM is currently in a dynamic stage; several new tenured group leaders have been appointed over the last three years, whereas seven such scientists left IFOM during 2009 - 2012. The goal has been to further improve the excellent scientific establishment at IFOM. One young group leader, Simona Polo, successfully applied for tenure at the end of 2011, and three group leaders were similarly promoted in the early part of 2013. However, there were no such appointments at IFOM, Milan, during 2012.

SAB MEMBERS (2012)

Tomas Lindahl (Chairman), Director Emeritus of the Clare Hall laboratories of the London Research Institute of Cancer Research UK. Lindahl is an expert on DNA damage and DNA repair mechanisms.

Ralf Adams, Director of the Max Planck Institute for Molecular Biomedicine in Münster, Germany. Adams is an expert on signal transduction pathways and angiogenesis, often employing transgenic mice to investigate cancer-related problems.

Julian Downward, Deputy Director of the Lincoln's Inn Fields laboratories of the London Research Institute, Cancer Research UK. Downward is an expert on the cell biology and drug sensitivity of transformed cells, and signal transduction with emphasis on Ras oncogenes.

Jan Hoeijmakers, Director of Department of Cell Biology and Genetics, Erasmus University, Rotterdam, the Netherlands. Hoeijmakers is an expert on the molecular mechanisms of the ageing process, genomic instability in cancer cells, and the pathology of defective DNA repair.

Michael Neuberger, Director of the Immunology Section, MRC Laboratory of Molecular Biology, Cambridge, U.K. Neuberger is an expert on antibody hypervariability and the cellular processing of genes encoding antibodies. Dr Neuberger passed away on October 26th, 2013

An institute in a dynamic stage

The author:

Tomas Lindahl

Emeritus Director of Cancer Research UK, Clare Hall Laboratories

Tomas Lindahl completed medical studies at the Karolinska Institute in Stockholm and has consistently been active in research. He worked as a post-doctoral fellow on nucleic acid biochemistry with J. Fresco at Princeton and G. Edelman at Rockefeller University, joining the faculty of the Karolinska Institute in 1969.

He became Professor of Medical Chemistry at the University of Gothenburg in 1978. In 1981 he was appointed Head of the Mutagenesis Laboratory at the ICRF Mill Hill Laboratories in London. From 1984 to 2006 he was Director of the Clare Hall Laboratories at ICRF and Cancer Research UK, also serving as Deputy Director of Research. Amongst many honors, Tomas Lindahl is a member of EMBO, a fellow of the Royal Swedish Academy of Sciences, and the Royal Society, London. He was the Royal Society Croonian Lecturer in 1996 and received a Royal Medal in 2007; INSERM the Prix Etranger in 2009, and the Copley Medal in 2010 of the Royal Society.

He is now Emeritus Director of Cancer Research UK, Clare Hall Laboratories, and involved in various scientific activities.

2009 - 2012 Visiting Professor of the Chinese Academy of Science 2010 - Scientific Advisor, Beijing Inst. of Genomics, China 2010 - 2012 Scientific Advisory Board, IFOM Milan 2010 - Scientific Advisory Board, Cancer and Ageing Centre, University of Nice, France 2010 - 2012 Hon. Professor in Medical Oncology, University of Sheffield.

Connecting Science: the agreement between IFOM and InStem

Commentary on the launch of the IFOM-InStem Joint Research Laboratory in Bangalore

by K. VijayRaghavan

InStem, the Institute for Stem Cell Biology and Regenerative Medicine, is a major initiative of the Indian Government and is growing collaboratively in a joint campus with the National Centre for Biological Sciences (NCBS).

In its 20 years of growth, NCBS has carved a place for itself as a place of quality scientific research. Satyajit 'Jitu' Mayor, is the dynamic new director of NCBS (and of InStem) Upi Bhalla, an accomplished neuroscientist is NCBS Dean. InStem has grown with Jyotsna Dhawan and S. 'Rams' Ramaswamy as Deans. Jyotsna has recently handed over to Apurva Sarin as a new Dean at InStem. This team at InStem and at NCBS, and their colleagues, have made the campus an example of excellence are working hard to ensure that it continues to lead in very challenging times.

The challenge for InStem, and for all of in biomedical research is simple: what special perspective do we bring to the research stable that makes our presence, in a world of big players, meaningful? We believe that the key to new discoveries in science is one's ability to think well, to keep excellent company and to be nimble.

Resources are very important, but resources without the above do not help. InStem's plan is for effective research through the highest quality in hiring and collaborating. Through this way we may define questions and define new directions, which may well elude much bigger players.

The international collaborations of NCBS and InStem range from Kyoto, Kobe, Singapore. Cambridge, Edinburgh, Stanford, Montana, Dresden, Barcelona and, of course, Milan. It is no coincidence that IFOM's own collaborations overlap substantially with ours!

IFOM is a great centre for Cancer biology: it has quickly become world-famous and, importantly, has a sense of adventure and internationalism rare in older staid institutes.

We expect that together we will address problems of such complexity that neither can address independently. IFOM is an inspiration for us at Bangalore. IFOM is nimble, brilliant, has depth and shares with us a desire to address the most fundamental questions in cancer biology and succeed. Our friends in IFOM are an amazingly collegial lot: we are fantastically lucky to be able to partner with such committed and dedicated people.

Our joint lab will be amongst the best anywhere, and we are sure that Professor Colin Jamora, who leads it, will fly IFOM's flag high in Bangalore. Its been a year since Colin started his lab in Bangalore and it been a difficult year. I have moved on to Delhi and Jitu has taken over at NCBS and InStem. Such transitions, when one is a new investigator, can be difficult. In addition, India, like Italy is going through difficult times. Nevertheless, Colin has done a stellar job settling in, with the help of his colleagues at InStem and NCBS, and is well on his way to establishing a great research team.

Our collaborations may have a special place in a world, which is churning with uncertainty. In such uncertain times, science can have major effects on policy and even on the planet's future.

The first is a very deep social and cultural one, similar to that of music and the arts. A society without scientific enquiry is like a society without music, without poetry and the arts: a graveyard of a society. Our quest to understand the universe and our origins is very deeply embedded in our blood and culturally strengthened in most countries. Of all places in the world, Italy in the West and India in the East have been historically iconic in communicating the value of questioning and scientific inquiry. It is wonderful that our institutions, InStem/NCBS and IFOM are, in a very small way, working together in this quest for understanding and scholarship. Science, and we in a small way, can be a unifying moral and rational force in a tumultuous world.

IFOM Network

India represents one of the most promising incubators of scientific and technological development in the world. Starting from 2012 IFOM has established agreements of collaboration with the most innovative indian research institutes and integrate the Partners' skills in the cutting-edge science area of regenerative medicine.

The second, and equally important, role of science is to translate our understanding of nature for the good: for the good of humanity, and of the planet. Many of our planet's problems can principally be addressed through good politics, good planning and good governance: Science and Technology can be an effective and responsible partner here.

NCBS, India

Connecting Science: the agreement between IFOM and InStem
by K. VijayRaghavan

It has often been said that science is value-neutral and its manner of use by society decides whether it is for the good or not. While, this may be a truism, I feel that it is vital for us, as scientists, to engage with society at every level. We must work with society to identify important questions and not hesitate to see how science can aid in their solution. We should also protest against misuse of science. We must make sure that evidence comes to bear on policy and is not squelched by ideology or misplaced idealism.

The third role science can play is in stressing the importance of internationalism and cooperation. In today's world, each of our strengths belong to the entire world and the problems each country faces also must be solved by international cooperation. The world's human population will be 9 Billion in the not too distant future. We must work together to make this populous world sustainable for all and science can glue good politics rather than be a force for greed and consequent despair.

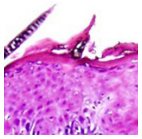
Mahatma Gandhi is supposed to have said that there is always enough on this planet for everyone's need, but not enough to satisfy everyone's greed. The financial crisis has complex underpinnings of course and it may too simplistic to attribute it to just greed, but it is true that we must now work hard to focus on sensible ways to address the needs of our planet. Scientists must work with society to ensure effective ways to develop technologies that will allow us to cut waste while delivering quality.

The financial crisis has brought much suffering, but now that we have it we should view it as an opportunity to make our societies more energy efficient, have better biomedical technologies and create jobs through entrepreneurship in a sustainable world. For example, if an Italian engineer develops an effective way of saving rainwater in India, its implementation can create jobs in Italy and in India while solving a major problem.
An early diagnostic for oral cancer coming from Milan could make for good public health and good economics. A breakthrough in computational biology or in skin stem cells could come from India and create new understanding for the whole world.

The world is in transition and China, India, Brazil and other countries will become major powers, hopefully in the best sense of the term. These 'Rising Powers' have much to learn from America, Europe and Japan. Amongst these America is special. America's success in science and innovation is phenomenal, historical and has many causes. The decline of America has been predicted for at least two hundred years and may still be a premature prediction. However, three aspects of its success are pertinent for China, India and even perhaps Europe.

The first is democracy. While it may be difficult to repress geniuses, a broad culture of innovation cannot come from an oppressed society. India is a democracy where there is much social oppression.

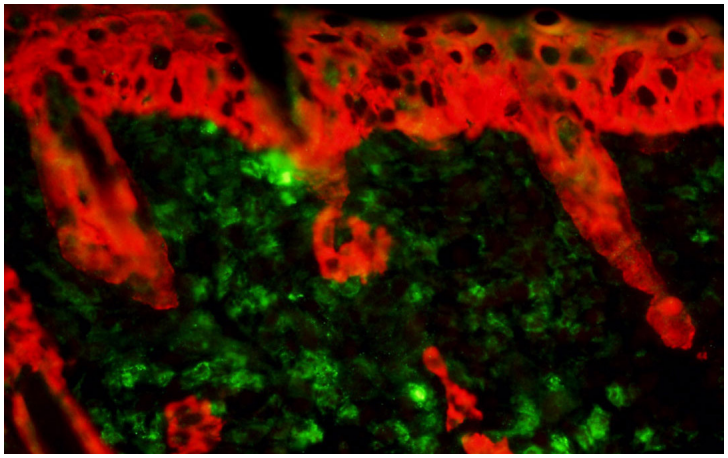
IFOM Network, Bangalore, Colin Jamora



We must change. China is not a democracy and it will change. Europe must not let its democracy slip into intellectual isolationism. America too can learn from itself. Some say that it seems to be grasping at anti-intellectual mirages.
This can cause its decline faster than any economic policy.

The second lesson we all can learn from America is openness. If India welcomes the best scientists in the world, the best economists, the best entrepreneurs, irrespective of nationality, we can change in a decade. If we become xenophobic, we will take a hundred years to change. Similarly, Europe can benefit from the welcoming openness America has towards the best and the brightest.

The third lesson we can learn from America is not to worry about failure in entrepreneurship. One reason why America is innovative is simply because it tries and fails far, far more often that similar ecosystems elsewhere. In India, despite the winds of change, there is still a tendency to feel assured that a venture will not fail before we get support it. This fear of failure is a mental block that prevents innovation.



Stem cells (green) in the skin multiply in a wound

Finally as China and India grow as economies, there is no guarantee that they will also become engines of innovation and leadership in science technology. It is possible to grow by neglecting the environment, with inequitable distribution of opportunity and by amplifying social and income disparities.

Such growth, in India and China, will be disastrous for the world. For meaningful transformation, deep socio-cultural changes and a change in China and India's education and research ecosystems are needed.
For this to happen rapidly in China and India (and in South America and Africa), a partnership of peace and collaboration between America-Europe and the rest of the world is needed.

This enters the realm of politics, but there is a danger we must recognize. Growing economies, which relinquish cultural, intellectual and moral connections are not good for anyone. Europe, and Italy, as the fountainheads of modern science and technology, have a great responsibility in this context. Europe can engage with the developing economies of the world and with America to ensure that innovation and technology is both global and calibrated for sustainable equitable change.

Science, then, is not a race between China and the world, but a team event for mutual sustenance and benefit. We must, therefore move past the ears of brain-drain, brain-gain and brain-circulation and seek the ideal of one cooperative brain for one sustainable planet.

Connecting Science: the agreement between IFOM and InStem

The author:

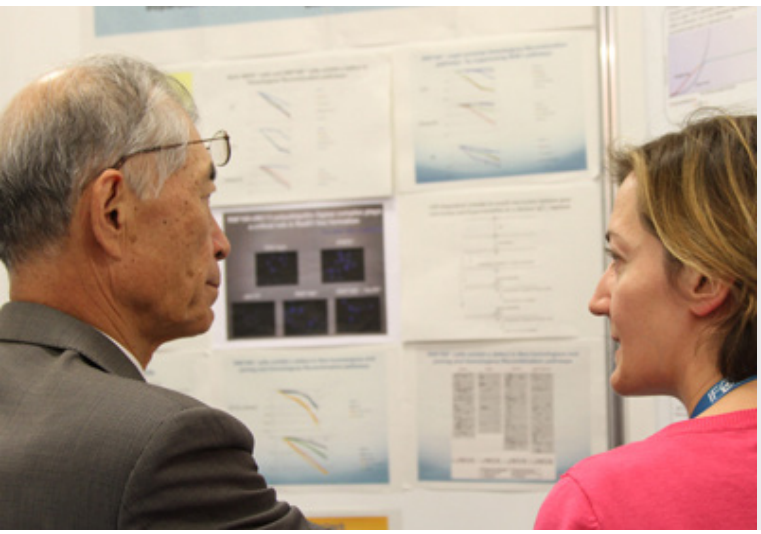
K. VijayRaghavan

Former Director of NCBS and InStem

K. (Vijay) Vijay Raghavan's research aims to understand motor- and olfactory-circuit assembly: from deciphering how each component is made, interacts, and stabilizes to functioning in the animal to allowing behavior for in the real world. Related to the development of network function in the maintenance in the mature animal; another aspect of the work in the laboratory addresses how mature neurons and muscles are maintained. The laboratory uses a genetic approach, mainly using the fruit fly but also collaborating with those using mouse and cell-culture.

VijayRaghavan is Distinguished Professor of the National Centre for Biological Sciences (NCBS) of the Tata Institute of Fundamental Research (TIFR) in Bangalore, India and, since January 28, 2013, Secretary of the Department of Biotechnology Government of India. Before VijayRaghavan was the Director of NCBS and the interim head of InStem, a new institute being nurtured by NCBS. He continues to be active in research with his research laboratory at the NCBS in Bangalore.
He studied engineering at the Indian Institute of Technology, Kanpur. His doctoral work was at TIFR, Mumbai (Bombay University) and postdoctoral work at the California Institute of Technology.

VijayRaghavan is a member of the Science Advisory Council to the Prime Minister of India, Associate Member of the EMBO, Fellow of the Indian Academies of Sciences and a Fellow of the Royal Society. He is a JC Bose fellow of the Government of India.



Mechanisms of cell transformation and metastasis

The IFOM-Kyoto University Joint Symposium

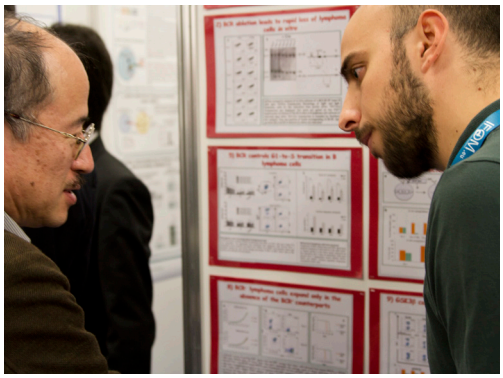
by Francesco Blasi

Within the framework of its International Asia Program, IFOM is exploring the possibility of joint ventures with the Kyoto University Medical School (Japan).

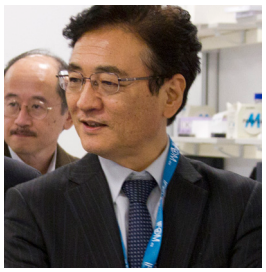
This step was finalized to offer to the japanese colleagues a representation of the science carried out at IFOM and to confront it with a selection of the Kyoto Medical School.

For this reason, with the help of FIRC and of the Kyoto University Medical School, IFOM organized a meeting on "Mechanisms of Cell transformation and metastasis" on October 25-26, 2012, in Milano on the IFOM premises.

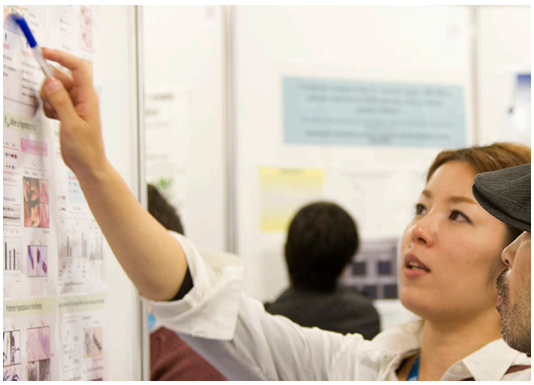
The speakers included 6 from the Kyoto Universuty delegation including Prof. Tasuku Honjo, 15 from IFOM including Institute's Director Marco Foiani, 4 from non-IFOM Milan Institutions, IEO-IIT, H San Raffaele and Istituto Clinico Humanitas.



Some pictures from the event



Nagahiro Minato and Makoto Noda during the lab tour



Poster session

Finally the Directors of the two Institutions with whom IFOM has already an operating collaboration-agreement, Sir David Lane from A*Star (Singapore) and Prof. Satiajit Mayor from NCBS (Bangalore, India) also delivered lectures.

In addition about 10 young japanese and 15 young Italian scientists presented their work in the form of porters.

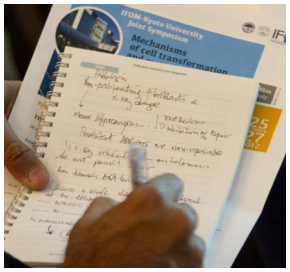
IFOM Network
IFOM-Kyoto University Joint Symposium

The meeting covered topics like genome stability and cancer, stem cells and cancer stem cells, inflammation and cancer, cell motility and metastasis, mechanisms of tumor suppression, signalling in cancer, genome stability syndromes and new frontiers in cancer therapy.

It therefore promoted a high-level multidisciplinary confrontation on new research frontiers in particular on cancer. In addition, the meeting succeeded in its goal to initiate a process that will hopefully lead to tighter cooperation between IFOM and Kyoto University.

The overall result of the meeting was the signature of an Agreement to implement the scientific exchanges between the two Institutions, which is now in the process of being realized in the form of IFOM scientists visiting Kyoto University laboratories.

Tomas Lindahl and Tasuku Honjo



Mechanisms of cell transformation and metastasis
by F. Blasi

Mechanisms of cell
transformation and metastasis

The author:

Francesco Blasi

IFOM Deputy Director

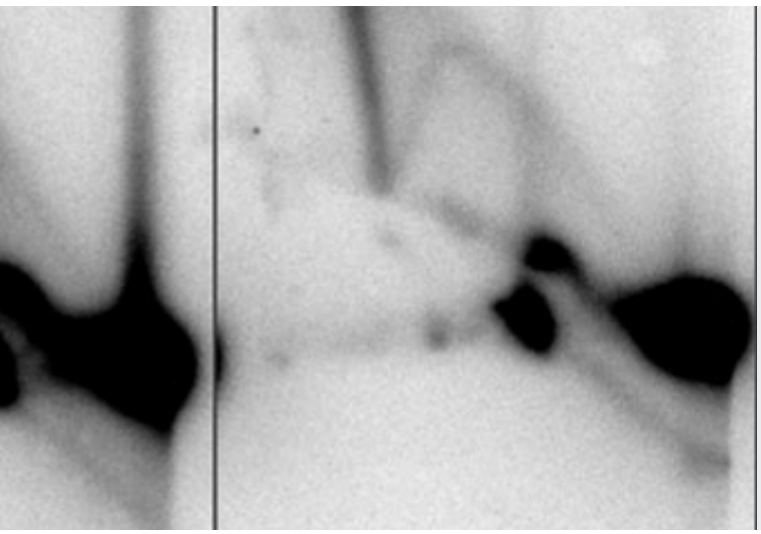
Born in Naples, October 19, 1937. MD from Naples University Medical School, then two post-Docs at the Max Planck Institut fuer Biophysik (Frankfurt, Germany) and NIH (National Institute of Arthritis and Metabolic Diseases) Bethesda, MD (U.S.A.). In 1970 back in Italy at the CNR Research Center in the Naples University Medical School, then in 1980 Full Professor at the II Faculty of Medicine of the University of Naples.

Subsequently, Professor at the University of Copenhagen, Denmark and finally in Milano since 1992.

Is at IFOM since 2004, Director of research program Transcriptional Regulation in Development and Cancer.
From 2007 to 2011 coordinates the Molecular Oncology PhD program of SEMM. In 2011 becomes Deputy Director for Science of IFOM.

Has previously been Director of the International Institute of Genetics and Biophysics of CNR in Naples (1980-1983), of the Molecular and Cellular Biology Center in Copenhagen (Denmark), (1988- 1992), and of the Department of Cellular Biology and Functional Genomics (1998-2006) at DIBIT, Ospedale San Raffaele.

In 1979 is elected member of EMBO, the prestigious European Molecular Biology Organization, and 1991-1993 of its Council.
Since 1992 is a member of Academia Europaea.
Has received national and international prizes and is Author of over 270 research articles in prestigious international Journals, including Nature and Cell.
Has been a member of the Advisory Board of AIRC, Associazione Italiana per la Ricerca sul Cancro, and of the Board of EMBO Journal.



The role of senataxin in cancer and ALS

science

Commentary on Marco Foiani and Giordano Liberi's paper published on Cell

by Giuseppe Biamonti

For a variety of reasons, my research has always been focused on two apparently distant topics: on one hand, analysis of DNA replication in human cells, and on the other, control of gene expression at the post-transcriptional level, primarily involving the splicing of transcripts. It was difficult to imagine that these two very different research fields would overlap.

However, a series of papers published over the past decade, many by Prof. Foiani, the Scientific Director of IFOM, have shown that there is a connection: proteins involved in the transcription and maturation of gene transcripts are important for preventing DNA damage during replication.

It has emerged that the integrity of the DNA molecule can become compromised when gene transcription and DNA replication are not coordinated, resulting in the collision of transcription and replication complexes.

Such a collision can give rise to DNA damage, recombination and chromosomal rearrangements, all events that are intimately connected with the onset of tumors. The factors involved in transcript maturation play an important role in this phenomenon.

They bind co-transciptionally to the RNA molecule and then, through a series of complex molecular processes, such as splicing, they produce a mature messenger RNA molecule that is exported from the nucleus to the cytoplasm where protein synthesis occurs. In the process, the transcript maturation factors also control the formation of particular structures, the so-called R-loops, which appear to have a physiological role in the termination of transcription but can be dangerous for genome integrity.

Senataxin associates with replication forks to protect fork integrity across RNA-polymerase-II-transcribed genes.
Transcription hinders replication fork progression and stability. The ATR checkpoint and specialized DNA helicases assist DNA synthesis across transcription units to protect genome integrity. Combining genomic and genetic approaches together with the analysis of replication intermediates, we searched for factors coordinating replication with transcription. We show that the Sen1/ Senataxin DNA/RNA helicase associates with forks, promoting their progression across RNA polymerase II (RNAPII)-transcribed genes. sen1 mutants accumulate aberrant DNA structures and DNA-RNA hybrids while forks clash head-on with RNAPII transcription units. These replication defects correlate with hyperrecombination and checkpoint activation in sen1 mutants. The Sen1 function at the forks is separable from its role in RNA processing. Our data, besides unmasking a key role for Senataxin in coordinating replication with transcription, provide a framework for understanding the pathological mechanisms caused by Senataxin deficiencies and leading to the severe neurodegenerative diseases ataxia with oculomotor apraxia type 2 and amyotrophic lateral sclerosis 4.
[PMID: 23141540]

R-loops form when the nascent transcript is not coated with proteins, but instead forms a stable hybrid with the DNA strand serving as the template for transcription, which leaves the other DNA strand unpaired.
R-loops are fragile elements in the genome because they cause DNA damage and recombination. Therefore, it is not surprising that the cell has many mechanisms for removing or preventing R-loop formation.

As Director of the Italian National Research Council's Institute of Molecular Genetics in Pavia, which has played an important role in national and international studies on DNA replication, genome stability, transcription and the maturation of transcripts, I thought it was important to introduce a new line of research aimed at analyzing precisely the relationship between replication and transcription.

This idea was realized in 2011 when it was possible to recruit Dr. Giordano Liberi, from the Foiani group. Dr. Liberi is one of the leading experts on DNA replication. He is studying senataxin - a protein mutated in two rare hereditary neurodegenerative diseases: one, a form of juvenile amyotrophic lateral sclerosis, and the other a rare ataxia with eye muscle defects (AOA2).

Dr. Liberi coordinates a project funded by AIRC and Telethon that investigates the role of senataxin in resolving conflicts between replication and transcription in the yeast model system. This project takes advantage of the close and valuable collaboration with the group of Professor Foiani at IFOM.

In 2012, the first joint IFOM-IGM article was published, with Liberi as the last author. It was a technically sophisticated article full of implications. Senataxin functions as a police officer 'directing traffic' during replication of regions of DNA that are particularly 'busy' from the transcriptional point of view. A role had already been demonstrated for senataxin in solving the R-loops that arise physiologically during the termination of transcription.

Liberi's research shows that the protein interacts directly with the replication complex and that this interaction is crucial for removing the R-loops that accumulate as a result of the clash between the replication and the transcription machinery.

Senataxin is the first protein shown to play a role both in the termination of transcripts and in progression of the replication fork, indicating that a strong connection exists between the two phenomena. It is conceivable that in the future other multitasking proteins will be identified that have roles in transcription, replication and transcript maturation. In fact, this is one of the topics at the leading edge of research. It remains to be determined whether its activity is important for the onset of neuronal diseases and if so, which cells in the nervous system contribute to the development of ALS and AOA2 ataxia as a result of DNA damage.

The role of senataxin
in cancer and ALS
by G. Biamonti

I want to end with two considerations.

The first is of a scientific nature. As the R-loop research demonstrates, much basic research is still needed to understand how the cell functions and to identify mechanisms that prevent the onset of pathologies such as cancer and neurodegenerative diseases.

Supporting excellence in research is certainly one of the objectives that we must pursue, also for the progress of the country.

Today, research in Italy is going through a very difficult time and we need to focus as much as possible on quality in order to encourage research and give hope to the country.

The ability of a public research center to recruit excellent scientists among those selected at IFOM may represent a good opportunity. It can support precarious promising researchers, while providing them access to the High Tech facilities at IFOM.

Local Network, Marco Foiani, Giordano Liberi

The second consideration is more institutional and the strategic choice to forge a relationship between a public research institute, the IGM-CNR in Pavia, and a private one, the IFOM in Milan.
This is how the signing of the Memorandum of Understanding in 2012 should be viewed. It involves not only the activities of Dr. Liberi, but also other researchers, foremost Dr. Fabrizio d'Adda di Fagagna who was hired with a fixed-term contract as a principle investigator at CNR.

The role of senataxin
in cancer and ALS
by G. Biamonti

The role of senataxin
in cancer and ALS

The author:

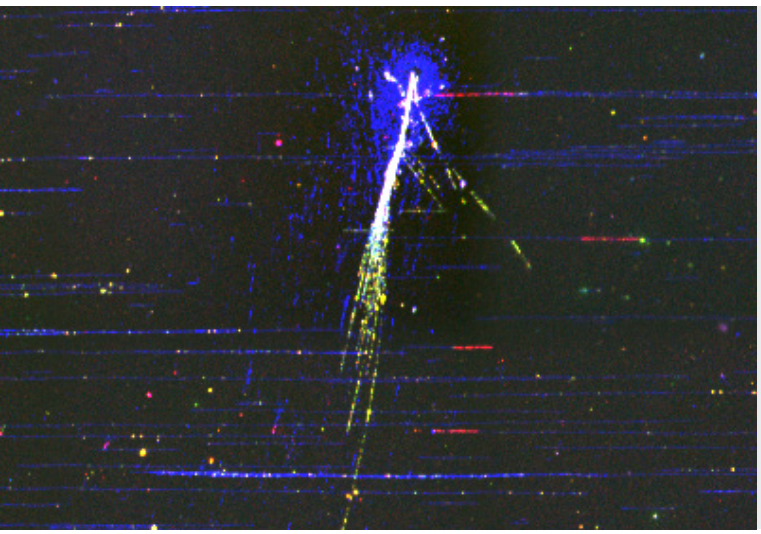
Giuseppe Biamonti

Scientific Director of IGM-CNR Pavia
(Institute of Molecular Genetics (IGM) of the Italian National Research Council)

Giuseppe Biamonti received his Ph.D. in genetics and molecular biology in 1985 from the University of Pavia, Italy.

From 1995 he was Director of Research at the Istituto di Genetica Molecolare, Consiglio Nazionale delle Ricerche (CNR) in Pavia. From April 2009 he is Director of the same Institute.

His main scientific interests include the analysis of DNA replication and RNA processing in human cells. Recently, he has focused on the relationship between nuclear function and structure, and on the involvement of alternative splicing programs in cancer progression.



DNA: in telomeres lesions of time are inevitable

science

Commentary on Fabrizio d'Adda di Fagagna's paper published on Nature Cell Biology

by Leonard Hayflick

The discovery by Fabrizio d'Adda di Fagagna *et al.* that the region at the ends of chromosomes, (telomeres), may suffer unrepaired damage is a significant finding that can only be understood in the context of the findings that preceded it.

It has been more than fifty years since I discovered that cultured normal human cells (HDC) had a finite capacity to divide. I called this phenomenon cellular senescence. My finding overturned a belief held since 1900 that all cultured cells were immortal and, if they died, it was because of failures in culture conditions. Significantly, if cultured normal cells are immortal then ageing must occur because of extracellular factors, - a belief held for sixty years. My findings led me to conclude that ageing, and the determination of longevity, are caused by internal cellular events and that only cancer cells are immortal.

I also found that fetal HDC could undergo only fifty population doublings and could be frozen retaining the memory of their doubling when frozen. Upon reconstitution, even after decades, they would undergo the remaining doublings to the maximum fifty. This, and other experiments, clearly indicated that the cells had a counting mechanism which we located in the nucleus.

This mechanism for my phenomenological discovery was found later by others. Telomeres do not carry genetic information. As HDC multiply, their telomeres, composed of thousands of repeats of the same four chemicals, shorten slightly at each cell division thus acting like a buffer protecting the downstream genes that would otherwise be lost. Unlike normal cells, immortal cancer cells express an enzyme called telomerase that reinserts many of the four chemicals at each cell division that a normal cell would have lost.

Telomeric DNA damage is irreparable and causes persistent DNA-damage-response activation.
The DNA-damage response (DDR) arrests cell-cycle progression until damage is removed. DNA-damage-induced cellular senescence is associated with persistent DDR. The molecular bases that distinguish transient from persistent DDR are unknown. Here we show that a large fraction of exogenously induced persistent DDR markers is associated with telomeric DNA in cultured cells and mammalian tissues. In yeast, a chromosomal DNA double-strand break next to a telomeric sequence resists repair and impairs DNA ligase 4 recruitment. In mammalian cells, ectopic localization of telomeric factor TRF2 next to a double-strand break induces persistent DNA damage and DDR. Linear, but not circular, telomeric DNA or scrambled DNA induces a prolonged checkpoint in normal cells. In terminally differentiated tissues of old primates, DDR markers accumulate at telomeres that are not critically short. We propose that linear genomes are not uniformly reparable and that telomeric DNA tracts, if damaged, are irreparable and trigger persistent DDR and cellular senescence.
[PMID: 22426077]

The telomere system is not a clock because it does not record the passage of time. It counts DNA replications. I have named this mechanism a "replicometer" because it meter's events.
It has been known for decades that the crucial DNA molecule suffers frequent errors as it replicates itself and even at rest. These errors could have profound effects on living cells but because this does not usually happen, efficient DNA repair systems are constantly at work.

Marzia Fumagalli and Francesca Rossiello, under the guidance of Fabrizio d'Adda di Fagagna, report the discovery of an important exception to the repair of DNA. They find that the telomeric region, much of which is not lost during DNA replication, suffers unrepaired damage or errors, Fumagalli *et al.* propose that their findings may reveal insights into ageing or cellular senescence. This proposal is compatible with ideas proposed earlier by several investigators that the fundamental cause of age changes is the result of The Second Law of Thermodynamics where ageing is caused by the accumulation of unrepaired molecular damage.

The basis for this belief is (1) there is no direct evidence that ageing is governed by genes, (2) everything in the universe changes or ages in space-time without being driven by a purposeful program and, (3) there is a huge body of knowledge indicating that age changes are characterized by the loss of molecular structure, hence function.

Loss of molecular fidelity is the result of the Second Law and, contrary to the old belief, it applies to both open and closed systems. The Second Law states that concentrated energy tends to disperse or spread out unless hindered. The hindrance is the relative strength of chemical bonds. The prevention of chemical bond breakage is essential for the maintenance of life.

Age changes occur as unrepaired or unreplaced molecules accumulate after reproductive maturation. If they accumulate before then, the loss of individual lives would cause the species to vanish. After reproductive maturation molecular fidelity becomes less important to species survival and the balance shifts such that repair processes can no longer keep up with accumulating errors. Furthermore, repair processes themselves are composed of complex molecules that also undergo the same fate as their substrate molecules.

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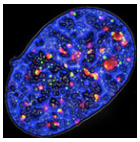
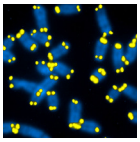
As Fumagalli *et al.* speculate, because the errors in telomeres are unrepaired, and accumulate over time, this phenomenon may be telling us something about ageing. However, it may also be telling us something about the determination of longevity. The two phenomena differ significantly.

Longevity is determined by how long molecular fidelity can be maintained. This is based on the efficiency of repair and synthesizing machinery which are also governed by the Second Law and prone to accumulating unrepaired errors.

Unlike the stochastic process that characterizes aging, longevity determination is not a random process. It is governed by the reserve physiological capacity reached at the time of sexual maturation





DNA Damage Response and Cellular Senescence, Fabrizio d'Adda di Fagagna

that, through natural selection, was achieved to better guarantee survival to that age. The determination of longevity is incidental to the main goal of the genome which is to reach reproductive maturity.

Genes govern the levels of physiological capacity, repair, and synthesis so they indirectly determine longevity. One might think of longevity determination as the energy state of molecules before they incur age changes and aging as the state of molecules after they have become dysfunctional.

Aging is a catabolic process that is chance driven and addresses the question: "Why do living things not live forever?" Longevity determination is an anabolic process that, indirectly, is genome driven and addresses the question: "Why do living things live as long as they do?"

Because the accumulation of errors in un-discarded telomeres discovered by Fumagalli *et al.* seem to be time dependent and not replication dependent they may very well contribute to aging, the limits of longevity or both.

DNA: in telomeres lesions of time are inevitable
by Leonard Hayflick

DNA: in telomeres lesions
of time are inevitable

The author:

Leonard Hayflick

Professor of Anatomy, UCSF

Leonard Hayflick, Ph.D., is Professor of Anatomy at the University of California, San Francisco.

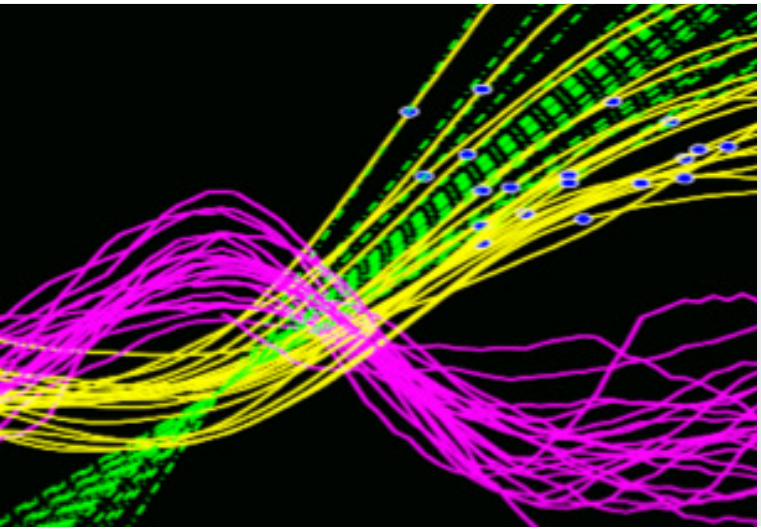
He is a past President of the Gerontological Society of America, a founding member of the Council of the National Institute on Aging, NIH, and a former consultant to the National Cancer Institute and the World Health Organization.

Hayflick is best known for his research in cell biology, virus vaccine development, and mycoplasmology. In 1962 he discovered that, contrary to what was believed since the turn of the century, cultured normal human and animal cells have a limited capacity for replication. This phenomenon is known as "The Hayflick Limit". The discovery overturned a dogma that existed since early in the 20th century and focused attention on the cell as the fundamental location of age changes. The molecular mechanism is telomere attrition for which the 2009 Nobel Prize in Medicine or Physiology was won by three of Hayflick's colleagues. Dr. Hayflick demonstrated for the first time that mortal and immortal mammalian cells existed. This distinction is the basis for much of modern cancer research.
Hayflick developed the first normal human diploid cell strain for studies on human aging and for research when a normal human cell is required. Hayflick's WI-38 cell strain was used by him to produce the first oral polio vaccine made on a continuously propagated cell strain. WI-38, or its imitators, is used today for the manufacture of most of the worlds' human virus vaccines including those for poliomyelitis, rubella, rubeola, varicella, mumps, rabies, adenoviruses and hepatitis A. Over one billion people have benefitted from vaccines produced on these cells. Hayflick is also recognized for his discovery of the etiological agent of Primary Atypical Pneumonia in humans ("Walking Pneumonia"). He showed that its' cause was not a virus as had been proposed but a mycoplasma, a member of the smallest free-living class of microorganisms. The etiological agent, Mycoplasma pneumoniae, was first grown by Hayflick on a medium he developed and that is now used world-wide for mycoplasma isolation and research.

Hayflick is the recipient of more than twenty-five major awards. He is an Academician and Foreign Member of the Ukrainian Academy of Medical Sciences, a corresponding member of the Société de Biologie of France, a Fellow of the American Association for the Advancement of Science and an Honorary Member of the Society for In Vitro Biology. The Institute of Scientific Information, notes that Hayflick is one of the most cited contemporary scientists in the world in the fields of biochemistry, biophysics, cell biology, genetics and molecular biology. He has authored over 275 scientific papers, book chapters and edited books of which four papers are among the 100 most cited scientific papers of the two million papers published in the basic biomedical sciences from 1961 to 1978.

The 1958 inverted microscope that Hayflick adapted from crystallography for use in cell culture is the prototype for all subsequent inverted microscopes used in the field. It has been accessioned by the Smithsonian Institution along with original ampoules of WI-38 and the labeled containers of poliomyelitis and rabies vaccines produced in these cells.

Dr. Hayflick is the author of the popular book, "How and Why We Age" published in August 1994 by Ballantine Books, NYC and in 1996 as a paperback. This book has been translated into nine languages and published in Japan, Brazil, Russia, Spain, Germany, the Czech Republic, Poland, Israel and Hungary. It was a selection of The Book-of-the-Month Club and has sold over 50,000 copies world-wide.



A new light on Spindle assembly checkpoint in chromosome distribution

science

Commentary on Andrea Ciliberto's paper published on Current Biology

by Silke Hauf

Science is not about proving an idea. Science is about disproving an idea. Any scientific truth is temporary; true only until disproven or 'falsified' as the Austro-British philosopher Karl Popper put it.

Although scientists work on disproving theories all day - and often all night -, they do not like their own theories to be disproven. In this whole game of disproving cherished believes, it is therefore most rewarding to disprove one's own idea. This is why the paper by Mariani, Chiroli, Ciliberto and colleagues is so beautiful. It is a very careful re-assessment of a cherished hypothesis, that was first put forward by some of the authors of this paper, was well accepted in the scientific community, was further substantiated by these authors, and was now disproven by them. But even more beautifully, like phoenix from the ashes, a new idea arises from these results - starting the scientific circle afresh. But let me explain from the beginning.

This paper investigates the cellular machinery that oversees the distribution of chromosomes into the emerging daughter cells at cell division. Both daughter cells need to receive exactly one copy of each chromosome. Any error in this process can lead to cell death, birth defects, or could promote tumorigenesis.

Not surprisingly, cells have developed an elaborate mechanism that makes sure that chromosomes are correctly distributed. This mechanism, called the 'spindle assembly checkpoint', monitors whether chromosomes are properly attached to the mitotic spindle. The spindle is a structure consisting of microtubules and motor proteins that will eventually pull the chromosomes into the two emerging daughter cells. Cells in our human body contain 46 chromosomes, and all of these need to become properly attached to the spindle.

Even if only a single chromosome fails to attach, the spindle assembly checkpoint reacts. Because of this high sensitivity, many researchers believe that the signaling mechanism must contain an amplification step. Interestingly, when an important part of the signaling mechanism was discovered (by the Musacchio group, formerly at IFOM-IEO as well), it became clear that the initial activation of the checkpoint, which happens at the contact point between chromosomes and mitotic spindle, releases a protein complex that has the potential to amplify the signal.

A key player in this model is the protein Mad2. Mad2 is the effector of the checkpoint: it binds to the protein Cdc20 and blocks the ability of Cdc20 to initiate the distribution of the chromosomes into the daughter cells. Mad2 can switch between two conformations, called open (O) and closed (C). When Mad2 is bound to Cdc20, it is in the closed conformation. Mad2 becomes proficient to bind Cdc20 through a dimerization reaction, where one O-Mad2 protein meets a C-Mad2 protein and thereby is converted into the Cdc20-bound C-conformation. This is what happens at chromosomes that fail to attach to the mitotic spindle: a complex between the proteins Mad1 and C-Mad2 activates O-Mad2 molecules to convert to C and bind Cdc20. When this was discovered, Musacchio and colleagues immediately realized that - just like the Mad1/C-Mad2-complex at chromosomes - Cdc20/C-Mad2 can in principle bind O-Mad2 and make it Cdc20-binding proficient, thereby creating more Cdc20-C-Mad2 and amplifying the signal.

A remarkable earlier paper by the Ciliberto group (Simonetta, Manzoni *et al.*, PLoS Biol 2009) subsequently demonstrated in elegant test tube experiments that both Mad1/C-Mad2 and Cdc20/C-Mad2 can strongly speed-up the conversion of O-Mad2 into the Cdc20-binding proficient C-Mad2. This paper had a strong influence on me, because it was the first study that analyzed spindle assembly checkpoint signaling quantitatively.

Role of the Mad2 dimerization interface in the spindle assembly checkpoint independent of kinetochores.
The spindle assembly checkpoint (SAC) arrests cells when kinetochores are unattached to spindle microtubules. The signaling pathway is initiated at the kinetochores by one SAC component, Mad2, which catalyzes the initial steps of the cascade via the conformational dimerization of its open and closed conformers. Away from kinetochores, the dimerization surface of Mad2 has been proposed, based on data in vitro, to either interact with SAC activators or inactivators and thus to contribute to SAC activation or silencing. Here, we analyze its role in vivo.
RESULTS: To analyze the putative pathway downstream of the kinetochores, we used two complementary approaches: we activated the SAC ectopically and independently from kinetochores, and we separated genetically the kinetochore-dependent and independent pools of Mad2. We found that the dimerization surface is required also downstream of kinetochores to mount a checkpoint response.
CONCLUSION: Our results show that away from kinetochores the dimerization surface is required for stabilizing the end-product of the pathway, the mitotic checkpoint complex. Surprisingly, downstream of kinetochores the surface does not mediate Mad2 dimerization. Instead, our results are consistent with a role of Mad3 as the main interactor of Mad2 via the dimerization surface.[PMID: 23000150]

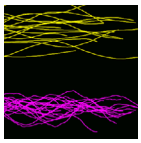
This paper also raised a big question that is still unanswered: In the test tube, generating a checkpoint signal takes hours, whereas in the cell it takes minutes.

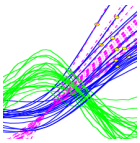
Nobody knows what explains the difference. But importantly, the paper lent further support to the amplification hypothesis, because clearly, both Mad1/C-Mad2 and Cdc20/C-Mad2 could speed up binding of Mad2 to Cdc20.

Yet, in the new paper by Mariani, Chiroli and colleagues, the authors now show that this is not the case in living yeast cells. This involved ingenious mutations within Mad2 that very specifically abolish its interaction with different interaction partners.

A new light on Spindle assembly checkpoint in chromosome distribution
by Silke Hauf

For example the authors modified the Mad1-Mad2 interaction surface by "humanizing" it (i.e. they made it resemble to the interaction site in human cells). Humanized Mad1 and humanized Mad2 work well together, whereas the humanized version of one does not interact well with the yeast version of the other. This allowed the authors for the first time to introduce two different pools of Mad2 into cells. One that would be able to interact with Mad1, and another one that would not.





Quantitative Biology of Cell Division, Andrea Ciliberto

Through such experiments they found that the dimerization interface of Mad2 in Cdc20/C-Mad2 is important for checkpoint signaling - not because it drives amplification of the signal, but because it interacts with yet another checkpoint protein Mad3.

The test tube experiments did not show this, because Mad3 had not been added when these experiments were done. This illustrates how important it is to not only rely on one type of analysis.

At around the same time as the paper by Mariani, Chiroli, Ciliberto and colleagues, the first structural analysis of the C-Mad2-Cdc20-Mad3 complex became available and confirmed that the dimerization interface of Mad2 is in contact with Mad3 - just as the cellular results had predicted. Researchers working with human cells additionally found evidence.

Together, these papers now make a strong case that a Cdc20/C-Mad2-mediated amplification does not exist. But despite this setback, the amplification idea survives. Other colleagues have already proposed a new mechanism how amplification of the checkpoint signal could be accomplished.

So now we spend our days and nights trying to falsify their theory.

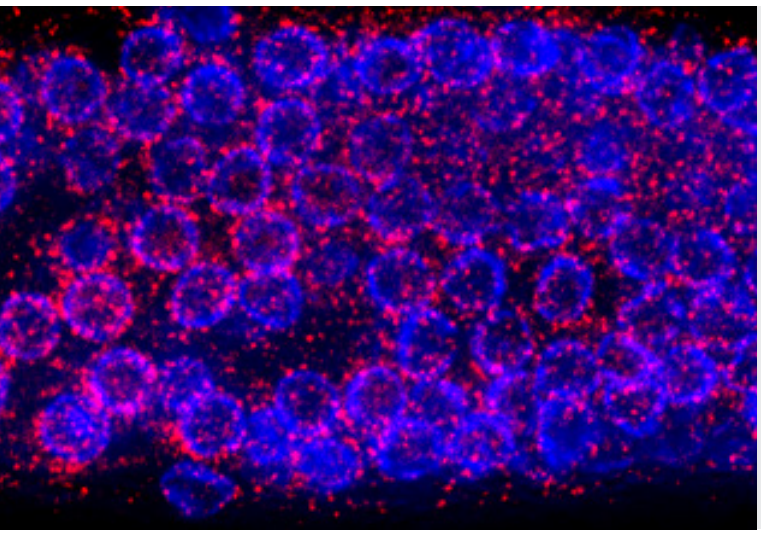
A new light on Spindle assembly checkpoint in chromosome distribution
by Silke Hauf

A new light on Spindle assembly checkpoint in chromosome distribution

The author:

Silke Hauf
Assistant Professor in Biological Sciences at Virginia Tech, Blacksburg, USA

Her group has an interest in the mechanisms that make cell division a highly reliable process. This includes how the spindle assembly checkpoint guards chromosome segregation. Following into the footsteps of the Ciliberto group, her lab combines experiments and computational modeling to understand the dynamics and regulation of mitosis.



A key insight on the enzymatic activity of AID

science

A commentary to Svend Petersen-Mahrt's paper published on Journal of Experimental Medicine

by Michael Neuberger

DNA alterations that lead to cancer are often generated via chemical or physical damage to our genomes and can be caused, for example, by smoking or UV light, which induce defined lesions into DNA. At the heart of our own defences against cancer lie a multitude of biochemical pathways that have evolved to repair this damage, keeping our genomes healthy. However, to ward off the invasive pathogens such as bacteria and viruses, evolution has also designed a system in which intentionally-induced DNA damage is a key step in producing a functional immune system.

The work from Dr. Petersen-Mahrt's laboratory provides a key insight into how this intentional DNA damage is introduced into the antibody genes, which in turn could also provide insight how such damage could lead to cancer. The breakthrough came from discovering how a small protein, AID, functions within the nucleus.

AID is a member of a family of proteins that induce DNA damage by removing an amino group (deaminating) from the base cytosine in our DNA. If this deamination is not corrected, then the deaminated cytosine will miscode for another base during DNA copying and mutations will arise. Should AID lose its focus on its usual target (the antibody genes), then deaminated cytosines will be generated throughout the genome and cause mutations predisposing to cancer development.

Using a novel approach to isolating AID protein from immune cells, Dr. Petersen-Mahrt's group was able, for the first time, to demonstrate the existence of a particular protein complex on chromatin containing AID and other members of the gene transcription machinery. By identifying an essential protein (PAF1) of the transcription machinery as an associated partner of AID, Dr. Petersen-Mahrt and his team were able to provide a model as to how the cell controls AID activity.

During the act of transcribing a gene, the RNA polymerase will slow down, stall and restart - processes influenced by PAF1. If AID associates with RNA polymerase during this time, the deaminated cytosines might not be repaired but could give rise to mutations and recombination. Such a mechanism is consistent with molecular observations made by other laboratories in the field.

A group from Rockefeller University had uncovered a complex that functions upstream of PAF1, while work of groups from Kyoto University and Harvard University identified downstream connections.

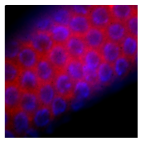
Dr. Petersen-Mahrt was able to confirm all the proposed connections, which should greatly assist the emergence of a coherent view of how AID is retained and functions at the antibody gene loci.

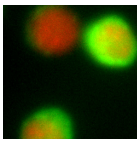
A role for the RNA pol II-associated PAF complex in AID-induced immune diversification.
Antibody diversification requires the DNA deaminase AID to induce DNA instability at immunoglobulin (Ig) loci upon B cell stimulation. For efficient cytosine deamination, AID requires single-stranded DNA and needs to gain access to Ig loci, with RNA pol II transcription possibly providing both aspects. To understand these mechanisms, we isolated and characterized endogenous AID-containing protein complexes from the chromatin of diversifying B cells. The majority of proteins associated with AID belonged to RNA polymerase II elongation and chromatin modification complexes. Besides the two core polymerase subunits, members of the PAF complex, SUPT5H, SUPT6H, and FACT complex associated with AID. We show that AID associates with RNA polymerase-associated factor 1 (PAF1) through its N-terminal domain, that depletion of PAF complex members inhibits AID-induced immune diversification, and that the PAF complex can serve as a binding platform for AID on chromatin. A model is emerging of how RNA polymerase II elongation and pausing induce and resolve AID lesions. [PMID: 23008333]

The role of AID in causing cancer has been well documented, but suitable pharmacological targets, aside from AID, have not been identified: PAF1 may prove a possible target. Because AID has been implicated in the development of chemo-drug resistance in patients, interrupting the PAF1-AID association might be a means to control AID mutability during therapy. The on-going work in Dr. Petersen-Mahrt is geared towards using high-throughput analysis to identify AID and AID function inhibitors.

Evolutionary offsprings of AID (APOBEC3 family of proteins) are known to inhibit viral infections such as HIV. A recent report has shown that PAF1 has an important function in HIV restriction, yet a functional mechanism was not proposed. In light of Dr. Petersen-Mahrt lab's finding, it could be that the interaction of the AID/APOBEC family with the RNA transcription machinery is ancient and conserved, and pharmacological characterisation could be beneficial for cancer as well as HIV therapy.

DNA Editing in Immunity and Epigenetics,
Svend Petersen-Mahrt

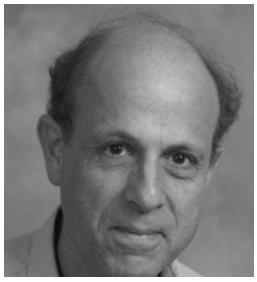




A key insight on the enzymatic activity of AID
by Michael Neuberger

A key insight on the enzymatic activity of AID

The author:



Michael Neuberger

Immunity and DNA deamination, MRC Cambridge

2 November 1953
26 October 2013

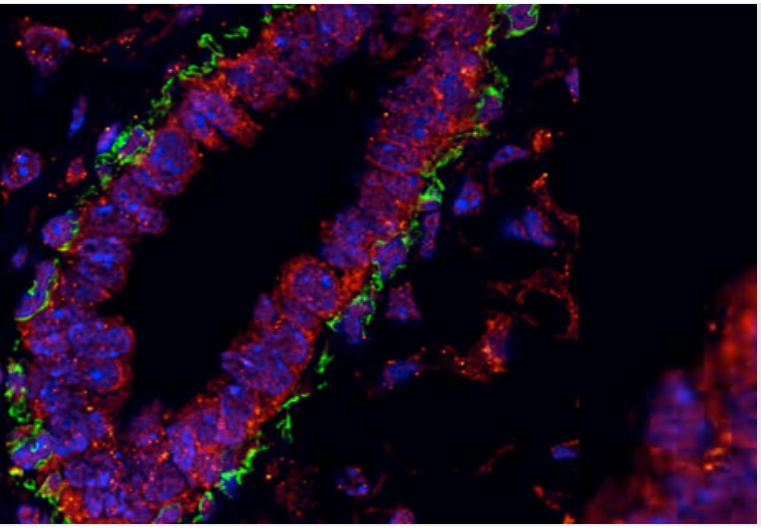
Prof. Michael Neuberger served as Joint Head of Division of Protein and Nucleic Acid Chemistry at the Medical Research Council Laboratory of Molecular Biology in Cambridge, UK and Honorary Professor of Molecular Immunology at the University of Cambridge.

Prof. Neuberger's major research interests were directed towards understanding the biochemical processes and the physiological pathways by which diversity is created within antibodies.

In his 25 years of work on antibodies, he made key discoveries on the molecular mechanisms of antibody gene expression and diversification as well as important contributions to the major technologies underpinning antibody engineering.

He published more than 150 manuscripts and is the inventor of several patents and applications in the field of antibody engineering. Up to his last days he served as Member of Scientific Advisory Board at Open Monoclonal Technology, Inc., at AnaptysBio, Inc. (formerly, Anaptys Biosciences, Inc) and at IFOM.

He was also a past or present member of a number of academic and editorial boards and consulted for various companies interested in antibody engineering including Cambridge Antibody Technology (CAT), Xenova-Cantab, and Therapeutic Human Polyclonals.



The role of MYBBP1A in early embryonic development

science

Commentary on Francesco Blasi's paper published on PloS one

by Tom Gonda

MYB binding protein 1A (MYBBP1A) was originally identified and cloned in 1998 in my laboratory by virtue of its ability to interact with the MYB transcription factor, which is encoded by the MYB oncogene. MYB in turn is a key regulator of normal and cancer cells of blood-forming, breast, colon and other tissues. Subsequently, a bewildering array of interactions and functions has been reported for MYBBP1A.

Some of these are interactions with other transcription factors, suggesting a relatively direct role in the regulation of gene expression. However a number of recent reports have implicated MYBBP1A in the synthesis and processing of ribosomal RNA, and in the responses to so-called "ribosomal stress", which can result from an imbalance between production of ribosomal RNA and protein components. Such functions are consistent with our original report that much - but not all - of MYBBP1A is found in the nucleolus, where ribosomes are assembled.

Intriguingly, the ribosomal stress response is mediated at least partly by the p53 tumour suppressor, which is activated by a process involving MYBBP1A. A function in such a fundamental process as ribosome biogenesis is consistent with the very early death of mouse embryos that lack the Mybbp1a gene, as reported by *Mori et al.*

Another important facet of MYBBP1A function that is emerging is its potential role as a tumour suppressor. Apart from its negative effect on MYB activity, as we originally reported, there are several more recent reports of a tumour suppressor role for MYBBP1A, including in breast cancer and head & neck cancer.

Here again the connection to p53 - probably the best-known tumour suppressor of all - becomes relevant. It is here also that the work of Mori et al sheds some new light by examining directly the

effects of reduced levels of MYBBP1A (MYBBP1A "knockdown") on malignant transformation of non-cancerous cells and also on the cell division cycle ("cell cycle") which underlies and drives cell growth. The results paint a somewhat complex picture which is consistent, though, with the multi-faceted function of this protein. Entirely consistent with a tumour suppressor function, the authors found that reducing Mybbp1a levels in the NIH3T3 mouse fibroblast cell line made it more susceptible to cancerous transformation by the well-known Ras oncogene, and increased the growth rate of tumours derived from these transformed cells in mice.

In apparent contrast, though, Mori *et al.* also found that in some other cell types, MYBBP1A knockdown actually inhibited cell proliferation and in some cases promoted cell death. Moreover, the effect on cell proliferation involved restricting progress through the late stages of the cell cycle (Gap2 and Mitosis or G2/M)) that follow DNA synthesis, during which chromosomes and the cell itself are prepared for division.

The expression of several genes involved in G2/M were affected by MYBBP1A knockdown, and a role at G2/M is also consistent with a report that MYBPP1A is a modified by the Aurora B protein, which plays critical roles during mitosis. Finally, like its role in ribosome biogenesis, such a role in the fundamental process of cell division may also be reflected in the requirement for this protein at the very earliest stages of embryonic development.

Myb-binding protein 1A (MYBBP1A) is essential for early embryonic development, controls cell cycle and mitosis, and acts as a tumor suppressor.
Abstract MYBBP1A is a predominantly nucleolar transcriptional regulator involved in rDNA synthesis and p53 activation via acetylation. However little further information is available as to its function. Here we report that MYBBP1A is developmentally essential in the mouse prior to blastocyst formation. In cell culture, down-regulation of MYBBP1A decreases the growth rate of wild type mouse embryonic stem cells, mouse embryo fibroblasts (MEFs) and of human HeLa cells, where it also promotes apoptosis. HeLa cells either arrest at G2/M or undergo delayed and anomalous mitosis. At mitosis, MYBBP1A is localized to a parachromosomal region and gene-expression profiling shows that its down-regulation affects genes controlling chromosomal segregation and cell cycle. However, MYBBP1A down-regulation increases the growth rate of the immortalized NIH3T3 cells. Such Mybbp1a down-regulated NIH3T3 cells are more susceptible to Ras-induced transformation and cause more potent Ras-driven tumors. We conclude that MYBBP1A is an essential gene with novel roles at the pre-mitotic level and potential tumor suppressor activity. [PMID: 23056166]

The report from Mori and colleagues, together with other recent findings on MYBBP1A, show some new roles for this protein, highlight its fundamental importance in cell function, and raise many intriguing questions and possibilities; here are just a few. First, why are there opposite effects of MYBBP1A knockdown on different cells types? This was not related to the absence or presence of p53 since growth inhibition was seen in cell lines that have and that lack p53.

Maybe some cancer and pre-cancerous (such as NIH3T3) cells have mutations that allow them to progress through mitosis in the presence of abnormally low levels of MYBBP1A, under which conditions its tumour-suppressive functions (perhaps related to its ability to activate p53), might become apparent.

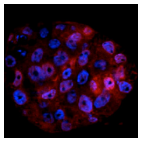
The role of MYBBP1A in early embryonic development
by Tom Gonda

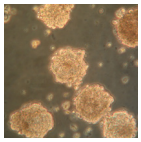
Secondly, does MYBBP1A directly regulate expression of cell cycle/mitotic genes, and if so, how? Does this reflect its ability to interact with and modulate the activity of specific transcription factors, or are the changes in G2/M gene expression a consequence of MYBBP1A's (other) effects on mitosis.

Third, is MYBBP1A's relationship to ribosomal stress and p53 involved in diseases where ribosomal stress appears to be involved, such as Diamond-Blackfan anaemia?

Another question relates to how MYBBP1A functions to modulate the activity of various transcription factors.
Does this reflect a distinct activity and set of interactions with other proteins, or is it in some way related to its nucleolar or other locations within the nucleus?

Many of us look forward to the answers to these and many other questions surrounding this ubiquitous and enigmatic protein.





Transcriptional Regulation in Development and Cancer, Francesco Blasi

The role of MYBBP1A in early embryonic development
by Tom Gonda

The role of MYBBP1A in early embryonic development

The author:

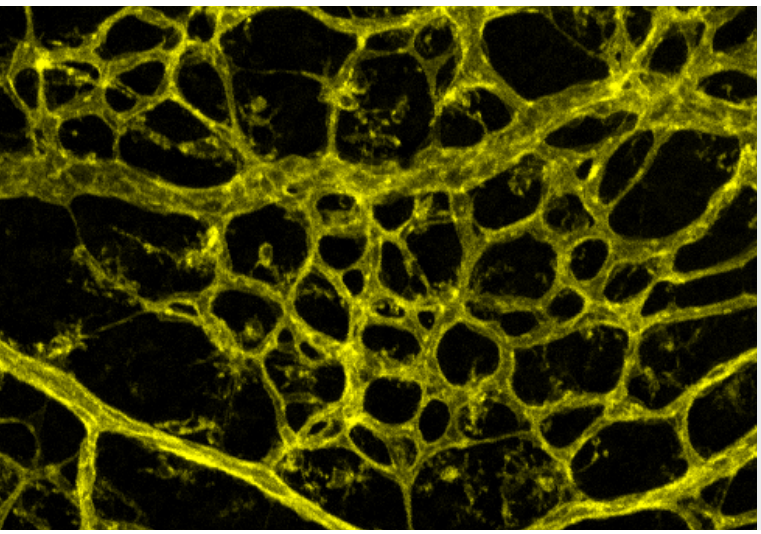
Tom Gonda

School of Pharmacy, University of Queensland, Brisbane Australia

Following his PhD in Adelaide, Prof. Gonda carried out postdoctoral research at UCSF with Nobel Laureate Prof. J. Michael Bishop. This position started his ongoing interest in haematology and the MYB oncogene. Prof. Gonda returned to Australia in 1982 to the Ludwig Institute, Melbourne, where he expanded his research to include retroviral vectors and cytokines.

Prof. Gonda continued these themes upon returning to Adelaide in 1990 at the Hanson Institute. From 2001-3 he gained biotechnology industry experience as Chief Scientist of Bionomics Ltd. He then returned to academia at the University of Queensland, first at the Diamantina Institute and now the School of Pharmacy. Prof. Gonda's research focuses on the role and therapeutic targeting of MYB in leukaemia and breast cancer. He has also been heavily involved in cancer gene discovery projects utilising functional genomics, genetic screens and genomic sequencing.

Prof. Gonda has contributed to the organisation of several scientific conferences including "New Directions in Leukaemia Research", which he co-founded. He has published in Nature, Cell, PNAS, EMBO J, Blood, Leukemia and Nature Reviews Cancer, and has obtained funding from major national and international agencies.



The role of VE-cadherin in vascular permeability

science

Commentary on Elisabetta Dejana's paper published on Nature Communications

by Michael Gimbrone

The vascular endothelium, the single-cell-thick lining of the human cardiovascular system, is a living membrane that comprises a container for blood. The integrity of this container is essential for the health of the various tissues and organs of the body, and changes in its permeability are a hallmark of acute and chronic inflammatory disease processes.

The building blocks of this dynamic barrier are individual endothelial cells, which are linked together by a complex of intercellular molecular bridges that serve as the "gate-keepers" for the trans-endothelial movement of proteins, fluid, and cells.
For many years it has been appreciated that this endothelial barrier function varies in the different types of vessels-arteries, veins, capillaries-that comprise the branching vascular tree. Interestingly, inflammatory mediators, such as histamine and bradykinin, show a selective effect on the venous side of the microcirculation.

The IFOM research group led by Professor Elisabetta Dejana has been at the forefront of dissecting the molecular components of these endothelial junctional complexes, and the mechanisms of their regulation in health and disease. In this report, they provide an in-depth analysis of the biochemical processes controlling the cell-cell "zipper" function of VE-cadherin, a key determinant of endothelial permeability, in the context of the inflammatory response.

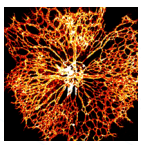
Specifically, they establish that phosphorylation of certain amino acids within the structure of VE-cadherin occurs constitutively within veins, but not arteries, in vivo, and that inflammatory mediators such as bradykinin, preferentially act to enhance the internalization/degradation of these phosphorylated junctional proteins, resulting in a localized, rapid but transient, increase in vascular permeability.

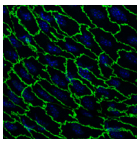
In effect, this provides a mechanistic explanation for the topography of increased permeability in inflammation. Further, they establish that differences in the magnitude of the fluid mechanical forces imparted by blood flow (lower in veins than in arteries) may be responsible for the observed spatial pattern of VE-cadherin phosphorylation that sensitizes vessels to the action of inflammatory mediators.

A major strength of this work is the skillful use of both in vitro (cultured cell models) and in vivo (intravital molecular microscopy) strategies to probe the cellular and molecular mechanisms of these fundamental vascular biological processes. Their novel results point the way to potential new pharmacologic interventions in inflammatory diseases.

Phosphorylation of VE-cadherin is modulated by haemodynamic forces and contributes to the regulation of vascular permeability in vivo.
Endothelial adherens junctions maintain vascular integrity. Arteries and veins differ in their permeability but whether organization and strength of their adherens junctions vary has not been demonstrated in vivo. Here we report that vascular endothelial cadherin, an endothelial specific adhesion protein located at adherens junctions, is phosphorylated in Y658 and Y685 in vivo in veins but not in arteries under resting conditions. This difference is due to shear stress-induced junctional Src activation in veins. Phosphorylated vascular endothelial-cadherin is internalized and ubiquitinated in response to permeability-increasing agents such as bradykinin and histamine. Inhibition of Src blocks vascular endothelial cadherin phosphorylation and bradykinin-induced permeability. Point mutation of Y658F and Y685F prevents vascular endothelial cadherin internalization, ubiquitination and an increase in permeability by bradykinin in vitro. Thus, phosphorylation of vascular endothelial cadherin contributes to a dynamic state of adherens junctions, but is not sufficient to increase vascular permeability in the absence of inflammatory agents. [PMID: 23169049]

New strategies to inhibit tumor angiogenesis,
Elisabetta Dejana





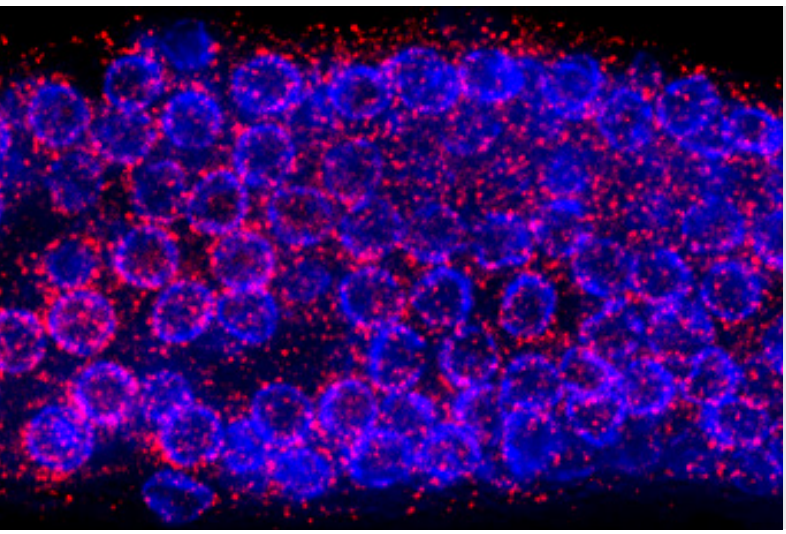
The role of VE-cadherin
in vascular permeability
By Michael Gimbrone

The role of VE-cadherin
in vascular permeability

The author:

Michael A. Gimbrone Jr., M.D.
Professor of Pathology at Harvard Medical School

Dr. Gimbrone is the Elsie T. Friedman Professor of Pathology at Harvard Medical School and the Director of the Center for Excellence in Vascular Biology at the Brigham and Women's Hospital, Boston, Massachusetts. He is a recognized leader in the field of vascular cell biology, and in particular the role of endothelial cells in inflammation and atherosclerosis.



Dark matter of the genome, a safeguard of genetic integrity

science

Commentary on Fabrizio d'Adda di Fagagna's paper published on Nature

by Geneviève Almouzni & Antonin Morillon

With the advances of DNA sequencing technologies, the realization that 99% of the human genome is non-protein coding has highlighted the under-appreciated potential that lies within the dark matter of the genome. More strikingly, the recent ENCODE project estimated that the number of expressed non-coding genes, so called pervasive transcripts, is now more prominent than the number of coding genes [1]. Thus, understanding how non-coding transcription can be associated with particular function in vivo is an area that is subject of debate [2] and deserves deeper investigations. In particular it is important to explore how the pervasive transcription that generates thousands of non-coding transcripts can regulate gene expression and have broad impacts on development and disease in many organisms [3]. Long and small non-coding RNAs have no protein-coding potential and do not overlap with characterized classes of non-coding RNAs [4, 5].

In contrast to RNAi, miRNA and piRNA-mediated gene regulation, the novel classes of long and short ncRNA are still poorly defined whether it is for their putative regulatory role(s) or for their systematic catalog in living cells. In addition, if the majority of the ncRNA do not have function yet associated with their expression, gene regulation-mediated by ncRNA remains the most studied activity, leaving as terra incognita the role of the ncRNA on general DNA maintenance and chromosome stability.

A few examples of DNA and chromatin territories modulation by long ncRNA have been described from X inactivation, DNA looping, chromosome pairing and epigenetic regulation [6]. Concerning small ncRNA, previous work on the filamentous fungus Neurospara crassa revealed the existence of short ncRNA (qiRNA), expressed from the rRNA locus, associated with argonaute protein and induced upon DNA damage [7].

Site-specific DICER and DROSHA RNA products control the DNA-damage response

Non-coding RNAs (ncRNAs) are involved in an increasingly recognized number of cellular events. Some ncRNAs are processed by DICER and DROSHA RNases to give rise to small double-stranded RNAs involved in RNA interference (RNAi). The DNA-damage response (DDR) is a signalling pathway that originates from a DNA lesion and arrests cell proliferation3. So far, DICER and DROSHA RNA products have not been reported to control DDR activation. Here we show, in human, mouse and zebrafish, that DICER and DROSHA, but not downstream elements of the RNAi pathway, are necessary to activate the DDR upon exogenous DNA damage and oncogene-induced genotoxic stress, as studied by DDR foci formation and by checkpoint assays. DDR foci are sensitive to RNase A treatment, and DICER- and DROSHA-dependent RNA products are required to restore DDR foci in RNase-A-treated cells. Through RNA deep sequencing and the study of DDR activation at a single inducible DNA double-strand break, we demonstrate that DDR foci formation requires site-specific DICER- and DROSHA-dependent small RNAs, named DDRNAs, which act in a MRE11–RAD50–NBS1-complex-dependent manner (MRE11 also known as MRE11A; NBS1 also known as NBN). DDRNAs, either chemically synthesized or in vitro generated by DICER cleavage, are sufficient to restore the DDR in RNase-A-treated cells, also in the absence of other cellular RNAs. Our results describe an unanticipated direct role of a novel class of ncRNAs in the control of DDR activation at sites of DNA damage. [PMID: 22722852]

However, if the biogenesis of qiRNAs has started to be deciphered and required the RNAi pathway, their precise function remains unknown and they are still considered as aberrant siRNA [8].

The team of Fabrizio d'Adda di Fagagna at IFOM, seeking for factors involved in DNA damage signaling pathways, explored why diverse human cells became sensitive to DNA damage when DICER and DROSHA, the two enzymes processing small ncRNA, are absent. Using high-throughput sequencing approaches in collaboration with the RIKEN institute in Japan, combined with appropriate genomic engineering on human and invertebrate systems, they identified the presence of novel small ncRNA, that they coined the DNA Damage RNA (DDRNA).

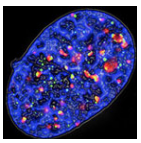
These RNAs are produced from the DNA damage site [9] and necessary for signaling the damage to the DNA repair machinery. Indeed, impairing the biogenesis of the DDRNA results in cells enabled to repair and cell-cycle arrested. Strikingly, the very same damaged cells when grown in presence of a set of artificially produced DDRNA corresponding to the DNA damage site, recover their ability to repair their broken DNA.

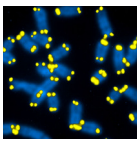
The authors propose that the DDRNA could trigger the molecular alarms through which the cell detects the problem and resolves it by repairing the damage. The exact molecular mechanism behind this DDRNA signaling pathway should be explored in the future.

Interestingly, two other teams, using two different model organisms, drosophila and Arabidopsis thaliana reached independently similar conclusions. Thus this novel DDRNA signaling pathway may have broad implications in various organisms.

In drosophila, DDRNA are generated from the DNA double-strand breaks at the end of chromosome, resulting from an active sense/antisense transcription and leading to gene silencing at the vicinity of the damage [10]. In plants, DSB-induced small RNAs, similar to DDRNA, are potentiated by argonaute for an unknown process [11].

Although in both studies the direct roles of DDRNA have not been explored in details, these works suggest that DDRNA is a conserved and widespread mechanism that relays the DNA repair machinery, opening new avenues for the function of small ncRNA in DNA maintenance regulation.





DNA Damage Response and Cellular Senescence, Fabrizio d'Adda di Fagagna

The notion that the dark matter of the genome represents a tremendous resource for various functions is now coming into a reality. It would not be surprising to soon realize that beyond DNA processes even unsuspected cellular functions will be demonstrated to be modulated by ncRNA. (nc) RNA should thus take a full space as a major actor in the molecular biology of the cell and the genetic world [12, 13].

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Geneviève Almouzni

Deputy Director of the Institut Curie (Paris, France)
Director of research at the CNRS, head of the Nuclear Dynamics and Genome Plasticity unit, a mixed structure between the Institut Curie and the CNRS.

Geneviève Almouzni is director of research at the CNRS, head of the Nuclear Dynamics and Genome Plasticity unit, a mixed structure between the Institut Curie and the CNRS. Her team, chromatin dynamics, over the years has conducted research on chromatin, histone variants, histone chaperones and nuclear organization with a particular interest on heterochromatin. Her general objective has been to dissect the mechanisms of chromatin assembly, from the basic structural unit, the nucleosome, up to the higher-order structures in the nucleus.

In addition, her work on specific nuclear domains has unveiled the importance of non-coding centromeric heterochromatic regions, which are of major importance for chromosome segregation and relevant for cancer. Her lab has exploited a variety of tools and models to understand the in vivo functions of chromatin dynamics (e.g. Xenopus, mouse) that combine biochemistry, cell biology, and developmental biology. These integrated approaches from molecules to tissue and a whole organism are actively pursued in particular within the network of excellence EpiGeneSys, to move epigenetics towards system biology (www.epigenesys.org) for which she acts as the scientific coordinator.

Dark matter of the genome,
a safeguard of genetic integrity

The authors:

Antonin Morillon

Centre National de la Recherche Scientifique
Director of Research (Paris, France)

Antonin Morillon is director of research at CNRS and group leader of the ncRNA, epigenetics and genome fluidity team at Institut Curie. He is an ERC starting grant laureate and member of Young EMBO investigator program. His interests are to understand the epigenetic functions of long non-coding (lnc)RNAs in eukaryotes, especially those antisense to genes. Using RNA-seq technology, his team defined a novel class of cryptic lncRNA in yeast, termed XUTs with a regulatory function on gene expression that might be conserved throughout the eukaryotic kingdom and might have a role on genomic instability. The activity of the team is mostly dedicated to yeast genetics but also to genomics in human cancer cells.

Ubiquitin and SUMO: an hands-on experience... by the sea

Personal memories for a memorable EMBO Practical Course organized by Simona Polo

by Ronald T. Hay

The 4th EMBO Practical Course on "Ubiquitin and SUMO" was run from 1-8th September, 2012 in Sardinia, Italy. It is difficult to imagine a more beautiful setting for the course than the Porto Conte Ricerche, Capo Caccia in Alghero, Sardinia.

The self-contained Research Centre has laboratories, lodgings, lecture halls as well as a bar and restaurant located on a single site within a nature reserve, that overlooks a beautiful bay on the coast of the small peninsula.

Simona Polo of IFOM, Milan organized the course and was ably assisted by her co-organisers Helle Ulrich (CRUK, London), Frauke Melchior (ZMBH, Heidelberg) and Ivan Dikic (Goethe University, Frankfurt). The whole course ran like clockwork and was a testament to the administrative skills of Daniela Ubezio of IFOM.

This was a truly international event with students coming from 12 European countries and lecturer/instructors coming from the USA and 4 European countries. Certainly the course was not for the faint-hearted. After an early breakfast course work started at 08.30 and was rarely finished by 23.00. The formal part of the proceedings consisted of 5 set experiments, one bioinformatics exercise and 9 lectures.

Topics covered in the practical experiments included "Properties of non-covalent binding between ubiquitin/Ubls and their binding domains" (Ivan Dikic and Jelena Korac), "Detection of ubiquitin and SUMO targets in yeast" (Helle Ulrich and Jonathan Lowther), "In vitro analysis of deubiquinating enzymes" (David Komander and Yogesh Kalathu, MRC, Cambridge), "Detection of ubiquitin targets in mammals" (Simona Polo, Sara Sigismund and Elena Maspero) and "in vitro SUMOylation" (Frauke Melchior and Annette Flotho).

About the pratical course
The chief objective of this course is to present the state-of-the-art methodology for the analysis of ubiquitination and sumoylation to scientists who are unfamiliar with this field. This will involve practical experiments demonstrating the use of modifying enzymes and ubiquitin receptors in vitro, the identification and analysis of in vivo targets in mammalian cells and yeast, and a tutorial on predictive and search tools for the bioinformatic analysis of components of the ubiquitin system.

A computer based "Bioinformatical approaches to the ubiquitin system" was led by Kay Hofmann (Cologne). Each of the practical sessions was supplemented by a lecture and an additional guest lecture was provided by Wade Harper of Harvard Medical School, Boston on his ubiquitin-related work. Within the course framework two seminars took place, co-sponsored by EMBO and Porto Conte Ricerche on "Proteomics of SUMOylation and other ubiquitin-like molecules."

The objective being to present the state-of-the-art methodologies for the application of proteomic techniques for the identification of the sites of modification by ubiquitin and ubiquitin-like proteins. Ron Hay (Dundee) discussed the challenges posed in mapping sites of SUMO modification, while Chuna Ram Choudhary (Copenhagen) discussed recent developments in mapping sites of ubiquitination.

Of course it wasn't all formal lectures or practical sessions and when we were all flagging in the late afternoon, proceedings were enlivened by "Meeting the teacher on the beach".

This involved far-reaching discussions on almost any aspect of science and when our voices finally gave out we all plunged into the crystal clear waters of the bay for a swim.

Getting back to the experiments after this demanded strong wills all round, but after the formal session finished everyone perked up and lively discussion continued, over refreshments, into the next day.

During a free afternoon a boat trip was organized to the spectacular Capo Caccia caves and I suspect all of us were impressed by the magnificence of the cave and its geologic structures.

Some pictures from the course

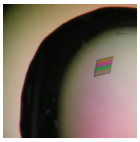
Ubiquitin and SUMO: an hands-on experience... by the sea
by Ronald T. Hay

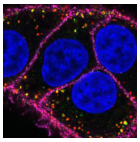
On a more cultural note a trip to Alghero was rounded off with a memorable dinner of traditional Sardinian food and wine.

As we wrapped up the course at the end of a busy week it was clear that the participants were going back to their labs with a bag full of useful constructs and a much better idea of how to tackle the problems posed by the members of the ubiquitin family.

The hope is that they will be better equipped to address problems in the field and will have made friendships and collaborations that will last for many years. We were all appreciative of the efforts of Simona and her co-organisers on putting together a great course.

The group of the participants





EMBO Global Activities, Simona Polo

Ubiquitin and SUMO: an hands-on experience... by the sea
by Ronald T. Hay

Ubiquitin and SUMO: an hands-on experience...
by the sea

The author:

Ronald T. Hay

Centre for Gene Regulation and Expression and Honourary member of Scottish Institute for Cell Signalling, College of Life Sciences, University of Dundee

Ron Hay was born and educated in Dundee and studied for a degree in Biochemistry at Heriot-Watt University, Edinburgh (1971-1975). His PhD was at the Medical Research Council Virology Unit in Glasgow (1975-1979) after which he was awarded a Damon Runyon-Walter Winchell Cancer Fund postdoctoral fellowship to work at Harvard Medical School, Boston on SV40 DNA replication (1979-1982). Returning to the MRC Virology Unit he established his independent laboratory (1982-1985), then moved to the University of St. Andrews where he held Lecturer and Reader positions before taking up the Chair in Molecular Biology and became Deputy Director of the new Centre for Biomolecular Sciences. In October 2005 he took up the Chair of Molecular Biology in the University of Dundee and is part of the Centre for Gene Regulation and Expression.

Ron's research has established conjugation with the Small Ubiquitin-like Modifier (SUMO) as an important regulatory mechanism in eukaryotes. A key role for SUMO and ubiquitin was uncovered in mediating the effects of arsenic when it is used therapeutically in the treatment of Acute Promyelocytic Leukaemia. Recently determination of the structure of a RING E3 ligase and ubiquitin-loaded E2 complex primed for catalysis has revealed the mechanism of ubiquitin modification.

Ron is a Wellcome Trust Senior Investigator and a fellow of the Royal Society, the Royal Society of Edinburgh, the Academy of Medical Sciences, Academia Europaea and is a member of the European Molecular Biology Organisation. In 2012 Ron was awarded the Novartis Medal and Prize of the Biochemical Society.

YouScientist: a live research program for science conscious citizens

The first year of the new IFOM Science & Society program

by Giorgio Scita

The aim of YouScientist is to widen the bridge connecting science with society by allowing a lay audience to live and experience the world of molecular biology firsthand, to hold test tubes and restriction enzymes. Participants work side-by-side with scientists and experience not only the passion and enthusiasm, but also the difficulties, frustrations and limitations of scientific research.

For centuries, science has been considered an activity driven primarily by curiosity on the part of the scientist. This attitude is at the heart of the mission at institutions like IFOM. At IFOM, the need to "understand cancer in order to treat it" translates into creating the conditions for individual researchers to develop instincts, passion and an unstoppable desire to explore and to go beyond the limits of current knowledge. Overturning dogmas, calling apparently acquired knowledge into question, taking the road less traveled - there are things that drive research, and especially cancer research.

This aspect is encoded in IFOM's genome, where another aspect has also gradually taken root: awareness that the link between the world of science and society has become increasingly intimate. There is increasing awareness that scientific discoveries influence everyday life, changing the lives and health of the public.

There is a growing need for researchers who are supported by public funds or donations to explain their activities and results. It follows that science must continually inform about the benefits that society can draw from its activities. Finally, there is a growing awareness among scientists that, along with their knowledge comes the responsibility to help solve public health, environmental, economic and educational problems. The stereotype of researchers hidden among test tubes on the bench has been replaced by that of 21st century scientists, aware of their role and above all their responsibilities towards society.

IFOM has established YouScientist in response to these needs and to the issues that scientists and society need to understand.
Leveraging decades of experience in communicating their science to students at high schools and others, 2012 was marked by efforts to expand this extraordinary audience.

The philosophy and strategy of the first initiatives was to transfer the training role typical of a school to a society thirsting for information. The strategy involved the use of methods and issues that rely on empathy, emotion and enthusiasm, which are the primary drivers of scientific activity, involving both rational and emotional spheres, gaming and entertainment.

Two new initiatives were launched in the context of the Researchers' Night.

IFOM was chosen as the institutional partner of "Meet Me Tonight" the Milan edition of Researchers' Night 2012, held on September 28, 2012. Researchers' Night is a European Commission initiative to promote contact between citizens and the world of research by involving them in games, lessons, experiments, competitions, demonstrations and seminars.

For IFOM, participating in Meet Me Tonight was an important opportunity to consolidate relationships with institutions and learning centers in the territory and a chance for greater openness towards society in general.

The first of these initiatives focused on projection of the documentary "The dark side of the sun" which was followed by a debate at the Spazio Oberdan, organized in collaboration with the Department of Culture of the Province of Milan.

This documentary by Carlo Shalom Hintermann, which received a special mention at the 2013 edition of the Rome International Film Festival, was sponsored by IFOM because of the high scientific and social interest of the topics discussed: *Xeroderma pigmentosum*, a rare disease that forces affected children to live in isolation, away from the daytime world of their peers. "The dark side of the sun" documents the positive experience of Camp Sundown, a summer camp established in upstate New York by the parents of an XP patient that receives patients from all over the world.

The event opened with an introduction by Novo Umberto Maerna, Commissioner for Culture for the Province of Milan. Viewing of the film was followed by a discussion stimulated by insights that had emerged, with topics ranging from the relationship between rare diseases and society, to effective advancement of knowledge in these areas of science, and the social and cultural contribution that a film can provide.

YouScientist:
a live research program for science conscious citizens
by Giorgio Scita

The debate, moderated by Eliana Liotta, Director of OK Salute, involved the film's director Carlo Hintermann, IFOM scientist Giorgio Scita, psychologist and director of IRIDe Gabriella Pravettoni, director of the Filmmaker Festival Luca Mosso, and director of the "Vedere la Scienza" Film Festival Pasquale Tucci.

Youscientist, IFOM Science & Society program

There was a very lively exchange of views among the participants in the debate. Film critic Morando Morandini was among the 70 spectators in the audience.

The second organized event was LAB GAME. This initiative is part of a project that aims to explain complex molecular biology concepts to the public by inviting people to improvise a performance of song, dance, mime, or acting. LAB GAME relies on the most recent advances in the cognitive field, which show that cognitive, emotional and creative involvement improves the capacity to learn and explain information, including scientific topics.

LAB GAME participants learned the scientific basis of biological phenomena important for cellular development and for the life of the organism. They also explore the correlations between lifestyle, genetic predisposition to the risk of a disease and health. This developed new awareness of their lifestyle and at the same time an unexpected interest in research, its discoveries and their impact in daily life.

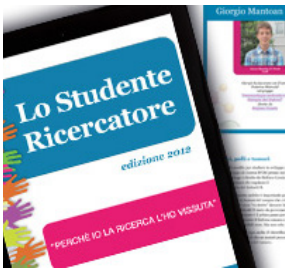
During "Meet Me Tonight", the public was offered a LAB GAME that involved the process of DNA replication and the health consequences of the damage that can occur during this process. LAB GAME had a great impact on the 90 participants, who also had fun playing it.

YouScientist:
a live research program for science conscious citizens
by Giorgio Scita

Activities and numbers

YouScientist program activities in 2012 included consolidation of a series of historical initiatives aimed at schools: educational workshops, scientific conferences, guided tours of IFOM research laboratories, Summer School and special events in the framework of national scientific events.

In particular, in 2012 YouScientist conducted 40 activities involving 2,633 people and 125 schools participated in these IFOM initiatives.



Among the program activities, note in particular the following projects:

"The student researcher", the IFOM summer school, now in its eighth edition and for the first time promoted nationwide. The project is aimed at students in the fourth year of secondary school. Selection is based on performance on school curriculum and scores on a particularly selective test. In 2012, of 313 applications from 202 schools in 70 Italian provinces, we selected 17 outstanding students, who completed a two-week internship in the IFOM research laboratories and attended a science communication training program.

The project concluded with the event "Poster Day, Science is an experience to communicate" during which the students discussed their scientific posters in front of an audience of non-experts. The project led to the publication of an e-book "Because I Have Experienced Research") and the promotional video of the YouScientist program. The project also received ample coverage in the local and national media.

The educational workshop "Discover your own DNA!" was aimed at thirty legal experts and implemented under the Advanced Training Course in Forensic Genetics, sponsored by the Superior Council of the Judiciary, by the Criminal Chamber of Milan, the European School of Molecular Medicine and the European Institute of Oncology. During the workshop, the legal experts undertook the purification of their own DNA from the buccal mucosa cells, exploring the scientific aspects of this procedure and its implications for genetic analysis.

The change in communication paradigms in science requires increasingly direct involvement by scientific research institutes, while maintaining their founding mission, which in the case of IFOM is the acquisition of knowledge on cancer as a step towards effective cancer therapy.

YouScientist:
a live research program for science conscious citizens
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YouScientist: a live research program
for science conscious citizens

The author:

Giorgio Scita

YouScientist program

A cell biologist and expert on the dynamics of cell movement, Giorgio Scita directs the Mechanisms of Tumor Cell Migration research unit at IFOM.

Born in 1963 near Parma, Scita enrolled in the Faculty of Biology at the University of Parma in 1982 with a precise intention: to study animal behavior alongside the famous Italian ethologist Danilo Mainardi.

However, this was the time of the great explosion of molecular biology: “They began to identify and clone genes, to move from genes to proteins, to study their functions. It was impossible not to be fascinated.”

Therefore, Scita focused on the behavior of proteins, graduating in 1986 with a thesis on the biochemistry of the metabolism of one of the most powerful antioxidants that protect cells from damage induced by free radicals: vitamin A.

In 1989, at the same University, he specialized in Chemistry and Food Technology and then left for the United States. There, in the laboratories of the Department of Nutritional Sciences at the University of California at Berkeley, he continued his studies on the effects of vitamin A and its derivatives - particularly beta-carotene and retinoic acid - on cell adhesion.

It was becoming increasingly apparent at the time that retinoic acid functions as a powerful molecular signal capable of influencing gene expression. Scita discovered that the cellular response to this signal could be altered following the activation of genes that promote tumor transformation.

To study these issues further, he left California in 1994 for Maryland to work in the Laboratory of Cellular Carcinogenesis and Tumor Promotion at the National Cancer Institute in Bethesda.

Meanwhile, in Milan, Italy a project to create a new organization was taking shape: a Department of Experimental Oncology at the European Institute of Oncology (IEO). Two scientists, in particular, were advocates: Pier Giuseppe Pelicci and Pier Paolo Di Fiore.

Attracted by the idea of studying beside them, Scita returned to Italy in 1995 to work on the staff of Pier Paolo Di Fiore.

In 2001, he left the IEO, accepting the offer by IFOM to develop his own line of research there. He established a new group to investigate how cancer cells acquire mobility, a feature essential for the spread of cancer in the body. This gave rise to the Mechanisms of Tumor Cell Migration research program at IFOM.

In 2006, after five years of significant contributions to the advancement of scientific knowledge, making important discoveries in his field, was confirmed as director of research at IFOM.

In the same year, he became Associate Professor of General Pathology in the Faculty of Medicine at the University of Milan.

He is also associated with various studies that deepen our understanding of the mechanisms by which cells perceive their external environments and transduce signals, in response to which they change their behavior, especially that of migration.

In particular, he was responsible for the discovery that highlighted the fundamental connection between tumor cell mobility and the cellular process of endocytosis, traditionally considered to act in quite different cellular events.

Author of over 80 publications, Scita is among the more productive and cited Italian scientists.

Publications

5-Methylcytosine DNA demethylation: more than losing a methyl group.

Franchini Don-Marc - Schmitz Kerstin-Maike - Petersen-Mahrt Svend K

Annual Review of Genetics | 2012 jan 1 | doi: 10.1146/annurev-genet-110711-155451 | ISSN: 1545-2948 | Vol. 46 Issue nd

[PMID: 22974304] IF: 17,436

Activation of β-catenin by oncogenic PIK3CA and EGFR promotes resistance to glucose deprivation by inducing a strong antioxidant response.

Cardone Luca - Bardelli Alberto - Avvedimento Vittorio Enrico

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0037526 | ISSN: 1932-6203 | Vol. 7 Issue 5

[PMID: 22662165] IF: 3,730

Active PI3K pathway causes an invasive phenotype which can be reversed or promoted by blocking the pathway at divergent nodes.

Wallin Jeffrey J - Guan Jane - Edgar Kyle A - Zhou Wei - Francis Ross - Torres Anthony C - Haverty Peter M - Eastham-Anderson Jeffrey - Arena Sabrina - Bardelli Alberto - Griffin Sue - Goodall John E - Grimshaw Kyla M - Hoeflich Klaus P - Torrance Christopher - Belvin Marcia - Friedman Lori S

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0036402 | ISSN: 1932-6203 | Vol. 7 Issue 5

[PMID: 22570710] IF: 3,730

AID enzymatic activity is inversely proportional to the size of cytosine C5 orbital cloud.

Rangam Gopinath - Schmitz Kerstin-Maike - Cobb Alexander J A - Petersen-Mahrt Svend K

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0043279 | ISSN: 1932-6203 | Vol. 7 Issue 8

[PMID: 22916236] IF: 3,730

Circulating microRNAs: next-generation biomarkers for early lung cancer detection.

Bianchi F - Nicassio F - Veronesi G - di Fiore P P

Ecancermedicalscience | 2012 jan 1 | doi: 10.3332/ecancer.2012.246 | ISSN: 1754-6605 | Vol. 6 Issue nd

[PMID: 22518197]

Common variants at 12p11, 12q24, 9p21, 9q31.2 and in ZNF365 are associated with breast cancer risk for BRCA1 and/or BRCA2 mutation carriers.

Antoniou Antonis C - Kuchenbaecker Karoline B - Soucy Penny - Beesley Jonathan - Chen Xiaoqing - McGuffog Lesley - Lee Andrew - Barrowdale Daniel - Healey Sue - Sinilnikova Olga M - Caligo Maria A - Loman Niklas - Harbst Katja - Lindblom Annika - Arver Brita - Rosenquist Richard - Karlsson Per - Nathanson Kate - Domchek Susan - Rebbeck Tim - Jakubowska Anna - Lubinski Jan - Jaworska Katarzyna - Durda Katarzyna - Elżbieta Złowowcka-Perłowska - Osorio Ana - Durán Mercedes - Andrés Raquel - Benítez Javier - Hamann Ute - Hogervorst Frans B - van Os Theo A - Verhoef Senno - Meijers-Heijboer Hanne E J - Wijnen Juul - Gómez Garcia Encarna B - Ligtenberg Marjolijn J - Kriege Mieke - Collée J Margriet - Ausems Margreet G E M - Oosterwijk Jan C - Peock Susan - Frost Debra - Ellis Steve D - Platte Radka - Fineberg Elena - Evans D Gareth - Lalloo Fiona - Jacobs Chris - Eeles Ros - Adlard Julian - Davidson Rosemarie - Cole Trevor - Cook Jackie - Paterson Joan - Douglas Fiona - Brewer Carole - Hodgson Shirley - Morrison Patrick J - Walker Lisa - Rogers Mark T - Donaldson Alan - Dorkins Huw - Godwin Andrew K - Bove Betsy - Stoppa-Lyonnet Dominique - Houdayer Claude - Buecher Bruno - de Pauw Antoine - Mazoyer Sylvie - Calender Alain - Léoné Mélanie - Bressac-de Paillerets Brigitte - Caron Olivier - Sobol Hagay - Frenay Marc - Prieur Fabienne - Ferrer Sandra U - Mortemousque Isabelle - Buys Saundra - Daly Mary - Miron Alexander - Terry Mary U - Hopper John L - John Esther M - Southey

Melissa - Goldgar David - Singer Christian F - Fink-Retter Anneliese - Tea Muy-Kheng - Kaulich Daphne U - Hansen Thomas V - Nielsen Finn C - Barkardottir Rosa B - Gaudet Mia - Kirchhoff Tomas - Joseph Vijai - Dutra-Clarke Ana - Offit Kenneth - Piedmonte Marion - Kirk Judy - Cohn David - Hurteau Jean - Byron John - Fiorica James - Toland Amanda E - Montagna Marco - Oliani Cristina - Imyanitov Evgeny - Isaacs Claudine - Tihomirova Laima - Blanco Ignacio - Lazaro Conxi - Teulé Alex - Valle J Del - Gayther Simon A - Odunsi Kunle - Gross Jenny - Karlan Beth Y - Olah Edith - Teo Soo-Hwang - Ganz Patricia A - Beattie Mary S - Dorfling Cecelia M - van Rensburg Elizabeth U - Diez Orland - Kwong Ava - Schmutzler Rita K - Wappenschmidt Barbara - Engel Christoph - Meindl Alfons - Ditsch Nina - Arnold Norbert - Heidemann Simone - Niederacher Dieter - Preisler-Adams Sabine - Gadzicki Dorothea - Varon-Mateeva Raymonda - Deissler Helmut - Gehrig Andrea - Sutter Christian - Kast Karin - Fiebig Britta - Schäfer Dieter - Caldes Trinidad - de la Hoya Miguel - Nevanlinna Heli - Muranen Taru A - Lespérance Bernard - Spurdle Amanda B - Neuhausen Susan L - Ding Yuan C - Wang Xianshu - Fredericksen Zachary - Pankratz Vernon S - Lindor Noralane M - Peterlongo Paolo - Manoukian Siranoush - Peissel Bernard - Zaffaroni Daniela - Bonanni Bernardo - Bernard Loris - Dolcetti Riccardo - Papi Laura - Ottini Laura - Radice Paolo - Greene Mark H - Loud Jennifer T - Andrulis Irene L - Ozcelik Hilmi - Mulligan Anna U - Glendon Gord - Thomassen Mads - Gerdes Anne-Marie - Jensen Uffe B - Skytte Anne-Bine - Kruse Torben A - Chenevix-Trench Georgia - Couch Fergus J - Simard Jacques - Easton Douglas F - CIMBA - SWE-BRCA - HEBON - EMBRACE - GEMO Collaborators Study - kConFab Investigators

Breast Cancer Research : BCR | 2012 jan 1 | doi: 10.1186/bcr3121 | ISSN: 1465-542X | Vol. 14 Issue 1

[PMID: 22348646] IF: 5,872

Comparison of 6q25 breast cancer hits from Asian and European Genome Wide Association Studies in the Breast Cancer Association Consortium (BCAC).

Hein Rebecca - Maranian Melanie - Hopper John L - Kapuscinski Miroslaw K - Southey Melissa C - Park Daniel J - Schmidt Marjanka K - Broeks Annegien - Hogervorst Frans B L - Bueno-de-Mesquita H Bas - Bueno-de-Mesquit H Bas - Muir Kenneth R - Lophatananon Artitaya - Rattanamongkongul Suthee - Puttawibul Puttisak - Fasching Peter A - Hein Alexander - Ekici Arif B - Beckmann Matthias W - Fletcher Olivia - Johnson Nichola - dos Santos Silva Isabel - Peto Julian - Sawyer Elinor - Tomlinson Ian - Kerin Michael - Miller Nicola - Marmee Frederick - Schneeweiss Andreas - Sohn Christof - Burwinkel Barbara - Guénel Pascal - Cordina-Duverger Emilie - Menegaux Florence - Truong Thérèse - Bojesen Stig E - Nordestgaard Børge G - Flyger Henrik - Milne Roger L - Perez Jose Ignacio Arias - Zamora M Pilar - Benítez Javier - Anton-Culver Hoda - Ziogas Argyrios - Bernstein Leslie - Clarke Christina A - Brenner Hermann - Müller Heiko - Arndt Volker - Stegmaier Christa - Rahman Nazneen - Seal Sheila - Turnbull Clare - Renwick Anthony - Meindl Alfons - Schott Sarah - Bartram Claus R - Schmutzler Rita K - Brauch Hiltrud - Hamann Ute - Ko Yon-Dschun - GENICA Network - Wang-Gohrke Shan - Dörk Thilo - Schürmann Peter - Karstens Johann H - Hillemanns Peter - Nevanlinna Heli - Heikkinen Tuomas - Aittomäki Kristiina - Blomqvist Carl - Bogdanova Natalia V - Zalutsky Iosif V - Antonenkova Natalia N - Bermisheva Marina - Prokovieva Darya - Farahtdinova Albina - Khusnutdinova Elza - Lindblom Annika - Margolin Sara - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana - Chen Xiaoqing - Beesley Jonathan - Kconfab Investigators - AOCS Group - Lambrechts Diether - Zhao Hui - Neven Patrick - Wildiers Hans - Nickels Stefan - Flesch-Janys Dieter - Radice Paolo - Peterlongo Paolo - Manoukian Siranoush - Barile Monica - Couch Fergus J - Olson Janet E - Wang Xianshu - Fredericksen Zachary - Giles Graham G - Baglietto Laura - McLean Catriona A - Severi Gianluca - Offit Kenneth - Robson Mark - Gaudet Mia M - Vijai Joseph - Alnæs Grethe Grenaker - Kristensen Vessela - Børresen-Dale Anne-Lise - John Esther M - Miron Alexander - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Grip Mervi - Andrulis Irene L - Knight Julia A - Glendon Gord - Mulligan Anna Marie - Figueroa Jonine D - García-Closas Montserrat - Lissowska Jolanta - Sherman Mark E - Hooning Maartje - Martens John W M - Seynaeve Caroline - Collée Margriet - Hall Per - Humpreys Keith - Czene Kamila - Liu Jianjun - Cox Angela - Brock Ian W - Cross Simon S - Reed Malcolm W R - Ahmed Shahana - Ghoussaini Maya - Pharoah Paul D P - Kang Daehee - Yoo Keun-Young - Noh Dong-Young - Jakubowska Anna - Jaworska Katarzyna - Durda Katarzyna - Złowocka Elżbieta - Sangrajrang Suleeporn - Gaborieau Valerie - Brennan Paul - McKay James - Shen Chen-Yang - Yu Jyh-Cherng - Hsu Huan-Ming - Hou Ming-Feng - Orr Nick - Schoemaker Minouk - Ashworth Alan - Swerdlow Anthony - Trentham-Dietz Amy - Newcomb Polly A - Titus Linda - Egan Kathleen M - Chenevix-Trench Georgia - Antoniou Antonis C - Humphreys Manjeet K - Morrison Jonathan - Chang-Claude Jenny - Easton Douglas F - Dunning Alison M

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0042380 | ISSN: 1932-6203 | Vol. 7 Issue 8

[PMID: 22879957] IF: 3,730

Endocytosis and signaling: cell logistics shape the eukaryotic cell plan.

Sigismund Sara - Confalonieri Stefano - Ciliberto Andrea - Polo Simona - Scita Giorgio - Di Fiore Pier Paolo

Physiological Reviews | 2012 Jan 1 | doi: 10.1152/physrev.00005.2011 | ISSN: 1522-1210 | Vol. 92 Issue 1

[PMID: 22298658] IF: 30,174

Functional purification of human and mouse mammary stem cells.

Tosoni Daniela - Di Fiore Pier Paolo - Pece Salvatore

Methods in Molecular Biology (Clifton, N.J.) | 2012 jan 1 | doi: 10.1007/978-1-61779-980-8_6 | ISSN: 1940-6029 | Vol. 916 Issue nd

[PMID: 22914933]

Myb-binding protein 1A (MYBBP1A) is essential for early embryonic development, controls cell cycle and mitosis, and acts as a tumor suppressor.

Mori Silvia - Bernardi Rosa - Laurent Audrey - Resnati Massimo - Crippa Ambra - Gabrieli Arianna - Keough Rebecca - Gonda Thomas J - Blasi Francesco

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0039723 | ISSN: 1932-6203 | Vol. 7 Issue 10

[PMID: 23056166] IF: 3,730

Phosphorylation of VE-cadherin is modulated by haemodynamic forces and contributes to the regulation of vascular permeability in vivo.

Orsenigo Fabrizio - Giampietro Costanza - Ferrari Aldo - Corada Monica - Galaup Ariane - Sigismund Sara - Ristagno Giuseppe - Maddaluno Luigi - Koh Gou Young - Franco Davide - Kurtcuoglu Vartan - Poulikakos Dimos - Baluk Peter - McDonald Donald - Grazia Lampugnani Maria - Dejana Elisabetta

Nature Communications | 2012 jan 1 | doi: 10.1038/ncomms2199 | ISSN: 2041-1723 | Vol. 3 Issue nd

[PMID: 23169049] IF: 10,015

Reduction of Prep1 levels affects differentiation of normal and malignant B cells and accelerates Myc driven lymphomagenesis.

Iotti Giorgio - Mejetta Stefania - Modica Livia - Penkov Dmitry - Ponzoni Maurilio - Blasi Francesco

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0048353 | ISSN: 1932-6203 | Vol. 7 Issue 10

[PMID: 23133585] IF: 3,730

Sequencing analysis of SLX4/FANCP gene in Italian familial breast cancer cases.

Catucci Irene - Colombo Mara - Verderio Paolo - Bernard Loris - Ficarazzi Filomena - Mariette Frederique - Barile Monica - Peissel Bernard - Cattaneo Elisa - Manoukian Siranoush - Radice Paolo - Peterlongo Paolo

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0031038 | ISSN: 1932-6203 | Vol. 7 Issue 2

[PMID: 22383991] IF: 3,730

Signaling-mediated control of ubiquitin ligases in endocytosis.

Polo Simona

BMC Biology | 2012 jan 1 | doi: 10.1186/1741-7007-10-25 | ISSN: 1741-7007 | Vol. 10 Issue nd

[PMID: 22420864] IF: 6,531

The endocytic adaptor Eps15 controls marginal zone B cell numbers.

Pozzi Benedetta - Amodio Stefania - Lucano Caterina - Sciullo Anna - Ronzoni Simona - Castelletti Daniela - Adler Thure - Treise Irina - Betsholtz Ingrid Holmberg - Rathkolb Birgit - Busch Dirk H - Wolf Eckhard - Fuchs Helmut - Gailus-Durner Valérie - de Angelis Martin Hrabě - Betsholtz Christer - Casola Stefano - Di Fiore Pier Paolo - Offenhäuser Nina

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0050818 | ISSN: 1932-6203 | Vol. 7 Issue 11

[PMID: 23226392] IF: 3,730

The Kiss-and-Run Model of Intra-Golgi Transport.

Mironov Alexander A - Beznoussenko Galina V

International Journal of Molecular Sciences | 2012 jan 1 | doi: 10.3390/ijms13066800 | ISSN: 1422-0067 | Vol. 13 Issue 6

[PMID: 22837664] IF: 2,464

Topoisomerase I poisoning results in PARP-mediated replication fork reversal.

Ray Chaudhuri Arnab - Hashimoto Yoshitami - Herrador Raquel - Neelsen Kai J - Fachinetti Daniele - Bermejo Rodrigo - Cocito Andrea - Costanzo Vincenzo - Lopes Massimo

Nature Structural & Molecular Biology | 2012 jan 1 | doi: 10.1038/nsmb.2258 | ISSN: 1545-9985 | Vol. 19 Issue 4

[PMID: 22388737] IF: 11,902

TPT1/ TCTP-regulated pathways in phenotypic reprogramming.

Amson Robert - Pece Salvatore - Marine Jean-Christophe - Di Fiore Pier Paolo - Telerman Adam

Trends in Cell Biology | 2013 Jan 1 | doi: 10.1016/j.tcb.2012.10.002 | ISSN: 1879-3088 | Vol. 23 Issue 1

[PMID: 23122550] IF: 11,721

Ve-ptp modulates vascular integrity by promoting adherens junction maturation.

Carra Silvia - Foglia Efrem - Cermenati Solei - Bresciani Erica - Giampietro Costanza - Lora Lamia Carla - Dejana Elisabetta - Beltrame Monica - Cotelli Franco

PloS one | 2012 jan 1 | doi: 10.1371/journal.pone.0051245 | ISSN: 1932-6203 | Vol. 7 Issue 12

[PMID: 23251467] IF: 3,730

Accelerated endothelial wound healing on microstructured substrates under flow.

Franco Davide - Milde Florian - Klingauf Mirko - Orsenigo Fabrizio - Dejana Elisabetta - Poulikakos Dimos - Cecchini Marco - Koumoutsakos Petros - Ferrari Aldo - Kurtcuoglu Vartan

Biomaterials | 2013 Feb 1 | doi: 10.1016/j.biomaterials.2012.10.007 | ISSN: 1878-5905 | Vol. 34 Issue 5

[PMID: 23182348] IF: 7,604

BMP2/BMP4 colorectal cancer susceptibility loci in northern and southern European populations.

Fernandez-Rozadilla Ceres - Palles Claire - Carvajal-Carmona Luis - Peterlongo Paolo - Nici Carmela - Veneroni Silvia - Pinheiro Manuela - Teixeira Manuel R - Moreno Victor - Lamas Maria-Jesus - Baiget Montserrat - Lopez-Fernandez LA - Gonzalez Dolors - Brea-Fernandez Alejandro - Clofent Juan - Bujanda Luis - Bessa Xavier - Andreu Montserrat - Xicola Rosa - Llor Xavier - EPICOLON Consortium - Jover Rodrigo - Castells Antoni - Castellvi-Bel Sergi - Carracedo Angel - Tomlinson Ian - Ruiz-Ponte Clara

Carcinogenesis | 2013 Feb 1 | doi: 10.1093/carcin/bgs357 | ISSN: 1460-2180 | Vol. 34 Issue 0

[PMID: 23161572] IF: 5,635

Immune surveillance and therapy of lymphomas driven by Epstein-Barr virus protein LMP1 in a mouse model.

Zhang Baochun - Kracker Sven - Yasuda Tomoharu - Casola Stefano - Vanneman Matthew - Hömig-Hölzel Cornelia - Wang Zhe - Derudder Emmanuel - Li Shuang - Chakraborty Tirtha - Cotter Shane E - Koyama Shohei - Currie Treeve - Freeman Gordon J - Kutok Jeffery L - Rodig Scott J - Dranoff Glenn - Rajewsky Klaus

Cell | 2012 Feb 17 | doi: 10.1016/j.cell.2011.12.031 | ISSN: 1097-4172 | Vol. 148 Issue 4

[PMID: 22341446] IF: 31,957

Noncanonical role of the 9-1-1 clamp in the error-free DNA damage tolerance pathway.

Karras Georgios Ioannis - Fumasoni Marco - Sienski Grzegorz - Vanoli Fabio - Branzei Dana - Jentsch Stefan

Molecular Cell | 2013 Feb 7 | doi: 10.1016/j.molcel.2012.11.016 | ISSN: 1097-4164 | Vol. 49 Issue 3

[PMID: 23260657] IF: 15,280

Acetylation: a novel link between double-strand break repair and autophagy.

Shubassi Ghadeer - Robert Thomas - Vanoli Fabio - Minucci Saverio - Foiani Marco

Cancer Research | 2012 Mar 15 | doi: 10.1158/0008-5472.CAN-11-3172 | ISSN: 1538-7445 | Vol. 72 Issue 6

[PMID: 22422989] IF: 8,650

During replication stress, non-SMC element 5 (NSE5) is required for Smc5/6 protein complex functionality at stalled forks.

Bustard Denise E - Menolfi Demis - Jeppsson Kristian - Ball Lindsay G - Dewey Sidney Carter - Shirahige Katsuhiko - Sjögren Camilla - Branzei Dana - Cobb Jennifer A

The Journal of Biological Chemistry | 2012 Mar 30 | doi: 10.1074/jbc.M111.336263 | ISSN: 1083-351X | Vol. 287 Issue 14

[PMID: 22303010] IF: 4,651

Genome-wide association analysis identifies three new breast cancer susceptibility loci.

Ghoussaini Maya - Fletcher Olivia - Michailidou Kyriaki - Turnbull Clare - Schmidt Marjanka K - Dicks Ed - Dennis Joe - Wang Qin - Humphreys Manjeet K - Luccarini Craig - Baynes Caroline - Conroy Don - Maranian Melanie - Ahmed Shahana - Driver Kristy - Johnson Nichola - Orr Nicholas - dos Santos Silva Isabel - Waisfisz Quinten - Meijers-Heijboer Hanne - Uitterlinden Andre G - Rivadeneira Fernando - Netherlands Collaborative Group on Hereditary Breast and Ovarian Cancer (HEBON) - Hall Per - Czene Kamila - Irwanto Astrid - Liu Jianjun - Nevanlinna Heli - Aittomäki Kristiina - Blomqvist Carl - Meindl Alfons - Schmutzler Rita K - Müller-Myhsok Bertram - Lichtner Peter - Chang-Claude Jenny - Hein Rebecca - Nickels Stefan - Flesch-Janys Dieter - Tsimiklis Helen - Makalic Enes - Schmidt Daniel - Bui Minh - Hopper John L - Apicella Carmel - Park Daniel J - Southey Melissa - Hunter David J - Chanock Stephen J - Broeks Annegien - Verhoef Senno - Hogervorst Frans B L - Fasching Peter A - Lux Michael P - Beckmann Matthias W - Ekici Arif B - Sawyer Elinor - Tomlinson Ian - Kerin Michael - Marme Frederik - Schneeweiss Andreas - Sohn Christof - Burwinkel Barbara - Guénel Pascal - Truong Thérèse - Cordina-Duverger Emilie - Menegaux Florence - Bojesen Stig E - Nordestgaard Børge G - Nielsen Sune F - Flyger Henrik - Milne Roger L - Alonso M Rosario - González-Neira Anna - Benítez Javier - Anton-Culver Hoda - Ziogas Argyrios - Bernstein Leslie - Dur Christina Clarke - Brenner Hermann - Müller Heiko - Arndt Volker - Stegmaier Christa - Familial Breast Cancer Study (FBCS) - Justenhoven Christina - Brauch Hiltrud - Brüning Thomas - Gene Environment Interaction of Breast Cancer in Germany

(GENICA) Network - Wang-Gohrke Shan - Eilber Ursula - Dörk Thilo - Schürmann Peter - Bremer Michael - Hillemanns Peter - Bogdanova Natalia V - Antonenkova Natalia N - Rogov Yuri I - Karstens Johann H - Bermisheva Marina - Prokofieva Darya - Khusnutdinova Elza - Lindblom Annika - Margolin Sara - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - Lambrechts Diether - Yesilyurt Betul T - Floris Giuseppe - Leunen Karin - Manoukian Siranoush - Bonanni Bernardo - Fortuzzi Stefano - Peterlongo Paolo - Couch Fergus J - Wang Xianshu - Stevens Kristen - Lee Adam - Giles Graham G - Baglietto Laura - Severi Gianluca - McLean Catriona - Alnaes Grethe Grenaker - Kristensen Vessela - Børrensen-Dale Anne-Lise - John Esther M - Miron Alexander - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Kauppila Saila - Andrulis Irene L - Glendon Gord - Mulligan Anna Marie - Devilee Peter - van Asperen Christie J - Tollenaar Rob A E M - Seynaeve Caroline - Figueroa Jonine D - Garcia-Closas Montserrat - Brinton Louise - Lissowska Jolanta - Hooning Maartje J - Hollestelle Antoinette - Oldenburg Rogier A - van den Ouweland Ans M W - Cox Angela - Reed Malcolm W R - Shah Mitul - Jakubowska Ania - Lubinski Jan - Jaworska Katarzyna - Durda Katarzyna - Jones Michael - Schoemaker Minouk - Ashworth Alan - Swerdlow Anthony - Beesley Jonathan - Chen Xiaoqing - kConFab Investigators - Australian Ovarian Cancer Study Group - Muir Kenneth R - Lophatananon Artitaya - Rattanamongkongul Suthee - Chaiwerawattana Arkom - Kang Daehee - Yoo Keun-Young - Noh Dong-Young - Shen Chen-Yang - Yu Jyh-Cherng - Wu Pei-Ei - Hsiung Chia-Ni - Perkins Annie - Swann Ruth - Velentzis Louiza - Eccles Diana M - Tapper Will J - Gerty Susan M - Graham Nikki J - Ponder Bruce A J - Chenevix-Trench Georgia - Pharoah Paul D P - Lathrop Mark - Dunning Alison M - Rahman Nazneen - Peto Julian - Easton Douglas F

Nature Genetics | 2012 Mar 1 | doi: 10.1038/ng.1049 | ISSN: 1546-1718 | Vol. 44 Issue 3

[PMID: 22267197] IF: 35,209

Highly penetrant melanoma in a zebrafish model is independent of ErbB3b signaling.

Santoriello Cristina - Anelli Viviana - Alghisi Elisa - Mione Marina

Pigment Cell & Melanoma Research | 2012 Mar 1 | doi: 10.1111/j.1755-148X.2012.00973.x | ISSN: 1755-148X | Vol. 25 Issue 2

[PMID: 22248380] IF: 5,839

Hormones and AID: balancing immunity and autoimmunity.

Incorvaia Elisabetta - Sicouri Lara - Petersen-Mahrt Svend K - Schmitz Kerstin-Maike

Autoimmunity | 2013 Mar 1 | doi: 10.3109/08916934.2012.748752 | ISSN: 1607-842X | Vol. 46 Issue 2

[PMID: 23181348] IF: 2,767

Overlapping and divergent signaling pathways of N-cadherin and VE-cadherin in endothelial cells.

Giampietro Costanza - Taddei Andrea - Corada Monica - Sarra-Ferraris Gian Maria - Alcalay Myriam - Cavallaro Ugo - Orsenigo Fabrizio - Lampugnani Maria Grazia - Dejana Elisabetta

Blood | 2012 Mar 1 | doi: 10.1182/blood-2011-09-381012 | ISSN: 1528-0020 | Vol. 119 Issue 9

[PMID: 22246030] IF: 9,060

Preventing replication stress to maintain genome stability: resolving conflicts between replication and transcription.

Bermejo Rodrigo - Lai Mong Sing - Foiani Marco

Molecular Cell | 2012 Mar 30 | doi: 10.1016/j.molcel.2012.03.001 | ISSN: 1097-4164 | Vol. 45 Issue 6

[PMID: 22464441] IF: 15,280

Targeting metabolism for cancer treatment and prevention: metformin, an old drug with multi-faceted effects.

Pierotti M A - Berrino F - Gariboldi M - Melani C - Mogavero A - Negri T - Pasanisi P - Pilotti S

Oncogene | 2013 Mar 21 | doi: 10.1038/onc.2012.181 | ISSN: 1476-5594 | Vol. 32 Issue 12

[PMID: 22665053] IF: 7,357

Unresponsiveness of colon cancer to BRAF(V600E) inhibition through feedback activation of EGFR.

Prahallad Anirudh - Sun Chong - Huang Sidong - Di Nicolantonio Federica - Salazar Ramon - Zecchin Davide - Beijersbergen Roderick L - Bardelli Alberto - Bernards René

Nature | 2012 Mar 1 | doi: 10.1038/nature10868 | ISSN: 1476-4687 | Vol. 483 Issue 7387

[PMID: 22281684] IF: 38,597

19p13.1 is a triple-negative-specific breast cancer susceptibility locus.

Stevens Kristen N - Fredericksen Zachary - Vachon Celine M - Wang Xianshu - Margolin Sara - Lindblom Annika - Nevanlinna Heli - Greco Dario - Aittomäki Kristiina - Blomqvist Carl - Chang-Claude Jenny - Vrieling Alina - Flesch-Janys Dieter - Sinn Hans-Peter - Wang-Gohrke Shan - Nickels Stefan - Brauch Hiltrud - GENICA Network - Ko Yon-Dschun - Fischer Hans-Peter - Schmutzler Rita K - Meindl Alfons - Bartram Claus R - Schott Sarah - Engel Christoph - Godwin Andrew K - Weaver Joellen - Pathak Harsh B - Sharma Priyanka - Brenner Hermann - Müller Heiko - Arndt Volker - Stegmaier Christa - Miron Penelope - Yannoukakos Drakoulis - Stavropoulou Alexandra - Fountzilas George - Gogas Helen J - Swann Ruth - Dwek Miriam - Perkins Annie - Milne Roger L - Benítez Javier - Zamora María Pilar - Pérez José Ignacio Arias - Bojesen Stig E - Nielsen Sune F - Nordestgaard Børge G - Flyger Henrik - Guénel Pascal - Truong Thérèse - Menegaux Florence - Cordina-Duverger Emilie - Burwinkel Barbara - Marmé Frederick - Schneeweiss Andreas - Sohn Christof - Sawyer Elinor - Tomlinson Ian - Kerin Michael J - Peto Julian - Johnson Nichola - Fletcher Olivia - Dos Santos Silva Isabel - Fasching Peter A - Beckmann Matthias W - Hartmann Arndt - Ekici Arif B - Lophatananon Artitaya - Muir Kenneth - Puttawibul Puttisak - Wiangnon Surapon - Schmidt Marjanka K - Broeks Annegien - Braaf Linde M - Rosenberg Efraim H - Hopper John L - Apicella Carmel - Park Daniel J - Southey Melissa C - Swerdlow Anthony J - Ashworth Alan - Orr Nicholas - Schoemaker Minouk J - Anton-Culver Hoda - Ziogas Argyrios - Bernstein Leslie - Dur Christina Clarke - Shen Chen-Yang - Yu Jyh-Cherng - Hsu Huan-Ming - Hsiung Chia-Ni - Hamann Ute - Dünnebier Thomas - Rüdiger Thomas - Ulmer Hans Ulrich - Pharoah Paul P - Dunning Alison M - Humphreys Manjeet K - Wang Qin - Cox Angela - Cross Simon S - Reed Malcom W - Hall Per - Czene Kamila - Ambrosone Christine B - Ademuyiwa Foluso - Hwang Helena - Eccles Diana M - Garcia-Closas Montserrat - Figueroa Jonine D - Sherman Mark E - Lissowska Jolanta - Devilee Peter - Seynaeve Caroline - Tollenaar Rob A E M - Hooning Maartje J - Andrulis Irene L - Knight Julia A - Glendon Gord - Mulligan Anna Marie - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Grip Mervi - John Esther M - Miron Alexander - Alnæs Grethe Grenaker - Kristensen Vessela - Børresen-Dale Anne-Lise - Giles Graham G - Baglietto Laura - McLean Catriona A - Severi Gianluca - Kosel Matthew L - Pankratz V S - Slager Susan - Olson Janet E - Radice Paolo - Peterlongo Paolo - Manoukian Siranoush - Barile Monica - Lambrechts Diether - Hatse Sigrid - Dieudonne Anne-Sophie - Christiaens Marie-Rose - Chenevix-Trench Georgia - kConFab Investigators - AOCS Group Beesley - Jonathan - Chen Xiaoqing - Mannermaa Arto - Kosma Veli-Matti - Hartikainen Jaana M - Soini Ylermi - Easton Douglas F - Couch Fergus J

Cancer Research | 2012 Apr 1 | doi: 10.1158/0008-5472.CAN-11-3364 | ISSN: 1538-7445 | Vol. 72 Issue 7

[PMID: 22331459] IF: 8,650

A 14-3-3_ dimer-based scaffold bridges CtBP1-S/BARS to PI(4)KIII_ to regulate post-Golgi carrier formation.

Valente Carmen - Turacchio Gabriele - Mariggiò Stefania - Pagliuso Alessandro - Gaibisso Renato - Di Tullio Giuseppe - Santoro Michele - Formiggini Fabio - Spanò Stefania - Piccini Daniele - Polishchuk Roman S - Colanzi Antonino - Luini Alberto - Corda Daniela

Nature Cell Biology | 2012 Apr 1 | doi: 10.1038/ncb2445 | ISSN: 1476-4679 | Vol. 14 Issue 4

[PMID: 22366688] IF: 20,761

Common variants at the 19p13.1 and ZNF365 loci are associated with ER subtypes of breast cancer and ovarian cancer risk in BRCA1 and BRCA2 mutation carriers.

Couch Fergus J - Gaudet Mia M - Antoniou Antonis C - Ramus Susan J - Kuchenbaecker Karoline B - Soucy Penny - Beesley Jonathan - Chen Xiaoqing - Wang Xianshu - Kirchhoff Tomas - McGuffog Lesley - Barrowdale Daniel - Lee Andrew - Healey Sue - Sinilnikova Olga M - Andrulis Irene L - OCGN - Ozcelik Hilmi - Mulligan Anna Marie - Thomassen Mads - Gerdes Anne-Marie - Jensen Uffe Birk - Skytte Anne-Bine - Kruse Torben A - Caligo Maria A - von Wachenfeldt Anna - Barbany-Bustinza Gisela - Loman Niklas - Soller Maria - Ehrencrona Hans - Karlsson Per - SWE-BRCA - Nathanson Katherine L - Rebbeck Timothy R - Domchek Susan M - Jakubowska Ania - Lubinski Jan - Jaworska Katarzyna - Durda Katarzyna - Zlowocka Elzbieta - Huzarski Tomasz - Byrski Tomasz - Gronwald Jacek - Cybulski Cezary - Górski Bohdan - Osorio Ana - Durán Mercedes - Tejada María Isabel - Benitez Javier - Hamann Ute - Hogervorst Frans B L - HEBON - van Os Theo A - van Leeuwen Flora E - Meijers-Heijboer Hanne E J - Wijnen Juul - Blok Marinus J - Kets Marleen - Hooning Maartje J - Oldenburg Rogier A - Ausems Margreet G E M - Peock Susan - Frost Debra - Ellis Steve D - Platte Radka - Fineberg Elena - Evans D Gareth - Jacobs Chris - Eeles Rosalind A - Adlard Julian - Davidson Rosemarie - Eccles Diana M - Cole Trevor - Cook Jackie - Paterson Joan - Brewer Carole - Douglas Fiona - Hodgson Shirley V - Morrison Patrick J - Walker Lisa - Porteous Mary E - Kennedy M John - Side Lucy E - EMBRACE - Bove Betsy - Godwin Andrew K - Stoppa-Lyonnet Dominique - GEMO Study Collaborators - Fassy-Colcombet Marion - Castera Laurent - Cornelis François - Mazoyer Sylvie - Léoné Mélanie - Boutry-Kryza Nadia - Bressac-de Paillerets Brigitte - Caron Olivier - Pujol Pascal - Coupier Isabelle - Delnatte Capucine - Akloul Linda - Lynch Henry T - Snyder Carrie L - Buys Saundra S - Daly Mary B - Terry Marybeth - Chung Wendy K - John Esther M - Miron Alexander - Southey Melissa C - Hopper John L - Goldgar David E - Singer Christian F - Rappaport Christine - Tea Muy-Kheng M - Fink-Retter Anneliese - Hansen Thomas V O - Nielsen Finn C - Arason Aðalgeir - Vijai Joseph - Shah Sohela - Sarrel Kara - Robson Mark E - Piedmonte Marion - Phillips Kelly - Basil Jack - Rubinstein Wendy S - Boggess John - Wakeley Katie - Ewart-Toland Amanda - Montagna Marco - Agata Simona - Imyanitov Evgeny N - Isaacs Claudine - Janavicius Ramunas - Lazaro Conxi - Blanco Ignacio - Feliubadalo Lidia - Brunet Joan - Gayther Simon A - Pharoah Paul P D - Odunsi Kunle O - Karlan Beth Y - Walsh Christine S - Olah Edith - Teo Soo Hwang - Ganz Patricia A - Beattie Mary S - van Rensburg Elizabeth J - Dorfling Cecelia M - Diez Orland - Kwong Ava - Schmutzler Rita K - Wappenschmidt Barbara - Engel Christoph - Meindl Alfons - Ditsch Nina - Arnold Norbert - Heidemann Simone - Niederacher Dieter - Preisler-Adams Sabine - Gadzicki Dorothea - Varon-Mateeva Raymonda - Deissler Helmut - Gehrig Andrea - Sutter Christian - Kast Karin - Fiebig Britta - Heinritz Wolfram - Caldes Trinidad - de la Hoya Miguel - Muranen Taru A - Nevanlinna Heli - Tischkowitz Marc D - Spurdle Amanda B - Neuhausen Susan L - Ding Yuan Chun - Lindor Noralane M - Fredericksen Zachary - Pankratz V Shane - Peterlongo Paolo - Manoukian Siranoush - Peissel Bernard - Zaffaroni Daniela - Barile Monica - Bernard Loris - Viel Alessandra - Giannini Giuseppe - Varesco Liliana - Radice Paolo - Greene Mark H - Mai Phuong L - Easton Douglas F - Chenevix-Trench Georgia - kConFab investigators - Offit Kenneth - Simard Jacques - Consortium of Investigators of Modifiers of BRCA1/2

Cancer Epidemiology, Biomarkers & Prevention | 2012 Apr 1 | doi: 10.1158/1055-9965.EPI-11-0888 | ISSN: 1538-7755 | Vol. 21 Issue 4

[PMID: 22351618] IF: 4,559

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miRNA profiling in colorectal cancer highlights miR-1 involvement in MET-dependent proliferation.

Reid James F - Sokolova Viktorija - Zoni Eugenio - Lampis Andrea - Pizzamiglio Sara - Bertan Claudia - Zanutto Susanna - Perrone Federica - Camerini Tiziana - Gallino Gianfrancesco - Verderio Paolo - Leo Ermanno - Pilotti Silvana - Gariboldi Manuela - Pierotti Marco A

Molecular Cancer Research : MCR | 2012 Apr 1 | doi: 10.1158/1541-7786.MCR-11-0342 | ISSN: 1557-3125 | Vol. 10 Issue 4

[PMID: 22343615] IF: 4,353

Ovarian cancer susceptibility alleles and risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers.

Ramus Susan J - Antoniou Antonis C - Kuchenbaecker Karoline B - Soucy Penny - Beesley Jonathan - Chen Xiaoqing - McGuffog Lesley - Sinilnikova Olga M - Healey Sue - Barrowdale Daniel - Lee Andrew - Thomassen Mads - Gerdes Anne-Marie - Kruse Torben A - Jensen Uffe Birk - Skytte Anne-Bine - Caligo Maria A - Liljegren Annelie - Lindblom Annika - Olsson Håkan - Kristoffersson Ulf - Stenmark-Askmalm Marie - Melin Beatrice - SWE-BRCA - Domchek Susan M - Nathanson Katherine L - Rebbeck Timothy R - Jakubowska Anna - Lubinski Jan - Jaworska Katarzyna - Durda Katarzyna - Złowocka Elżbieta - Gronwald Jacek - Huzarski Tomasz - Byrski Tomasz - Cybulski Cezary - Toloczko-Grabarek Aleksandra - Osorio Ana - Benitez Javier - Duran Mercedes - Tejada Maria-Isabel - Hamann Ute - Rookus Matti - van Leeuwen Flora E - Aalfs Cora M - Meijers-Heijboer Hanne E J - van Asperen Christi J - van Roozendaal K E P - Hoogerbrugge Nicoline - Collée J Margriet - Kriege Mieke - van der Luijt Rob B - HEBON - EMBRACE -Peock Susan - Frost Debra - Ellis Steve D - Platte Radka - Fineberg Elena - Evans D Gareth - Lalloo Fiona - Jacobs Chris - Eeles Ros - Adlard Julian - Davidson Rosemarie - Eccles Diana - Cole Trevor - Cook Jackie - Paterson Joan - Douglas Fiona - Brewer Carole - Hodgson Shirley - Morrison Patrick J - Walker Lisa - Porteous Mary E - Kennedy M John - Pathak Harsh - Godwin Andrew K - Stoppa-Lyonnet Dominique - Caux-Moncoutier Virginie - de Pauw Antoine - Gauthier-Villars Marion - Mazoyer Sylvie - Léoné Mélanie - Calender Alain - Lasset Christine - Bonadona Valérie - Hardouin Agnès - Berthet Pascaline - Bignon Yves-Jean - Uhrhammer Nancy - Faivre Laurence - Loustalot Catherine - GEMO - Buys Saundra - Daly Mary - Miron Alex - Terry Mary Beth - Chung Wendy K - John Esther M - Southey Melissa - Goldgar David - Singer Christian F - Tea Muy-Kheng - Pfeiler Georg - Fink-Retter Anneliese - Hansen Thomas v O - Ejlertsen Bent - Johannsson Oskar Th - Offit Kenneth - Kirchhoff Tomas - Gaudet Mia M - Vijai Joseph - Robson Mark - Piedmonte Marion - Phillips Kelly-Anne - Van Le Linda - Hoffman James S - Ewart Toland Amanda - Montagna Marco - Tognazzo Silvia - Imyanitov Evgeny - Issacs Claudine - Janavicius Ramunas - Lazaro Conxi - Blanco Iganacio - Tornero Eva - Navarro Matilde - Moysich Kirsten B - Karlan Beth Y - Gross Jenny - Olah Edith - Vaszko Tibor - Teo Soo-Hwang - Ganz Patricia A - Beattie Mary S - Dorfling Cecelia M - van Rensburg Elizabeth J - Diez Orland - Kwong Ava - Schmutzler Rita K - Wappenschmidt Barbara - Engel Christoph - Meindl Alfons - Ditsch Nina - Arnold Norbert - Heidemann Simone - Niederacher Dieter - Preisler-Adams Sabine - Gadzicki Dorotehea - Varon-Mateeva Raymonda - Deissler Helmut - Gehrig Andrea - Sutter Christian - Kast Karin - Fiebig Britta - Schäfer Dieter - Caldes Trinidad - de la Hoya Miguel - Nevanlinna Heli - Aittomäki Kristiina - Plante Marie - Spurdle Amanda B - kConFab - Neuhausen Susan L - Ding Yuan Chun - Wang Xianshu - Lindor Noralane - Fredericksen Zachary - Pankratz V Shane - Peterlongo Paolo - Manoukian Siranoush - Peissel Bernard - Zaffaroni Daniela - Bonanni Bernardo - Bernard Loris - Dolcetti Riccardo - Papi Laura - Ottini Laura - Radice Paolo - Greene Mark H - Mai Phuong L - Andrulis Irene L - Glendon Gord - Ozcelik Hilmi - OCGN- Pharoah Paul D P - Gayther Simon A - Simard Jacques - Easton Douglas F - Couch Fergus J - Chenevix-Trench Georgia - Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA)

Human Mutation | 2012 Apr 1 | doi: 10.1002/humu.22025 | ISSN: 1098-1004 | Vol. 33 Issue 4

[PMID: 22253144] IF: 5,213

Telomeric DNA damage is irreparable and causes persistent DNA-damage-response activation.

Fumagalli Marzia - Rossiello Francesca - Clerici Michela - Barozzi Sara - Cittaro Davide - Kaplunov Jessica M - Bucci Gabriele - Dobreva Miryana - Matti Valentina - Beausejour Christian M - Herbig Utz - Longhese Maria Pia - d'Adda di Fagagna Fabrizio

Nature Cell Biology | 2012 Apr 1 | doi: 10.1038/ncb2466 | ISSN: 1476-4679 | Vol. 14 Issue 4

[PMID: 22426077] IF: 20,761

The KL-VS sequence variant of Klotho and cancer risk in BRCA1 and BRCA2 mutation carriers.

Laitman Yael - Kuchenbaecker Karoline B - Rantala Johanna - Hogervorst Frans - Peock Susan - Godwin Andrew K - Arason Adalgeir - Kirchhoff Tomas - Offit Kenneth - Isaacs Claudine - Schmutzler Rita K - Wappenschmidt Barbara - Nevanlinna Heli - Chen Xiaoqing - Chenevix-Trench Georgia - Healey Sue - Couch Fergus - Peterlongo Paolo - Radice Paolo - Nathanson Katherine L - Caligo Maria Adelaide - Neuhausen Susan L - Ganz Patricia - Sinilnikova Olga M - McGuffog Lesley - Easton Douglas F - Antoniou Antonis C - Wolf Ido - Friedman Eitan

Breast Cancer Research and Treatment | 2012 Apr 1 | doi: 10.1007/s10549-011-1938-8 | ISSN: 1573-7217 | Vol. 132 Issue 3

[PMID: 22212556] IF: 4,469

Inhibition of MEK and PI3K/mTOR suppresses tumor growth but does not cause tumor regression in patient-derived xenografts of RAS-mutant colorectal carcinomas.

Migliardi Giorgia - Sassi Francesco - Torti Davide - Galimi Francesco - Zanella Eugenia R - Buscarino Michela - Ribero Dario - Muratore Andrea - Massucco Paolo - Pisacane Alberto - Risio Mauro - Capussotti Lorenzo - Marsoni Silvia - Di Nicolantonio Federica - Bardelli Alberto - Comoglio Paolo M - Trusolino Livio - Bertotti Andrea

Clinical Cancer Research: an Official Journal of the American Association for Cancer Research | 2012 May 1 | doi: 10.1158/1078-0432.CCR-11-2683 | ISSN: 1078-0432 | Vol. 18 Issue 9

[PMID: 22392911] IF: 7,837

Molecular pathways: old drugs define new pathways: non-histone acetylation at the crossroads of the DNA damage response and autophagy.

Botrugno Oronza Antonietta - Robert Thomas - Vanoli Fabio - Foiani Marco - Minucci Saverio

Clinical Cancer Research: an Official Journal of the American Association for Cancer Research | 2012 May 1 | doi: 10.1158/1078-0432.CCR-11-0767 | ISSN: 1078-0432 | Vol. 18 Issue 9

[PMID: 22512979] IF: 7,837

Vascular endothelial-cadherin and vascular stability.

Dejana Elisabetta - Giampietro Costanza

Current Opinion in Hematology | 2012 May 1 | doi: 10.1097/MOH.0b013e3283523e1c | ISSN: 1531-7048 | Vol. 19 Issue 3

[PMID: 22395663] IF: 4,111

Association of PHB 1630 C>T and MTHFR 677 C>T polymorphisms with breast and ovarian cancer risk in BRCA1/2 mutation carriers: results from a multicenter study.

Jakubowska A - Rozkrut D - Antoniou A - Hamann U - Scott R J - McGuffog L - Healy S - Sinilnikova O M - Rennert G - Lejbkowicz F - Flugelman A - Andrulis I L - Glendon G - Ozcelik H - Thomassen M - Paligo M - Aretini P - SWE-BRCA - Kantala J - Aroer B - von Wachenfeldt A - Liljegren A - Loman N - Herbst K - Kristoffersson U - Rosenquist R - Karlsson P - Stenmark-Askmalm M - Melin B - Nathanson K L - Domchek S M - Byrski T - Huzarski T - Gronwald J - Menkiszak J - Cybulski C - Serrano P - Osorio A - Cajal T R - Tsitlaidou M - Benítez J - Gilbert M - HEBON- Rookus M - Aalfs C M - Kluijt I - Boessenkool-Pape J L - Meijers-Heijboer H E J - Oosterwijk J C - van Asperen C J - Blok M J - Nelen M R - van den Ouweland A M W - Seynaeve C - van der Luijt R B - Devilee P - EMBRACE - Easton D F - Peock S - Frost D - Platte R - Ellis S D - Fineberg E - Evans D G - Lalloo F - Eeles R - Jacobs C - Adlard J - Davidson R - Eccles D - Cole T - Cook J - Godwin A - Bove B - GEMO Study Collaborators - Stoppa-Lyonnet D - Caux-Moncoutier V - Belotti M - Tirapo C - Mazoyer S - Barjhoux L - Boutry-Kryza N - Pujol P - Coupier I - Peyrat J-P - Vennin P - Muller D - Fricker J-P - Venat-Bouvet L - Johannsson O Th - Isaacs C - Schmutzler R - Wappenschmidt B - Meindl A - Arnold N - Varon-Mateeva R - Niederacher D - Sutter C - Deissler H - Preisler-Adams S - Simard J - Soucy P - Durocher F - Chenevix-Trench G - Beesley J - Chen

X - KConFab - Rebbeck T - Couch F - Wang X - Lindor N - Fredericksen Z - Pankratz V S - Peterlongo P - Bonanni B - Fortuzzi S - Peissel B - Szabo C - Mai P L - Loud J T - Lubinski J - CIMBA, the Consortium of Investigators of Modifiers of BRCA1/2-Related Cancer.

British journal of cancer | 2012 Jun 5 | doi: 10.1038/bjc.2012.160 | ISSN: 1532-1827 | Vol. 106 Issue 12

[PMID: 22669161] IF: 5,082

Dna2 offers support for stalled forks.

Lai Mong Sing - Foiani Marco

Cell | 2012 Jun 8 | doi: 10.1016/j.cell.2012.05.021 | ISSN: 1097-4172 | Vol. 149 Issue 6

[PMID: 22682239] IF: 31,957

Emergence of KRAS mutations and acquired resistance to anti-EGFR therapy in colorectal cancer.

Misale Sandra - Yaeger Rona - Hobor Sebastijan - Scala Elisa - Janakiraman Manickam - Liska David - Valtorta Emanuele - Schiavo Roberta - Buscarino Michela - Siravegna Giulia - Bencardino Katia - Cercek Andrea - Chen Chin-Tung - Veronese Silvio - Zanon Carlo - Sartore-Bianchi Andrea - Gambacorta Marcello - Gallicchio Margherita - Vakiani Efsevia - Boscaro Valentina - Medico Enzo - Weiser Martin - Siena Salvatore - Di Nicolantonio Federica - Solit David - Bardelli Alberto

Nature | 2012 Jun 28 | doi: 10.1038/nature11156 | ISSN: 1476-4687 | Vol. 486 Issue 7404

[PMID: 22722830] IF: 38,597

EuFishBioMed (COST Action BM0804): a European network to promote the use of small fishes in biomedical research.

Strähle Uwe - Bally-Cuif Laure - Kelsh Robert - Beis Dimitris - Mione Marina - Panula Pertti - Figueras Antonio - Gothilf Yoav - Brösamle Christian - Geisler Robert - Knedlitschek Gudrun

Zebrafish | 2012 Jun 1 | doi: 10.1089/zeb.2012.0742 | ISSN: 1557-8542 | Vol. 9 Issue 2

[PMID: 22537014] IF: 2,883

Is cellular senescence an example of antagonistic pleiotropy?

Giaimo Stefano - d'Adda di Fagagna Fabrizio

Aging Cell | 2012 Jun 1 | doi: 10.1111/j.1474-9726.2012.00807.x | ISSN: 1474-9726 | Vol. 11 Issue 3

[PMID: 22329645] IF: 5,705

Oncogene-induced telomere dysfunction enforces cellular senescence in human cancer precursor lesions.

Suram Anitha - Kaplunov Jessica - Patel Priyanka L - Ruan Haihe - Cerutti Aurora - Boccardi Virginia - Fumagalli Marzia - Di Micco Raffaella - Mirani Neena - Gurung Resham Lal - Hande Manoor Prakash - d'Adda di Fagagna Fabrizio - Herbig Utz

The EMBO Journal | 2012 Jun 29 | doi: 10.1038/emboj.2012.132 | ISSN: 1460-2075 | Vol. 31 Issue 13

[PMID: 22569128] IF: 9,822

Protecting normal cells from the cytotoxicity of chemotherapy.

Cheok Chit Fang

Cell Cycle (Georgetown, Tex.) | 2012 Jun 15 | doi: 10.4161/cc.20961 | ISSN: 1551-4005 | Vol. 11 Issue 12

[PMID: 22684296] IF: 5,243

The SNP rs895819 in miR-27a is not associated with familial breast cancer risk in Italians.

Catucci Irene - Verderio Paolo - Pizzamiglio Sara - Bernard Loris - Dall'olio Valentina - Sardella Domenico - Ravagnani Fernando - Galastri Laura - Barile Monica - Peissel Bernard - Zaffaroni Daniela - Manoukian Siranoush - Radice Paolo - Peterlongo Paolo

Breast Cancer Research and Treatment | 2012 Jun 1 | doi: 10.1007/s10549-012-2011-y | ISSN: 1573-7217 | Vol. 133 Issue 2

[PMID: 22415478] IF: 4,469

11q13 is a susceptibility locus for hormone receptor positive breast cancer.

Lambrechts Diether - Truong Therese - Justenhoven Christina - Humphreys Manjeet K - Wang Jean - Hopper John L - Dite Gillian S - Apicella Carmel - Southey Melissa C - Schmidt Marjanka K - Broeks Annegien - Cornelissen Sten - van Hien Richard - Sawyer Elinor - Tomlinson Ian - Kerin Michael - Miller Nicola - Milne Roger L - Zamora M Pilar - Pérez José Ignacio Arias - Benítez Javier - Hamann Ute - Ko Yon-Dschun - Brüning Thomas - GENICA Network - Chang-Claude Jenny - Eilber Ursel - Hein Rebecca - Nickels Stefan - Flesch-Janys Dieter - Wang-Gohrke Shan - John Esther M - Miron Alexander - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Grip Mervi - Chenevix-Trench Georgia - Beesley Jonathan - Chen Xiaoqing - Investigators kConFab - Australian Ovarian Cancer Study Group - Menegaux Florence - Cordina-Duverger Emilie - Shen Chen-Yang - Yu Jyh-Cherng - Wu Pei-Ei - Hou Ming-Feng - Andrulis Irene L - Selander Teresa - Glendon Gord - Mulligan Anna Marie - Anton-Culver Hoda - Ziogas Argyrios - Muir Kenneth R - Lophatananon Artitaya - Rattanamongkongul Suthee - Puttawibul Puttisak - Jones Michael - Orr Nicholas - Ashworth Alan - Swerdlow Anthony - Severi Gianluca - Baglietto Laura - Giles Graham - Southey Melissa - Marmé Federik - Schneeweiss Andreas - Sohn Christof - Burwinkel Barbara - Yesilyurt Betul T - Neven Patrick - Paridaens Robert - Wildiers Hans - Brenner Hermann - Müller Heiko - Arndt Volker - Stegmaier Christa - Meindl Alfons - Schott Sarah - Bartram Claus R - Schmutzler Rita K - Cox Angela - Brock Ian W - Elliott Graeme - Cross Simon S - Fasching Peter A - Schulz-Wendtland Ruediger - Ekici Arif B - Beckmann Matthias W - Fletcher Olivia - Johnson Nichola - Silva Isabel Dos Santos - Peto Julian - Nevanlinna Heli - Muranen Taru A - Aittomäki Kristiina - Blomqvist Carl - Dörk Thilo - Schürmann Peter - Bremer Michael - Hillemanns Peter - Bogdanova Natalia V - Antonenkova Natalia N - Rogov Yuri I - Karstens Johann H - Khusnutdinova Elza - Bermisheva Marina - Prokofieva Darya - Gancev Shamil - Jakubowska Anna - Lubinski Jan - Jaworska Katarzyna - Durda Katarzyna - Nordestgaard Børge G - Bojesen Stig E - Lanng Charlotte - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - Radice Paolo - Peterlongo Paolo - Manoukian Siranoush - Bernard Loris - Couch Fergus J - Olson Janet E - Wang Xianshu - Fredericksen Zachary - Alnaes Grethe Grenaker - Kristensen Vessela - Børresen-Dale Anne-Lise - Devilee Peter - Tollenaar Robert A E M - Seynaeve Caroline M - Hooning Maartje J - García-Closas Montserrat - Chanock Stephen J - Lissowska Jolanta - Sherman Mark E - Hall Per - Liu Jianjun - Czene Kamila - Kang Daehee - Yoo Keun-Young - Noh Dong-Young - Lindblom Annika - Margolin Sara - Dunning Alison M - Pharoah Paul D P - Easton Douglas F - Guénel Pascal - Brauch Hiltrud

Human Mutation | 2012 Jul 1 | doi: 10.1002/humu.22089 | ISSN: 1098-1004 | Vol. 33 Issue 7

[PMID: 22461340] IF: 5,213

A novel ubiquitin mark at the N-terminal tail of histone H2As targeted by RNF168 ubiquitin ligase.

Gatti Marco - Pinato Sabrina - Maspero Elena - Soffientini Paolo - Polo Simona - Penengo Lorenza

Cell Cycle (Georgetown, Tex.) | 2012 Jul 1 | doi: 10.4161/cc.20919 | ISSN: 1551-4005 | Vol. 11 Issue 13

[PMID: 22713238] IF: 5,243

Clinical and pathologic characteristics of BRCA-positive and BRCA-negative male breast cancer patients: results from a collaborative multicenter study in Italy.

Ottini Laura - Silvestri Valentina - Rizzolo Piera - Falchetti Mario - Zanna Ines - Saieva Calogero - Masala Giovanna - Bianchi Simonetta - Manoukian Siranoush - Barile Monica - Peterlongo Paolo - Varesco Liliana - Tommasi Stefania - Russo Antonio - Giannini Giuseppe - Cortesi Laura - Viel Alessandra - Montagna Marco - Radice Paolo - Palli Domenico

Breast Cancer Research and Treatment | 2012 Jul 1 | doi: 10.1007/s10549-012-2062-0 | ISSN: 1573-7217 | Vol. 134 Issue 1

[PMID: 22527108] IF: 4,469

Neural stem cells exposed to BrdU lose their global DNA methylation and undergo astrocytic differentiation.

Schneider Leonid - d'Adda di Fagagna Fabrizio

Nucleic Acids Research | 2012 Jul 1 | doi: 10.1093/nar/gks207 | ISSN: 1362-4962 | Vol. 40 Issue 12

[PMID: 22379135] IF: 8,278

A nonsynonymous polymorphism in IRS1 modifies risk of developing breast and ovarian cancers in BRCA1 and ovarian cancer in BRCA2 mutation carriers.

Ding Yuan C - McGuffog Lesley - Healey Sue - Friedman Eitan - Laitman Yael - Paluch-Shimon Shani- - Kaufman Bella - SWE-BRCA - Liljegren Annelie - Lindblom Annika - Olsson Håkan - Kristoffersson Ulf - Stenmark-Askmalm Marie - Melin Beatrice - Domchek Susan M - Nathanson Katherine L - Rebbeck Timothy R - Jakubowska Anna - Lubinski Jan - Jaworska Katarzyna - Durda Katarzyna - Gronwald Jacek - Huzarski Tomasz - Cybulski Cezary - Byrski Tomasz - Osorio Ana - Cajal Teresa Ramóny - Stavropoulou Alexandra V - Benítez Javier - Hamann Ute - HEBON - Rookus Matti - Aalfs Cora M - de Lange Judith L - Meijers-Heijboer Hanne E J - Oosterwijk Jan C - van Asperen Christi J - Gómez García Encarna B - Hoogerbrugge Nicoline - Jager Agnes - van der Luijt Rob B - EMBRACE - Easton Douglas F - Peock Susan - Frost Debra - Ellis Steve D - Platte Radka - Fineberg Elena - Evans D Gareth - Lalloo Fiona - Izatt Louise - Eeles Ros - Adlard Julian - Davidson Rosemarie - Eccles Diana - Cole Trevor - Cook Jackie - Brewer Carole - Tischkowitz Marc - Godwin Andrew K - Pathak Harsh - GEMO Study Collaborators - Stoppa-Lyonnet Dominique - Sinilnikova Olga M - Mazoyer Sylvie - Barjhoux Laure - Léoné Mélanie - Gauthier-Villars Marion - Caux-Moncoutier Virginie - de Pauw Antoine - Hardouin Agnès - Berthet Pascaline - Dreyfus Hélène - Ferrer Sandra Fert - Collonge-Rame Marie-Agnès - Sokolowska Johanna - Buys Saundra - Daly Mary - Miron Alex - Terry Mary Beth - Chung Wendy - John Esther M - Southey Melissa - Goldgar David - Singer Christian F - Tea Muy-Kheng Maria - Gschwantler-Kaulich Daphne - Fink-Retter Anneliese - Hansen Thomas V O - Ejlertsen Bent - Johannsson Oskar T - Offit Kenneth - Sarrel Kara - Gaudet Mia M - Vijai Joseph - Robson Mark - Piedmonte Marion R - Andrews Lesley - Cohn David - DeMars Leslie R - DiSilvestro Paul - Rodriguez Gustavo - Toland Amanda Ewart - Montagna Marco - Agata Simona - Imyanitov Evgeny - Isaacs Claudine - Janavicius Ramunas - Lazaro Conxi - Blanco Ignacio - Ramus Susan J - Sucheston Lara - Karlan Beth Y - Gross Jenny - Ganz Patricia A - Beattie Mary S - Schmutzler Rita K - Wappenschmidt Barbara - Meindl Alfons - Arnold Norbert - Niederacher Dieter - Preisler-Adams Sabine - Gadzicki Dorotehea - Varon-Mateeva Raymonda - Deissler Helmut - Gehrig Andrea - Sutter Christian - Kast Karin - Nevanlinna Heli - Aittomäki Kristiina - Simard Jacques - KConFab Investigators - Spurdle Amanda B - Beesley Jonathan - Chen Xiaoqing - Tomlinson Gail E - Weitzel Jeffrey - Garber Judy E - Olopade Olufunmilayo I - Rubinstein Wendy S - Tung Nadine - Blum Joanne L - Narod Steven A - Brummel Sean - Gillen Daniel L - Lindor Noralane - Fredericksen Zachary - Pankratz Vernon S - Couch Fergus J - Radice Paolo - Peterlongo Paolo - Greene Mark H - Loud Jennifer T - Mai Phuong L - Andrulis Irene L - Glendon Gord - Ozcelik Hilmi - OCGN - Gerdes Anne-Marie - Thomassen Mads - Jensen Uffe Birk - Skytte Anne-Bine - Caligo Maria A - Lee Andrew - Chenevix-Trench Georgia - Antoniou Antonis C - Neuhausen Susan L - Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA)

Cancer Epidemiology, Biomarkers & Prevention | 2012 Aug 1 | doi: 10.1158/1055-9965.EPI-12-0229 | ISSN: 1538-7755 | Vol. 21 Issue 8

[PMID: 22729394] IF: 4,559

AIDing the immune system-DIAbolic in cancer.

Schmitz Kerstin-Maike - Petersen-Mahrt Svend K

Seminars in Immunology | 2012 Aug 1 | doi: 10.1016/j.smim.2012.07.001 | ISSN: 1096-3618 | Vol. 24 Issue 4

[PMID: 22841422] IF: 5,926

Publishing: Alarming shift away from sharing results.

Boniolo Giovanni - Vaccari Thomas

Nature | 2012 Aug 9 | doi: 10.1038/488157d | ISSN: 1476-4687 | Vol. 488 Issue 7410

[PMID: 22874955] IF: 38,597

Rad5-dependent DNA repair functions of the Saccharomyces cerevisiae FANCM protein homolog Mph1.

Daee Danielle L - Ferrari Elisa - Longerich Simonne - Zheng Xiao-feng - Xue Xiaoyu - Branzei Dana - Sung Patrick - Myung Kyungjae

The Journal of Biological Chemistry | 2012 Aug 3 | doi: 10.1074/jbc.M112.369918 | ISSN: 1083-351X | Vol. 287 Issue 32

[PMID: 22696213] IF: 4,651

Site-specific DICER and DROSHA RNA products control the DNA-damage response.

Francia Sofia - Michelini Flavia - Saxena Alka - Tang Dave - de Hoon Michiel - Anelli Viviana - Mione Marina - Carninci Piero - d'Adda di Fagagna Fabrizio

Nature | 2012 Aug 9 | doi: 10.1038/nature11179 | ISSN: 1476-4687 | Vol. 488 Issue 7410

[PMID: 22722852] IF: 38,597

The young and happy marriage of membrane traffic and cell polarity.

Thompson Barry J - Perez Franck - Vaccari Thomas

EMBO Reports | 2012 Aug 1 | doi: 10.1038/embor.2012.98 | ISSN: 1469-3178 | Vol. 13 Issue 8

[PMID: 22777496] IF: 7,189

Germline mutations in BRIP1 and PALB2 in Jewish high cancer risk families.

Catucci Irene - Milgrom Roni - Kushnir Anya - Laitman Yael - Paluch-Shimon Shani - Volorio Sara - Ficarazzi Filomena - Bernard Loris - Radice Paolo - Friedman Eitan - Peterlongo Paolo

Familial Cancer | 2012 Sep 1 | doi: 10.1007/s10689-012-9540-8 | ISSN: 1573-7292 | Vol. 11 Issue 3

[PMID: 22692731] IF: 1,935

Investigation of in vitro cytotoxicity of the redox state of ionic iron in neuroblastoma cells.

Singh Ajay Vikram - Vyas Varun - Montani Erica - Maontani Erica - Cartelli Daniele - Parazzoli Dario - Oldani Amanda - Zeri Giulia - Orioli Elisa - Gemmati Donato - Zamboni Paolo

Journal of Neurosciences in Rural Practice | 2012 Sep 1 | doi: 10.4103/0976-3147.102611 | ISSN: 0976-3155 | Vol. 3 Issue 3

[PMID: 23188983] IF: 6,908

Preserving the genome by regulating chromatin association with the nuclear envelope.

Bermejo Rodrigo - Kumar Amit - Foiani Marco

Trends in Cell Biology | 2012 Sep 1 | doi: 10.1016/j.tcb.2012.05.007 | ISSN: 1879-3088 | Vol. 22 Issue 9

[PMID: 22771046] IF: 11,721

Sedlin controls the ER export of procollagen by regulating the Sar1 cycle.

Venditti Rossella - Scanu Tiziana - Santoro Michele - Di Tullio Giuseppe - Spaar Alexander - Gaibisso

Renato - Beznoussenko Galina V - Mironov Alexander A - Mironov Alexander - Zelante Leopoldo - Piemontese Maria Rosaria - Notarangelo Angelo - Malhotra Vivek - Vertel Barbara M - Wilson Cathal - De Matteis Maria Antonietta

Science (New York, N.Y.) | 2012 Sep 28 | doi: 10.1126/science.1224947 | ISSN: 1095-9203 | Vol. 337 Issue 0

[PMID: 23019651] IF: 31,027

The role of genetic breast cancer susceptibility variants as prognostic factors.

Fasching Peter A - Pharoah Paul D P - Cox Angela - Nevanlinna Heli - Bojesen Stig E - Karn Thomas - Broeks Annegien - van Leeuwen Flora E - van\'t Veer Laura J - Udo Renate - Dunning Alison M - Greco Dario - Aittomäki Kristiina - Blomqvist Carl - Shah Mitul - Nordestgaard Børge G - Flyger Henrik - Hopper John L - Southey Melissa C - Apicella Carmel - Garcia-Closas Montserrat - Sherman Mark - Lissowska Jolanta - Seynaeve Caroline - Huijts Petra E A - Tollenaar Rob A E M - Ziogas Argyrios - Ekici Arif B - Rauh Claudia - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - Andrulis Irene L - Ozcelik Hilmi - Mulligan Anna-Marie - Glendon Gord - Hall Per - Czene Kamila - Liu Jianjun - Chang-Claude Jenny - Wang-Gohrke Shan - Eilber Ursula - Nickels Stefan - Dörk Thilo - Schiekel Maria - Bremer Michael - Park-Simon Tjoung-Won - Giles Graham G - Severi Gianluca - Baglietto Laura - Hooning Maartje J - Martens John W M - Jager Agnes - Kriege Mieke - Lindblom Annika - Margolin Sara - Couch Fergus J - Stevens Kristen N - Olson Janet E - Kosel Matthew - Cross Simon S - Balasubramanian Sabapathy P - Reed Malcolm W R - Miron Alexander - John Esther M - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Kauppila Saila - Burwinkel Barbara - Marme Frederik - Schneeweiss Andreas - Sohn Christof - Chenevix-Trench Georgia - kConFab Investigators - Lambrechts Diether - Dieudonne Anne-Sophie - Hatse Sigrid - van Limbergen Erik - Benitez Javier - Milne Roger L - Zamora M Pilar - Pérez José Ignacio Arias - Bonanni Bernardo - Peissel Bernard - Loris Bernard - Peterlongo Paolo - Rajaraman Preetha - Schonfeld Sara J - Anton-Culver Hoda - Devilee Peter - Beckmann Matthias W - Slamon Dennis J - Phillips Kelly-Anne - Figueroa Jonine D - Humphreys Manjeet K - Easton Douglas F - Schmidt Marjanka K

Human Molecular Genetics | 2012 Sep 1 | doi: 10.1093/hmg/dds159 | ISSN: 1460-2083 | Vol. 21 Issue 17

[PMID: 22532573] IF: 7,692

The SUMO protease SENP1 is required for cohesion maintenance and mitotic arrest following spindle poison treatment.

Era Saho - Abe Takuya - Arakawa Hiroshi - Kobayashi Shunsuke - Szakal Barnabas - Yoshikawa Yusuke - Motegi Akira - Takeda Shunichi - Branzei Dana

Biochemical and Biophysical Research Communication | 2012 Sep 28 | doi: 10.1016/j.bbrc.2012.08.066 | ISSN: 1090-2104 | Vol. 426 Issue 3

[PMID: 22943854] IF: 2,406

9q31.2-rs865686 as a susceptibility locus for estrogen receptor-positive breast cancer: evidence from the Breast Cancer Association Consortium.

Warren Helen - Dudbridge Frank - Fletcher Olivia - Orr Nick - Johnson Nichola - Hopper John L - Apicella Carmel - Southey Melissa C - Mahmoodi Maryam - Schmidt Marjanka K - Broeks Annegien - Cornelissen Sten - Braaf Linda M - Muir Kenneth R - Lophatananon Artitaya - Chaiwerawattana Arkom - Wiangnon Surapon - Fasching Peter A - Beckmann Matthias W - Ekici Arif B - Schulz-Wendtland Ruediger - Sawyer Elinor J - Tomlinson Ian - Kerin Michael - Burwinkel Barbara - Marme Frederik - Schneeweiss Andreas - Sohn Christof - Guénel Pascal - Truong Thérèse - Laurent-Puig Pierre - Mulot Claire - Bojesen Stig E - Nielsen Sune F - Flyger Henrik - Nordestgaard Børge G - Milne Roger L - Benítez Javier - Arias-Pérez José-Ignacio - Zamora M Pilar - Anton-Culver Hoda - Ziogas Argyrios - Bernstein Leslie - Dur Christina Clarke - Brenner Hermann - Müller Heiko - Arndt Volker - Langheinz Anne - Meindl Alfons - Golatta Michael - Bartram Claus R - Schmutzler Rita K - Brauch Hiltrud - Justenhoven Christina - Brüning Thomas - GENICA Network - Chang-Claude Jenny - Wang-Gohrke Shan - Eilber Ursula - Dörk Thilo - Schürmann Peter - Bremer Michael - Hillemanns Peter - Nevanlinna Heli - Muranen Taru A - Aittomäki Kristiina - Blomqvist Carl - Bogdanova Natalia - Antonenkova Natalia - Rogov Yuriy - Bermisheva Marina - Prokofyeva Darya - Zinnatullina Guzel - Khusnutdinova Elza - Lindblom Annika - Margolin Sara - Mannermaa Arto - Kosma Veli-Matti - Hartikainen Jaana M -

Kataja Vesa - Chenevix-Trench Georgia - Beesley Jonathan - Chen Xiaoqing - kConFab Investigators - Australian Ovarian Cancer Study Group - Lambrechts Diether - Smeets Ann - Paridaens Robert - Weltens Caroline - Flesch-Janys Dieter - Buck Katharina - Behrens Sabine - Peterlongo Paolo - Bernard Loris - Manoukian Siranoush - Radice Paolo - Couch Fergus J - Vachon Celine - Wang Xianshu - Olson Janet - Giles Graham - Baglietto Laura - McLean Cariona A - Severi Gianluca - John Esther M - Miron Alexander - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Grip Mervi - Andrulis Irene L - Knight Julia A - Mulligan Anna Marie - Weerasooriya Nayana - Devilee Peter - Tollenaar Robert A E M - Martens John W M - Seynaeve Caroline M - Hooning Maartje J - Hollestelle Antoinette - Jager Agnes - Tilanus-Linthorst Madeleine M A - Hall Per - Czene Kamila - Liu Jianjun - Li Jingmei - Cox Angela - Cross Simon S - Brock Ian W - Reed Malcolm W R - Pharoah Paul - Blows Fiona M - Dunning Alison M - Ghoussaini Maya - Ashworth Alan - Swerdlow Anthony - Jones Michael - Schoemaker Minouk - Easton Douglas F - Humphreys Manjeet - Wang Qin - Peto Julian - dos-Santos-Silva Isabel

Cancer Epidemiology, Biomarkers & Prevention | 2012 Oct 1 | doi: 10.1158/1055-9965.EPI-12-0526 | ISSN: 1538-7755 | Vol. 21 Issue 10

[PMID: 22859399] IF: 4,559

A role for the RNA pol II-associated PAF complex in AID-induced immune diversification.

Willmann Katharina L - Milosevic Sara - Pauklin Siim - Schmitz Kerstin-Maike - Rangam Gopinath - Simon Maria T - Maslen Sarah - Skehel Mark - Robert Isabelle - Heyer Vincent - Schiavo Ebe - Reina-San-Martin Bernardo - Petersen-Mahrt Svend K

The Journal of Experimental Medicine | 2012 Oct 22 | doi: 10.1084/jem.20112145 | ISSN: 1540-9538 | Vol. 209 Issue 11

[PMID: 23008333] IF: 13,214

Crosstalk between chromatin state and DNA damage response in cellular senescence and cancer.

Sulli Gabriele - Di Micco Raffaella - d'Adda di Fagagna Fabrizio

Nature Reviews. Cancer | 2012 Oct 1 | doi: 10.1038/nrc3344 | ISSN: 1474-1768 | Vol. 12 Issue 10

[PMID: 22952011] IF: 35,000

Differentiation-associated microRNAs antagonize the Rb-E2F pathway to restrict proliferation.

Marzi Matteo J - Puggioni Eleonora M R - Dall'olio Valentina - Bucci Gabriele - Bernard Loris - Bianchi Fabrizio - Crescenzi Marco - Di Fiore Pier Paolo - Nicassio Francesco

The Journal of Cell Biology | 2012 Oct 1 | doi: 10.1083/jcb.201206033 | ISSN: 1540-8140 | Vol. 199 Issue 1

[PMID: 23027903] IF: 10,822

LIN7 regulates the filopodium- and neurite-promoting activity of IRSp53.

Crespi Arianna - Ferrari Ilaria - Lonati Paola - Disanza Andrea - Fornasari Diego - Scita Giorgio - Padovano Valeria - Pietrini Grazia

Journal of Cell Science | 2012 Oct 1 | doi: 10.1242/jcs.106484 | ISSN: 1477-9137 | Vol. 125 Issue Pt 19

[PMID: 22767515] IF: 5,877

Rare variants in XRCC2 as breast cancer susceptibility alleles.

Hilbers Florentine S - Wijnen Juul T - Hoogerbrugge Nicoline - Oosterwijk Jan C - Collee Margriet J - Peterlongo Paolo - Radice Paolo - Manoukian Siranoush - Feroce Irene - Capra Fabio - Couch Fergus J - Wang Xianshu - Guidugli Lucia - Offit Kenneth - Shah Sohela - Campbell Ian G - Thompson Ella R - James Paul A - Trainer Alison H - Gracia Javier - Benitez Javier - van Asperen Christi J - Devilee Peter

Journal of Medical Genetics | 2012 Oct 1 | doi: 10.1136/jmedgenet-2012-101191 | ISSN: 1468-6244 | Vol. 49 Issue 10

[PMID: 23054243] IF: 5,703

Role of the Mad2 dimerization interface in the spindle assembly checkpoint independent of kinetochores.

Mariani Luca - Chiroli Elena - Nezi Luigi - Müller Heiko - Piatti Simonetta - Musacchio Andrea - Ciliberto Andrea

Current Biology : CB | 2012 Oct 23 | doi: 10.1016/j.cub.2012.08.028 | ISSN: 1879-0445 | Vol. 22 Issue 20

[PMID: 23000150] IF: 9,494

Seeking synergy in p53 transcriptional activation for cancer therapy.

Cheok Chit Fang - Lane David P

Discovery Medicine | 2012 Oct 1 | doi: | ISSN: 1944-7930 | Vol. 14 Issue 0

[PMID: 23114582] IF: 2,965

A molecularly annotated platform of patient-derived xenografts ("xenopatien ts") identifies HER2 as an effective therapeutic target in cetuximab-resistant colorectal cancer.

Bertotti Andrea - Migliardi Giorgia - Galimi Francesco - Sassi Francesco - Torti Davide - Isella Claudio - Corà Davide - Di Nicolantonio Federica - Buscarino Michela - Petti Consalvo - Ribero Dario - Russolillo Nadia - Muratore Andrea - Massucco Paolo - Pisacane Alberto - Molinaro Luca - Valtorta Emanuele - Sartore-Bianchi Andrea - Risio Mauro - Capussotti Lorenzo - Gambacorta Marcello - Siena Salvatore - Medico Enzo - Sapino Anna - Marsoni Silvia - Comoglio Paolo M - Bardelli Alberto - Trusolino Livio

Cancer Discovery | 2011 Nov 1 | doi: 10.1158/2159-8290.CD-11-0109 | ISSN: 2159-8290 | Vol. 1 Issue 0

[PMID: 22586653] IF: 10,143

Differential regulation of DNA damage response activation between somatic and germline cells in Caenorhabditis elegans.

Vermezovic J - Stergiou L - Hengartner M O - d'Adda di Fagagna Fabrizio

Cell Death and Differentiation | 2012 Nov 1 | doi: 10.1038/cdd.2012.69 | ISSN: 1476-5403 | Vol. 19 Issue 11

[PMID: 22705849] IF: 8,371

Senataxin associates with replication forks to protect fork integrity across RNA-polymerase-II-transcribed genes.

Alzu Amaya - Bermejo Rodrigo - Begnis Martina - Lucca Chiara - Piccini Daniele - Carotenuto Walter - Saponaro Marco - Brambati Alessandra - Cocito Andrea - Foiani Marco - Liberi Giordano

Cell | 2012 Nov 9 | doi: 10.1016/j.cell.2012.09.041 | ISSN: 1097-4172 | Vol. 151 Issue 4

[PMID: 23141540] IF: 31,957

The H3K27 demethylase JMJD3 is required for maintenance of the embryonic respiratory neuronal network, neonatal breathing, and survival.

Burgold Thomas - Voituron Nicolas - Caganova Marieta - Tripathi Prem Prakash - Menuet Clement - Tusi Betsabeh Khoramian - Spreafico Fabio - Bévengut Michelle - Gestreau Christian - Buontempo Serena - Simeone Antonio - Kruidenier Laurens - Natoli Gioacchino - Casola Stefano - Hilaire Gérard - Testa Giuseppe

Cell Reports | 2012 Nov 29 | doi: 10.1016/j.celrep.2012.09.013 | ISSN: 2211-1247 | Vol. 2 Issue 5

[PMID: 23103168]

The spindle-assembly checkpoint and the beauty of self-destruction.

Musacchio Andrea - Ciliberto Andrea

Nature Structural & Molecular Biology | 2012 Nov 1 | doi: 10.1038/nsmb.2429 | ISSN: 1545-9985 | Vol. 19 Issue 11

[PMID: 23132380] IF: 11,902

The V-ATPase-inhibitor archazolid abrogates tumor metastasis via inhibition of endocytic activation of the Rho-GTPase Rac1.

Wiedmann Romina M - von Schwarzenberg Karin - Palamidessi Andrea - Schreiner Laura - Kubisch Rebekka - Liebl Johanna - Schempp Christina - Trauner Dirk - Vereb Gyorgy - Zahler Stefan - Wagner Ernst - Müller Rolf - Scita Giorgio - Vollmar Angelika M

Cancer Research | 2012 Nov 15 | doi: 10.1158/0008-5472.CAN-12-1772 | ISSN: 1538-7445 | Vol. 72 Issue 22

[PMID: 22986742] IF: 8,650

Identification of fifteen novel germline variants in the BRCA1 3'UTR reveals a variant in a breast cancer case that introduces a functional miR-103 target site.

Brewster Brooke L - Rossiello Francesca - French Juliet D - Edwards Stacey L - Wong Ming - Wronski Ania - Whiley Phillip - Waddell Nic - Chen Xiaowei - Bove Betsy - kConFab - Hopper John L - John Esther M - Andrulis Irene - Daly Mary - Volorio Sara - Bernard Loris - Peissel Bernard - Manoukian Siranoush - Barile Monica - Pizzamiglio Sara - Verderio Paolo - Spurdle Amanda B - Radice Paolo - Godwin Andrew K - Southey Melissa C - Brown Melissa A - Peterlongo Paolo

Human Mutation | 2012 Dec 1 | doi: 10.1002/humu.22159 | ISSN: 1098-1004 | Vol. 33 Issue 12

[PMID: 22753153] IF: 5,213

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