

2013

A YEAR IN REVIEW

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Introducing the 2013 edition of IFOM Review

The idea of publishing an annual report for the institute has been in the air for a very long time. However, we did not like producing every year a cold document highlighting our own results with plain scientific data.

Thus, we came to the conclusion that it would have been better to receive a sincere and frank opinion on our work from external colleagues and collect these commentaries in an editorial product.

Therefore, we consider the IFOM Review a chance for reflection on the progress of knowledge, moving from IFOM activities and results.

A special thanks goes to the authors who generously spent their time and energy to share their views on the progress and perspectives of our research.

Marco Foiani



Francesco Blasi



IFOM Review: deep in the background of science

The authors:



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 Biophysics 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.



Francesco Blasi

IFOM Deputy Director

Francesco Blasi 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.

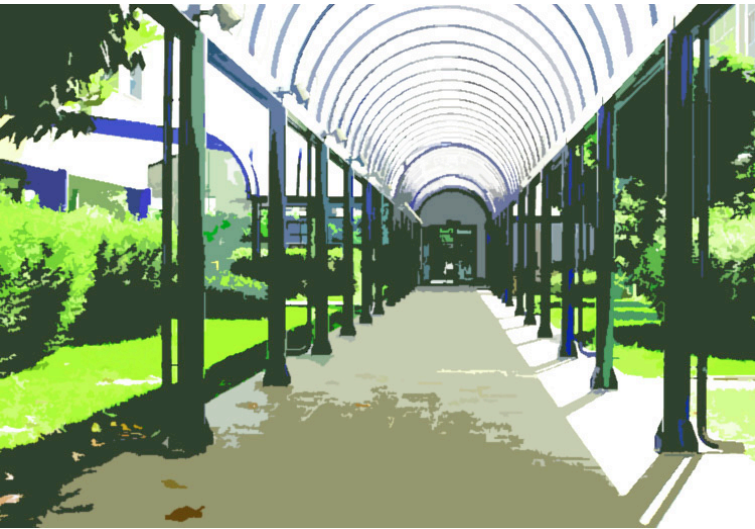
Is at IFOM since 2004, Director of research program Transcriptional Regulation in Development and Cancer.

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.



An expanding research institute of increasing impact

A view from the Scientific Advisory Board

by Tomas Lindahl

IFOM, the FIRC Institute of Molecular Oncology in Milan, is currently in a challenging and expansive phase, thanks to the impressive work by the international scientific staff, the generous supportive funding from FIRC and related sources, and the dynamic leadership by Marco Foiani and his close colleagues.

In addition to the essential core activities and basic research in Milan, translational research has been strengthened by closer links with Alberto Bardelli's IFOM unit localised in Turin, about 1 - 1.5 hour travel distance from the IFOM campus in Milan.

Three successful young scientists in Milan were awarded tenured posts in 2013, after the usual detailed scrutiny. They are Dana Branzei, Andrea Ciliberto and Stefano Casola. We congratulate them!

Dana Branzei was considered by a committee chaired by Jiri Bartek (Copenhagen). Dana is an expert on cellular responses to DNA damage, employing yeast genetics with complementary

experiments in the chicken DT40 cell line. The work is elegant, clarifying template switching during recombination and replication as an important strategy to avoid copying damaged DNA. Dana's group publishes in the leading journals, and she is frequently invited to speak at the major meetings in her field. She has the unusual talent of being fluent in Japanese, although she has a European background, and she is an important participant in several of IFOM's international activities.

Andrea Ciliberto was reviewed by a committee chaired by Sir Tim Hunt (London). Andrea obtained thorough training in applied mathematics and bioinformatics, and then decided to complement this approach with experimental work in molecular biology, especially in yeast. He investigates cell cycle key events, such as the spindle assembly checkpoint and cellular exit from mitosis. The data are leading to novel theoretical work, and Andrea has a close-to-perfect background for such ventures.

Stefano Casola has investigated B lymphocyte development, especially with regard to lymphomagenesis. He had a long collaboration with Klaus Rajewsky before setting up his own group in Milan. At IFOM, Stefano has played a key role in establishing top class mouse genetics, and new ventures in developmental biology. Stefano was reviewed by a committee chaired by Michael Neuberger (LMB Cambridge). Since Michael was frail due to the myeloma that later killed him, this tenure review was unusually carried out by Skype. The participants were impressed with Casola's deep insights, but perhaps even more so by the brilliant, constructive and helpful scholarly reviewing by Neuberger.

The death of Michael Neuberger is a great loss to the whole scientific community. He contributed invaluable to the work of the IFOM Scientific Advisory Board. Michael's former mentor, Klaus Rajewsky (Berlin) has kindly agreed to replace Michael on the SAB, under these sad circumstances.

In view of the increasing international profile of IFOM, and the ongoing collaborative activities in Asia, especially in Singapore and Bangalore, we are extremely pleased that Professor Krishnaswamy VijayRaghavan FRS agreed to join the Board to strengthen IFOM developmental biology, in spite of parallel new commitments, in particular recently becoming Secretary of Department of Biotechnology in the Indian Government.

We look forward to broad scientific discussions!



An expanding research institute
of increasing impact
by Tomas Lindahl

An expanding research institute
of increasing impact

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.

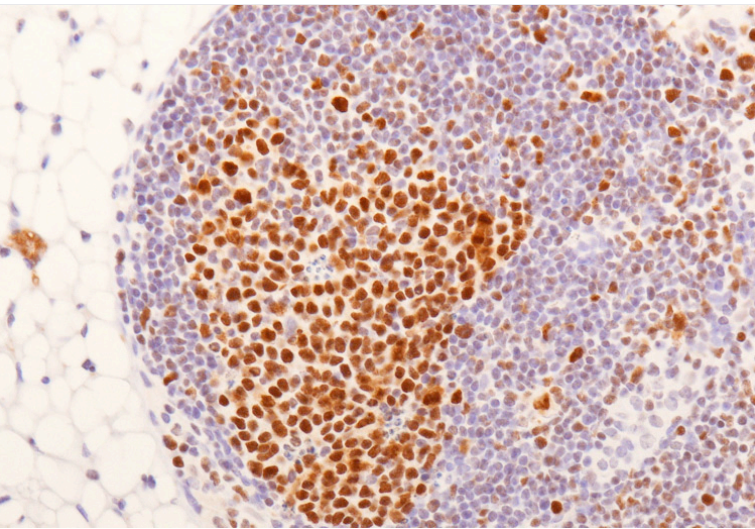
He became Professor of Medical Chemistry at the University of Gothenburg in 1978. In 1981 he was appointed Head of the Mutagenesis Laboratory at the ICRF Mill Hill Laboratories in London. From 1984 to 2006 he was Director of the Clare Hall

Laboratories at ICRF and Cancer Research UK, also serving as Deputy Director of Research. Amongst many distinctions, 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 Prix Etranger in 2009, and the Copley Medal in 2010 of the Royal Society.

He has received honorary doctorates from the Universities of Gothenburg, Oslo, Sheffield, and Sussex. He is now Emeritus Director of Cancer Research

UK, Clare Hall Laboratories, and involved in various scientific activities.

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



Germinal center dysregulation by histone methyltransferase EZH2 promotes lymphomagenesis

Commentary on Stefano Casola's paper published on *The Journal of Clinical Investigation*

by Riccardo Dalla-Favera

Our ability to produce antibodies with high specificity for foreign substances (antigens) is dependent on Germinal Centers (GC), a highly specialized structure that forms in response to certain antigens in lymphoid organs, including tonsils and lymphnodes. GC are generated when B lymphocytes (also called B cells), the cells that will eventually produce antibodies, encounter for the first time an antigen for which they have some, usually low, degree of affinity. Once recruited to the GC, B cells rapidly proliferate in the so-called dark zone and, notably, actively modify their DNA, specifically the Variable (antigen encountering) region of their antibody genes by the process of somatic hypermutation (SHM). As a consequence of these DNA modifications, the original specificity of the antibody for the challenging antigen will either be lost or greatly increased in different B cells within the GC.

B cells will then move to the Light Zone of the GC, where they encounter the antigen again: cells carrying on their cell surface an antibody with

high-affinity for the antigen will be selected for survival and differentiation into memory cells and plasma cells, the final producers of high affinity antibodies; B cells carrying antibodies that have lost affinity will miss the encounter with the antigen and die. In the GC, B cells also undergo a second DNA modification in their antibody genes, namely class-switch recombination (CSR), a DNA remodeling event that confers distinct biological properties to antibodies with identical specificities. SHM and CSR represent highly-specialized functions unique to B cells; they are both performed by an enzyme, activation-induced cytidine deaminase (AID), whose function involves the creation of DNA breaks, an event that is normally not tolerated in other cell types.

The ability of GC B cells to control proliferation and differentiation while performing sophisticated genomic remodeling functions is critical to ensure the selection of antibody-producing cells as well as the elimination of dangerous cells producing antibodies against self components or carrying

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excessive DNA damage and mutations that may lead to cancer. Thus, a thorough understanding of the mechanisms regulating the GC is important for the understanding of the physiology of antibody production as well as of the mechanisms that lead to pathology, including autoimmune diseases and lymphomas deriving from the malignant transformation of GC B cells.

Toward this end, important insights into GC physiology and pathology have been provided by the study of Caganova et al. in the research team led by Stefano Casola at IFOM (Caganova *et al.* J. Clinical Investigation, 123: 5009-5022, 2013). Their research has focused on the function of EZH2, a gene encoding an enzyme (methyltransferase) that contributes to the regulation of specific target genes by posing repressive markers on chromatin, the protein structure that coats DNA and regulates its activity. Casola and colleagues have selected to study EZH2 based on two important observations: first, the EZH2 gene is expressed at high levels in GC B cells, suggesting an important and specific function; second, its structure and function is altered in various types of lymphomas, suggesting a role of these alterations in tumor development.

In order to identify the normal function of EZH2 in the GC, Casola and colleagues generated mice in which this gene was specifically deleted in GC B cells. These mice displayed specific defects in the formation of GC and in the generation of memory B cells, leading to greatly impaired antibody-dependent immunological responses.

Germinal center dysregulation by histone methyltransferase EZH2 promotes lymphomagenesis

Protection against deadly pathogens requires the production of high-affinity antibodies by B cells, which are generated in germinal centers (GCs). Alteration of the GC developmental program is common in many B cell malignancies. Identification of regulators of the GC response is crucial to develop targeted therapies for GC B cell dysfunctions, including lymphomas. The histone H3 lysine 27 methyltransferase enhancer of zeste homolog 2 (EZH2) is highly expressed in GC B cells and is often constitutively activated in GC-derived non-Hodgkin lymphomas (NHLs). The function of EZH2 in GC B cells remains largely unknown. Herein, we show that Ezh2 inactivation in mouse GC B cells caused profound impairment of GC responses, memory B cell formation, and humoral immunity. EZH2 protected GC B cells against activation-induced cytidine deaminase (AID) mutagenesis, facilitated cell cycle progression, and silenced plasma cell determinant and tumor suppressor B-lymphocyte-induced maturation protein 1 (BLIMP1). EZH2 inhibition in NHL cells induced BLIMP1, which impaired tumor growth. In conclusion, EZH2 sustains AID function and prevents terminal differentiation of GC B cells, which allows antibody diversification and affinity maturation. Dysregulation of the GC reaction by constitutively active EZH2 facilitates lymphomagenesis and identifies EZH2 as a possible therapeutic target in NHL and other GC-derived B cell diseases.

[PMID 24200695]

In a series of remarkably precise and sophisticated investigations, they also showed that the function of EZH2 in GC control is based on multiple mechanisms, among which two appear particularly relevant: first, EZH2 protects the genome of B cells from the excessive genomic damage produced by the remodeling functions of AID, thus preventing or repairing genetic lesions that are dangerous for malignant transformation. Second EZH2 represses the expression of BLIMP1, a gene required for the differentiation of B cells in memory and antibody-secreting plasma cells, thus preventing the premature exit of B cells from the GC prior to their selection for the production of high-affinity antibodies.

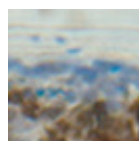


Germinal center dysregulation by histone methyltransferase EZH2 promotes lymphomagenesis
by Riccardo Dalla-Favera

These results identify EZH2 as one of the most important regulators of GC development and therefore of the development of physiologic antibody-mediated responses to foreign antigens. The results of the Casola's group have also important implications for the pathogenesis and the therapeutic treatment of lymphomas. Both Follicular Lymphoma and Diffuse Large B-Cell Lymphoma, the two most common types of human lymphomas, express the EZH2 gene and protein, and a fraction of them carry a mutant form of the EZH2 gene that alters its activity. As suggested by the authors, the roles of EZH2 in protecting from AID-induced DNA damage and in preventing differentiation imply that genotoxic drugs, in combination with differentiation-inducing agents, may be useful complements in anti-lymphoma regimens.

More importantly, drugs specifically targeting and inactivating normal or mutant EZH2 are already available and have been shown to have activity against lymphoma cells. The results of the Casola's group provide important insights into their mechanism of action and identify potential biomarkers to monitor their activity.

Figure (page 10): Germinal center in lymph node. Germinal center B cells are identified on the basis of Ezh2 expression (brown).



Genetics of B Cells and Lymphomas
Stefano Casola



Germinal center dysregulation by histone methyltransferase EZH2 promotes lymphomagenesis
by Riccardo Dalla-Favera

Germinal center dysregulation by histone methyltransferase EZH2 promotes lymphomagenesis

The author:



Riccardo Dalla-Favera

Professor and Director, Institute for Cancer Genetics

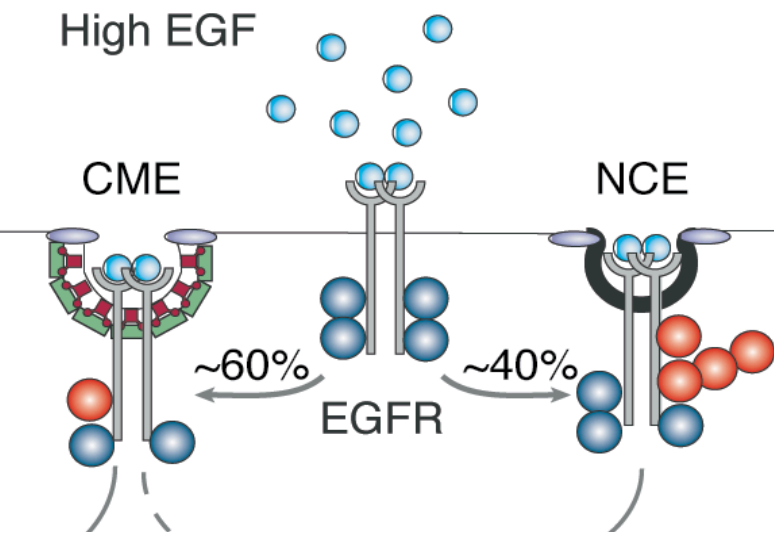
Dr. Dalla-Favera has provided key leadership to the cancer research community at Columbia University Medical Center, particularly in his roles as founding Director of the Institute for Cancer Genetics, and from 2005-2011, as Director of the Herbert Irving Comprehensive Cancer Center.

As a researcher, he has contributed much of the current knowledge on the genetic lesions responsible for human B cell lymphoma.

The molecular lesions identified by Dr. Dalla-Favera have led to the development of diagnostic tests and are being tested as targets in clinical trials with lymphoma patients. His work is widely quoted in scientific publications and in medicine and oncology textbooks.

Dr. Dalla-Favera has been recognized with several national awards, including the 2006 William Dameshek Prize for Outstanding Contribution to

Hematology from The American Society of Hematology. In 2011 he was elected to the Institute of Medicine of the National Academy of Sciences, USA, and in 2012, received the National Cancer Institute's Alfred Knudson Award



Endocytosis-setting the course with Ubiquitin

Commentary on Pier Paolo Di Fiore's paper published on *The Embo Journal*

by Ivan Dikic

My first encounter with Pier Paolo di Fiore dates back to 2002. It was a memorable dinner at the FEBS meeting in Istanbul that sparked the start of an interesting and productive collaboration. Our conversation revolved around the question why and how ubiquitination regulates internalization and trafficking (=endocytosis) of active growth factor receptors. We shared the same scientific enthusiasm and engaged in quite stimulating discussions that were continued during the visit to the blue mosque (and admittedly hampered our capacity to appreciate its cultural beauty). In the following year our labs reported a common work showing that epidermal growth factor receptors (EGFRs) are multiply monoubiquitinated and that this modification determines the kinetics and fidelity of the endocytic process.

What is endocytosis and what makes us so enthusiastic about it? In simple words endocytosis is a logistics process committed to the transport of plasmamembrane proteins and different types

of extracellular molecules to the inside of the cell followed by the shuttling to their intracellular destinations. This process is often *ligand-induced*, i.e. happens only when a ligand interacts with its cognate cell surface receptor. This type of internalization is observed for signalling receptors (e.g. the receptors for hormones, growth factors or cytokines) that trigger an intracellular signalling cascade upon binding to an extracellular ligand ultimately leading to a certain cellular response.

Internalization of these activated receptors serves primarily to extinguish the signal by removing the signalling receptor through lysosomal degradation. This is crucial to avoid overstimulation of the cell that would cause serious problems such as malignant transformation. An important signal that drives lysosomal targeting of the plasma-membrane receptors is provided by ubiquitin, a small molecule that is attached to the activated receptors. Those receptors that escape ubiquitination are recycled back to the

plasmamembrane and can be activated again.

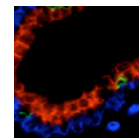
A seminal theme - and here the excitement starts - is the unexpectedly tight connection between endocytosis and signalling: It is thought that the receptor, being associated with its ligand and thus active, continues to emit signals inside the cells until it reaches the lysosomes. These signals are distinct from those emitted from the cell surface and have thus distinct outcomes. Importantly, there are different routes that the ligand-activated receptor can take to enter and travel inside the cell and it became clear that the very early decision which way to go will impact on receptor signalling.

For a very long time our understanding of these internalization routes was very simplistic. Yet, by combining computational modelling, experimental work and a very original, unbiased view Paolo has challenged and significantly expanded the canonical knowledge. In his pioneering work on the endocytic adaptor Eps15 he shed light on the molecular mechanism that governs the Ub-dependent transport of activated receptors towards the lysosome. He was also the first one to question the ingrained notion that the Clathrin-dependent entry route required ubiquitination of the activated EGFR. Instead, he proposed that ubiquitination provided a short-cut signal to destruction via a Clathrin-independent pathway.

Threshold-controlled ubiquitination of the EGFR directs receptor fate

How the cell converts graded signals into threshold-activated responses is a question of great biological relevance. Here, we uncover a nonlinear modality of epidermal growth factor receptor (EGFR)-activated signal transduction, by demonstrating that the ubiquitination of the EGFR at the PM is threshold controlled. The ubiquitination threshold is mechanistically determined by the cooperative recruitment of the E3 ligase Cbl, in complex with Grb2, to the EGFR. This, in turn, is dependent on the simultaneous presence of two phosphotyrosines, pY1045 and either one of pY1068 or pY1086, on the same EGFR moiety. The dose-response curve of EGFR ubiquitination correlate precisely with the non-clathrin endocytosis (NCE) mode of EGFR internalization. Finally, EGFR-NCE mechanistically depends on EGFR ubiquitination, as the two events can be simultaneously re-engineered on a phosphorylation/ubiquitination-incompetent EGFR backbone. Since NCE controls the degradation of the EGFR, our findings have implications for how the cell responds to increasing levels of EGFR signalling, by varying the balance of receptor signalling and degradation/attenuation. [PMID 23799367]

Cellular Logistics in Cancer
Pier Paolo Di Fiore



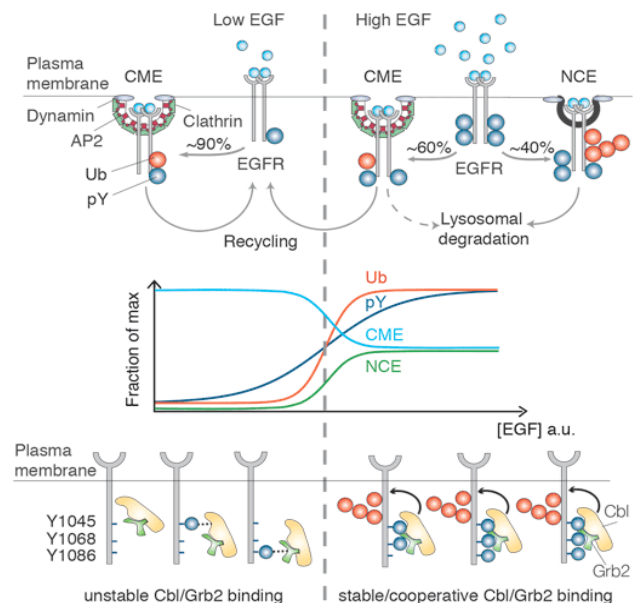
Endocytosis-setting the course with Ubiquitin
by Ivan Dikic

In Paolo's recent paper (EMBO J, 2013) his team has described the mechanism that creates a switch-like degradation signal from a graded signal, i.e. explains how a cell that is exposed to variable concentrations of extracellular ligand ensures a sharp response (ON/OFF) to the signal.

Phosphorylation-dependent ubiquitination of the EGFR constitutes the heart of this process. Only if the concentration of EGF is sufficient to ensure phosphorylation of two specific sites within one receptor molecule, i.e. the threshold concentration is reached, the Ub ligase Cbl can be recruited to ubiquitinate the receptor, the ultimate signal that drives rapid lysosomal degradation. Receptors that do not fulfil the criterion are directed to a clathrin-mediated entry portal and remain much longer in a signalling-competent mode.

This and previous discoveries of Paolo's group have important biological implications as endocytosis and signalling are inseparable processes. It has become clear that alterations in the endocytic program are indeed implicated in diseases that include cancer, infectious diseases, immune system disorders and neurodegenerative diseases. Paolo's work has set the stage for manipulating the endocytic process to obtain a desired outcome. On the way there, a number of exciting unresolved issues await their solution: For example, how the ubiquitinated receptor is coupled to the non-clathrin mediated endocytic pathway and whether threshold-controlled ubiquitination functions as a switch for other signalling molecules as well.

Figure: Top, pathways of EGFR internalization at low and high EGF concentration (CME, clathrin-mediated endocytosis, NCE, non-clathrin endocytosis). Middle, schematic representation of EGFR ubiquitination (Ub), phosphorylation (pY) and endocytic routes, as a function of ligand concentration. Bottom, cooperativity mechanism responsible for the EGFR-Ub threshold. Three phosphotyrosines (pYs) are critical for the cooperative recruitment of Cbl to active EGFR: pY1045 binds directly to Cbl, pY1068/pY1086 bind indirectly to Cbl:Grb2 complex.



Endocytosis –setting the course with Ubiquitin

The authors:

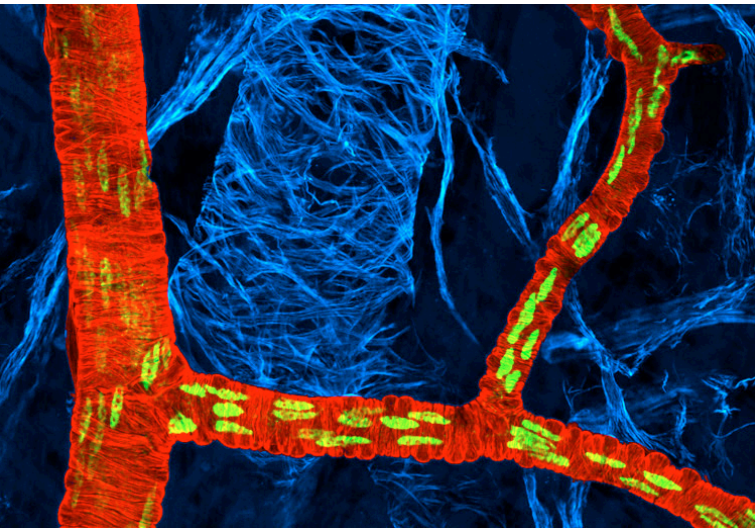


Ivan Dikic

Ivan Dikic grew up in Croatia, where he trained as a medical doctor. He obtained his PhD in molecular biology from the University of Zagreb and New York University Medical Center. He is currently a Professor at Goethe University Medical School and Founding Director of the Buchmann Institute for Molecular Life Sciences in Frankfurt, Germany. His research focuses on the role of ubiquitin (Ub), a small protein that is covalently attached to thousands of cellular proteins.

His pioneering work explained how Ub acts as a multivalent cellular signal that is recognized by an expanding number of Ub-binding proteins, which in turn translate this molecular signal into appropriate cellular phenotypes. His group demonstrated the importance of Ubiquitin in the regulation of DNA repair, inflammation, cancer, infection, receptor endocytosis, and proteasomal degradation. Most recently, they revealed mechanisms by which linear ubiquitination can regulate the

NF- κ B pathway making a decision between cell survival and death pathways and how selective autophagy pathways remove specific cargoes to the lysosome for degradation. His recent recognitions and awards include the AACR Award for Outstanding Achievement in Cancer Research in 2006, the Hans Krebs Prize 2010, the Leibniz Award (2013) and Ernst Jung Award in Medicine 2013 as well election in the German Academy Leopoldina (2010).



Arterial fate decision revised: Sox17 links Wnt/ β -catenin and Notch signaling

Commentary on Elisabetta Dejana's paper published on *Nature Communications*

by Stefan Liebner

The blood vascular system of higher vertebrates is crucial for the nourishment of organs throughout the organism, as well as for the removal and excretion of metabolic waste products. With the heart as the central pumping organ, the circulation is divided in a high-pressure arterial system that, with exception of the lung circulation, carries the oxygenized blood, and a low-pressure venous system that returns the deoxygenated blood back to the heart. Between arteries and veins a highly organ-specific network of capillaries mediate the exchange between blood and interstitial compartment. Due to their function as high- and low-pressure “tubing”, arteries and veins differ considerably in their morphology and in their molecular signature. For example smooth muscle cells (SMCs) are mainly attached to arteries, supporting the endothelium as the innermost layer of blood vessels to resist pressure and to modulate vessel diameter.

Veins instead develop valves, which reinsure unidirectional blood flow in absence of sufficient pressure as a driving force. Because of the apparent coupling of blood pressure to vessel

morphology, physical parameters were considered to induce the vascular differentiation into arteries and veins via flow-/pressure-sensing pathways. In the present article in *Nature Communications*, Corada and colleagues of the research group headed by Professor Elisabetta Dejana at IFOM report that arterial determination of endothelial cells is blood flow-/pressure-independent, providing novel insight in vascular signaling and differentiation. The group of Professor Dejana has been working at the cutting edge of vascular research with major contribution to the molecular dissection of endothelial junctional complexes and their role during developmental angiogenesis as well as in health and disease.

Particularly, *Corada et al.* could show that the HMG-box transcription factor Sox17 determines arterial fate by directly regulating Notch4 and delta-like 1 in endothelial cells. The Notch pathway has been shown to be crucial for the regulation of angiogenic processes, influencing the “sensitivity” of endothelial cells for the growth factor VEGF in their environment and contributing to vascular maturation. In a previous publication Professor

science

Dejana's group has shown that the Wnt/ β -catenin pathway can directly regulate the Notch ligand delta-like 4 (Dll4). Interestingly, in the present publication the authors show that Sox17 acts downstream of the Wnt/ β -catenin pathway and in turn activates Notch/Dll signaling. Apparently, this neat, consecutive interaction of different pathways is independent of blood flow, as the first arterial markers (such as ephrinB2 etc.) are detectable even before blood circulation starts during embryogenesis in the mouse. This novel finding establishes the transcriptional regulator Sox17 as a crucial link in the chain of signaling events leading to arterial differentiation.

A major strength of this work is the smart combination of *in vivo* and *in vitro* experiments to decipher the molecular crosstalk of Wnt/ β -catenin, Sox17 and Notch/Dll signaling pathway. These exciting findings also raise a number of further questions for example which are the upstream events initiating Wnt/ β -catenin signaling in a subset of endothelial cells and which other arterial genes are influenced by Sox17.

From a medical point of view, these findings will be critical for the further understanding and eventually therapy of deleterious arteriovenous malformations, which may lead to spontaneous bleeding often in the brain -hemorrhagic stroke- of affected patients.

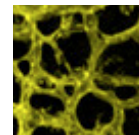
Sox17 is indispensable for acquisition and maintenance of arterial identity.

The functional diversity of the arterial and venous endothelia is regulated through a complex system of signalling pathways and downstream transcription factors. Here we report that the transcription factor Sox17, which is known as a regulator of endoderm and hemopoietic differentiation, is selectively expressed in arteries, and not in veins, in the mouse embryo and in mouse postnatal retina and adult. Endothelial cell-specific inactivation of Sox17 in the mouse embryo is accompanied by a lack of arterial differentiation and vascular remodelling that results in embryo death in utero. In mouse postnatal retina, abrogation of Sox17 expression in endothelial cells leads to strong vascular hypersprouting, loss of arterial identity and large arteriovenous malformations. Mechanistically, Sox17 acts upstream of the Notch system and downstream of the canonical Wnt system. These data introduce Sox17 as a component of the complex signalling network that orchestrates arterial/venous specification.
[PMID 24153254]

Conflict-of-interest disclosure:

The author declares no competing financial interests.

New strategies to inhibit tumor angiogenesis
Elisabetta Dejana



Arterial fate decision revised: Sox17 links
Wnt/ β -catenin and Notch signaling

The author:



Stefan Liebner

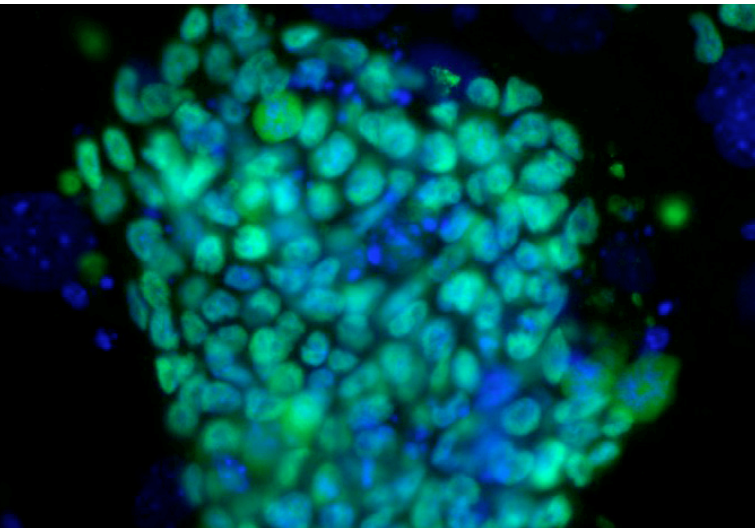
Blood-Brain Barrier Signaling Group, Edinger Institute Goethe University Clinic Frankfurt

Subsequent to his PhD at the Institute of Pathology in Tübingen, Germany, Dr. Liebner carried out postdoctoral training at IFOM with Prof. Elisabetta Dejana. During his research in the group of Prof. Dejana he started his ongoing interest in the Wnt/ β -catenin pathway. When Dr. Liebner moved as a group leader to the Edinger Institute Frankfurt, Germany in 2005, he expanded his research to study signaling pathways, such as Wnt/ β -catenin, in the differentiation of barrier

properties of endothelial cells in the central nervous system, specifically the blood-brain barrier (BBB).

Dr. Liebner continued these themes to understand BBB malfunction under pathological conditions, such as in brain tumors and Alzheimer's disease. Dr. Liebner has been invited as Keynote speaker to the biannual Cerebral Vascular Biology Meeting in 2013 and has contributed to the organization of scientific

conferences including the "2014 Cold Spring Harbor Laboratory Meeting on Blood Brain Barrier". He has published in prestigious international journals and has obtained funding from major national and international agencies.



Cell Reprogramming Requires Silencing of a Core Subset of Polycomb Targets

Commentary on Stefano Casola's paper published on *PLoS genetics*

by Gustavo Mostoslavsky

The beginning of the 21st century will most likely be remembered in biomedical history as the time when stem cells took center stage, thanks to the incredible discovery of induced pluripotency. Immediately after the now seminal 2006 report of Yamanaka *et al.*, scientists around the world started asking how a somatic cell could change its identity in such a dramatic fashion. It was suspected - in part thanks to the “rediscovered” Waddington's epigenetic landscape - that chromatin modifiers may be mechanistically involved in reprogramming. In recent years, several histone posttranslational modifications including methylation, acetylation, phosphorylation and others have all been implicated in gene regulation, and whether or not any of them participate in the process of induced pluripotency has become a topic of intense research.

In this regard the manuscript by Stefano Casola and Giuseppe Testa's labs represents a key advance in our understanding of how chromatin

remodeling regulates reprogramming. Before their studies came to light it was generally accepted that a wave of dimethylation of lysine-4 of histone H3 (H3K4me2) was established at enhancers and promoters of genes important for pluripotency preceding reprogramming, but that chromatin state differed in established induced pluripotent stem cells (iPSC) which showed Polycomb-mediated trimethylation of lysine 27 of histone 3 (H3K27me3) (Boyer *et al.*, 2006; Maherali *et al.*, 2007; Mansour *et al.*, 2012; Onder *et al.*, 2012).

Hence, a major role was attributed to the gene silencing activity of the PRC2 complex (mainly mediated by Ezh2) in establishing this H3K27me3 signature, which became the chromatin hallmark of iPSC. The elegant studies by the Casola and Testa's labs utilizing conditional Ezh2 knock-out cells, revealed that in actuality, Ezh2 and global H3K27me3 were dispensable for reprogramming to occur, except for a highly specific H3K27me3 mark on a defined core of Polycomb targets that ultimately enables nuclear reprogramming. More

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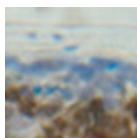
surprisingly, they showed for the first time that this gene repression mark was achieved through an alternative PRC2, most likely Ezh1, providing the first functional validation of the role of PRC2 in the establishment of pluripotency. This was further confirmed by their findings that downregulation of EED, an essential component of PRC2 significantly reduced H3K27me3 and prevented reprogramming.

The concepts illuminated by Stefano and Giuseppe's manuscript provide the basis for and in some cases explained several recent articles (Gafni *et al.*, 2013; Malouf *et al.*, 2013; Tiwari *et al.*, 2013; Ding *et al.*, 2014), confirming the significance and importance of their original findings. Indeed, the fact that H3K27me3 marks are retained in specific hotspots and that is mediated independently of Ezh2, opens new exciting opportunities to advance our understanding of the basic processes of reprogramming and provides novel targets for the manipulation of cell fate. I have been lucky to know Stefano and Giuseppe for many years and I am proud to have played a small part in this seminal paper.

Cell reprogramming requires silencing of a core subset of polycomb targets.

Transcription factor (TF)-induced reprogramming of somatic cells into induced pluripotent stem cells (iPSC) is associated with genome-wide changes in chromatin modifications. Polycomb-mediated histone H3 lysine-27 trimethylation (H3K27me3) has been proposed as a defining mark that distinguishes the somatic from the iPSC epigenome. Here, we dissected the functional role of H3K27me3 in TF-induced reprogramming through the inactivation of the H3K27 methylase EZH2 at the onset of reprogramming. Our results demonstrate that surprisingly the establishment of functional iPSC proceeds despite global loss of H3K27me3. iPSC lacking EZH2 efficiently silenced the somatic transcriptome and differentiated into tissues derived from the three germ layers. Remarkably, the genome-wide analysis of H3K27me3 in Ezh2 mutant iPSC cells revealed the retention of this mark on a highly selected group of Polycomb targets enriched for developmental regulators controlling the expression of lineage specific genes. Erasure of H3K27me3 from these targets led to a striking impairment in TF-induced reprogramming. These results indicate that PRC2-mediated H3K27 trimethylation is required on a highly selective core of Polycomb targets whose repression enables TF-dependent cell reprogramming.
[PMID 23468641]

Figure (page 21): iPS reprogrammed cells



Genetics of B Cells and Lymphomas
Stefano Casola

Cell Reprogramming Requires Silencing
of a Core Subset of Polycomb Targets
by Gustavo Mostoslavsky

Cell Reprogramming Requires Silencing of a Core Subset of Polycomb Targets

The author:



Gustavo Mostoslavsky

After receiving his MD from the National University of Tucuman in Argentina, he moved to Israel to pursue a PhD degree at the Hebrew University of Jerusalem. During that time he specialized in Cellular and Molecular Immunology, and specifically in mechanisms of tissue injury mediated by autoantibodies in SLE.

In 2001, he moved to Boston to start a postdoctoral fellowship in gene therapy and stem cells, at Harvard University, where he developed and published several studies focused on the use of hematopoietic stem cells and their genetic modification for transplantation studies. In 2008 he received a faculty position at the School of Medicine of Boston University (BUSM) and in addition

to continue working with HSC and gene transfer, his laboratory has devoted significant efforts to the development of a methodology for the generation of clinically relevant induced Pluripotent Stem Cells (iPSCs) and their use for human disease modeling. Based on his previous expertise on the use of lentiviral vectors and the manipulation of stem cell populations, Mostoslavsky and his team designed several forms of a single, excisable lentiviral vector that are able to induce nuclear reprogramming of mouse and human cells with the highest efficiency published to date. These efforts resulted in the publication of several manuscripts (Sommer *et al.*, 2009; Sommer *et al.*, 2010; Somers *et al.*, 2010; Christodoulou *et al.*, 2011).

These vectors have been freely distributed for use in more than 500 laboratories across the world and the method has become the industry standard for reprogramming. In addition, he has launched and co-direct the Boston University Center for Regenerative Medicine (CRoM), featuring six research programs across Boston University and Boston Medical Center. Project areas in the lab focuses on the use of different stem cell populations, including embryonic stem cells, induced Pluripotent Stem (iPS) cells, hematopoietic stem cells and intestinal stem cells for disease modeling and discovery of novel therapies, as well as their genetic manipulation by lentiviral vectors.

by Miguel Torres Sánchez

The homeodomain was named after its discovery in genes belonging to the *Drosophila bithorax* and *antennapedia* gene complexes, whose mutations lead to so-called homeotic transformations.

There are two TALE subfamilies playing this role in vertebrates, the Pbx subfamily with 4 genes and the Meis/Prep with 3 Meis and 2 Prep genes (discovered by Francesco Blasi in 1988). Further analyses led to the identification of additional roles for Pbx and Meis/Prep TFs as cofactors of several other families of tissue-specific TFs. Not surprisingly, genetic alterations in members of the TALE-Hox network correlate both with congenital and acquired diseases such as cancer. Given their ability to regulate the activity of sets of TFs that control specific pathways, the TALE TFs occupy

a very high position in the genome regulatory hierarchy and can be regarded as super-regulators of the genome transcriptional specificity.

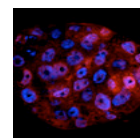
Most of the knowledge accumulated on the role of Meis-Prep and Pbx biochemical interactions had been addressed *in vitro* and was derived from the analysis of a few specific cases of gene regulation. The picture emerging for these previous studies mostly suggested similar DNA binding specificity and redundant roles in interactions with Hox proteins/genes for Meis and Prep factors; however, this view was in conflict with the mutant phenotypes found respectively by Blasi in *Prep1* mutants and by my own laboratory in *Meis1* mutants.

The situation required at this point a comprehensive and unbiased study of the *in vivo* specificity of TALE factors, something that could only be achieved through the coordination of several laboratories interested in this area. It was the initiative of Francesco Blasi that made this possible; we had recently obtained a COST grant for the coordination of research efforts across Europe towards the understanding of TALE homeodomain protein function, when I received a phone call from Francesco proposing a coordinated effort to achieve this important goal. He did not need much insistence to convince me of embarking on this project and we rapidly put together efforts from laboratories in Italy, Spain, Germany and Russia that had in hands the reagents and expertise required for this ambitious project. Main actors of this effort were Dmitry

Analysis of the DNA-binding profile and function of TALE homeoproteins reveals their specialization and specific interactions with Hox genes/proteins.

The interactions of Meis, Prep, and Pbx1 TALE homeoproteins with Hox proteins are essential for development and disease. Although Meis and Prep behave similarly in vitro, their in vivo activities remain largely unexplored. We show that Prep and Meis interact with largely independent sets of genomic sites and select different DNA-binding sequences, Prep associating mostly with promoters and housekeeping genes and Meis with promoter-remote regions and developmental genes. Hox target sequences associate strongly with Meis but not with Prep binding sites, while Pbx1 cooperates with both Prep and Meis. Accordingly, Meis1 shows strong genetic interaction with Pbx1 but not with Prep1. Meis1 and Prep1 nonetheless coregulate a subset of genes, predominantly through opposing effects. Notably, the TALE homeoprotein binding profile subdivides Hox clusters into two domains differentially regulated by Meis1 and Prep1. During evolution, Meis and Prep thus specialized their interactions but maintained significant regulatory coordination. [PMID 23602564]

*Transcriptional Regulation
in Development and Cancer
Francesco Blasi*



TALE homeodomain transcription factors:
super-regulators of the genome transcriptional specificity
By Miguel Torres Sánchez

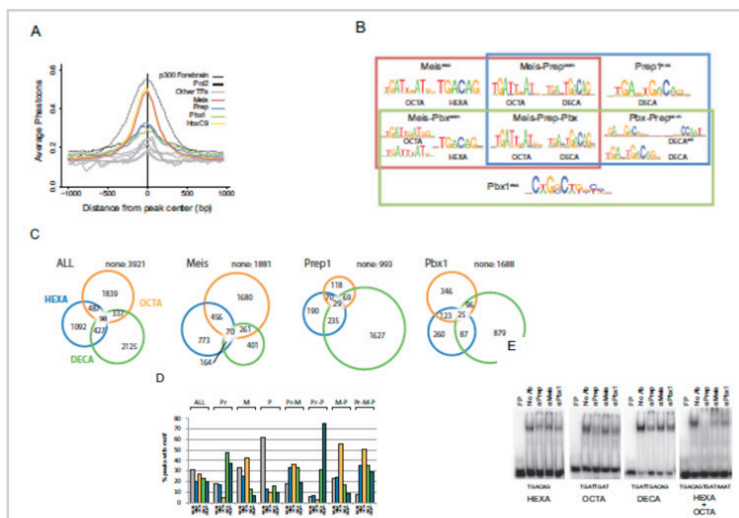
Penkov from the University of Moscow, a former Blasi lab postdoc and specialist in protein-DNA interactions, and Daniel Mateos San Martín, a PhD student in my lab with a special talent for bioinformatics.

Together we could generate ChIP-seq data addressing the DNA binding landscape of a majority of Meis-Prep and Pbx TFs. Importantly this was achieved *in vivo* and targeting the endogenous native proteins. The studies were complemented with phenotypic and transcriptional analyses of several single-factor mutant and compound mutant mice. The informatics analysis of the huge amount of data generated indicated a very different picture from previous conceptions in the field; Meis and Prep factors, not only were not redundant but they showed complementary DNA-binding patterns, different DNA sequence preference and, most importantly, different cofactor-binding preferences.

Not surprisingly, Meis/Prep compound mutants displayed no cooperative interactions in any organ/tissue studied. The differences identified affected especially the ability of Meis/Prep to interact with Hox proteins; Meis was the preferred DNA binding partner for Hox proteins and, surprisingly, the nearly exclusive factor binding on Hox clusters for Hox gene regulation. The structural analysis of the binding profiles

was not less surprising; while Prep was revealed as promoter-binding transcription factor, Meis bound with a strong preference to promoter-remote regions. Finally, the type of genes bound by each factor revealed that Prep bound mostly genes acting on basic cellular functions, while Meis preferentially bound developmentally regulated genes.

A recent example of the application of the knowledge generated in this work derives from the observation that a significant set of genes co-regulated by Meis and Prep displayed antagonistic regulation by these factors. Based on these observations the group of Francesco Blasi has recently described in PNAS the antagonistic activity of *Meis1* and *Prep1* in tumor formation. This study has thus modified the way we understand the regulatory interactions within a family of TFs essential for animal development and adult tissue homeostasis. Thanks to the vision of Francesco Blasi and a fruitful collaborative effort, the knowledge generated in this work is paving the way to new discoveries and will likely have a long-standing impact in several fields of research.



TALE homeodomain transcription factors:
super-regulators of the genome transcriptional specificity
By Miguel Torres Sánchez

TALE homeodomain transcription factors:
super-regulators of the genome transcriptional specificity

The author:



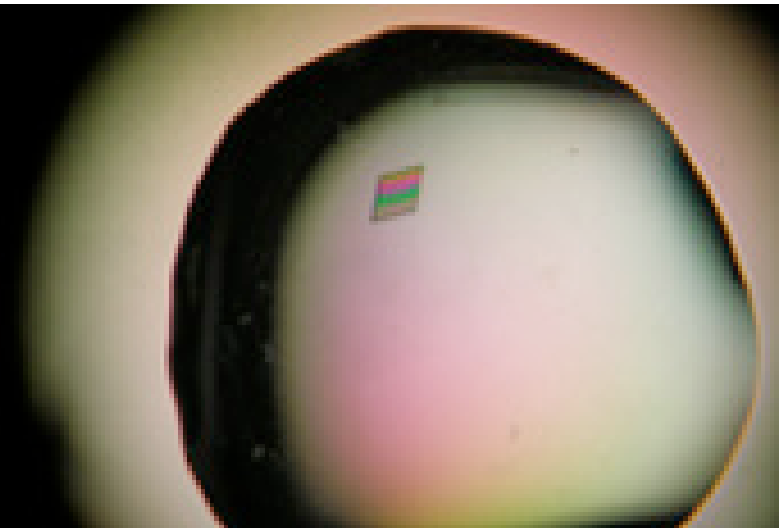
Miguel Torres Sánchez

*Director of the Department of Cardiovascular Development and Repair
at Centro Nacional de Investigaciones Cardiovasculares, CNIC*

Miguel Torres graduated in Biology (1986, Complutense University of Madrid) and obtained his PhD in Biochemistry and Molecular Biology (1991, Autonomous University of Madrid) for his studies on *Drosophila* developmental Genetics. During his postdoctoral stay with Peter Gruss at the Max Planck Institute for Biophysical Chemistry (1992-96, Göttingen,

Germany), he contributed to elucidating the function of Pax transcription factors in mammals and established a Program of insertional mutagenesis in Embryonic Stem Cells. After being appointed as CSIC Research Scientist at the Spanish National Center for Biotechnology, CNB (1996-2006, Madrid), he built an internationally recognized team specialized in the study of

transcription factors in vertebrate embryonic development. His studies on the role and regulation of the TALE transcription factors have led to new models of limb patterning and vascular development. His recent studies in Cell Competition have led to the first identification of endogenous Cell Competition in Vertebrates.



Illuminating a ubiquitin transfer relay, step-by-step

Commentary on Simona Polo's paper published on *Nature Structural & Molecular Biology*

by Brenda A. Schulman

A key way that protein activities are controlled in a spatiotemporal manner is by post-translational modification, such as by covalent ligation of the small protein ubiquitin. In some cases, a single monoubiquitin is attached. Alternatively, repeated rounds of ubiquitin ligation can form polyubiquitin chains with multiple ubiquitin molecules attached to each other. Chains can form on several different sites of ubiquitin.

Initially, polyubiquitin chains were mainly known for mediating interactions with the proteasome and directing degradation of the modified protein. However, it is now known that chains linked via lysine 63 on ubiquitin ("K63-linked chains") regulate diverse functions such as protein trafficking, DNA repair, and immune signaling. Likewise, monoubiquitin can bestow its targets with a wide-range of alternative fates. Therefore, a major question for understanding protein regulation is: how are specific ubiquitin modifications directed to their particular protein substrates? Simona Polo at IFOM and I came to

work on this question from different directions. I have long been interested in the biochemical and structural basis by which ubiquitin becomes attached to targets to regulate function. For over a dozen years, Simona Polo has been a leader in understanding numerous facets of ubiquitin signaling, although her path started with a quest to decipher regulation of and by the epidermal growth receptor. In seminal work performed initially with Pier Paolo Di Fiore, and then later in her own lab, Simona found that Kay Hofmann's predicted ubiquitin interacting motif (UIM) sequence in epsin family endocytic regulators both binds monoubiquitin, and is also responsible for Eps15 monoubiquitination. Simona's lab discovered a novel mechanism termed "coupled monoubiquitination", where Eps15 uses its UIM to bind ubiquitin on an E3 enzyme NEDD4. The burning follow-up problem was to understand how NEDD4 transfers ubiquitin.

NEDD4 belongs to the family of E3 enzymes known as HECT. NEDD4 and other HECT E3s

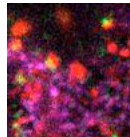
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function as part of multi-enzyme ubiquitin transfer cascades through a two-step mechanism. First, ubiquitin is transferred from the catalytic cysteine of an E2 enzyme to that on the E3 HECT domain.

This produces a transient HECT~ubiquitin intermediate that is linked by a thioester bond. Next, ubiquitin is transferred from the HECT E3 cysteine to either a substrate protein, or to a specific lysine on the surface of ubiquitin to generate a chain. This process is often likened to a relay, where ubiquitin is the baton transferred between athletes (e.g. E2, E3, substrate, and eventually ubiquitin linked to substrate). We had previously determined the structure transfer of ubiquitin from E2 to the HECT domain and subsequently of a downstream intermediate, and Simona's and Jon Huibregtse's labs had solved structures of other forms of HECT E3s bound to ubiquitin.

Structure of a ubiquitin-loaded HECT ligase reveals the molecular basis for catalytic priming.

Homologous to E6-AP C terminus (HECT) E3 ligases recognize and directly catalyze ligation of ubiquitin (Ub) to their substrates. Molecular details of this process remain unknown. We report the first structure, to our knowledge, of a Ub-loaded E3, the human neural precursor cell-expressed developmentally downregulated protein 4 (Nedd4). The HECT(Nedd4)~Ub transitory intermediate provides a structural basis for the proposed sequential addition mechanism. The donor Ub, transferred from the E2, is bound to the Nedd4 C lobe with its C-terminal tail locked in an extended conformation, primed for catalysis. We provide evidence that the Nedd4-family members are Lys63-specific enzymes whose catalysis is mediated by an essential C-terminal acidic residue.
[PMID: 23644597]



Ubiquitin and Signal Transduction
Simona Polo

However, several big questions remained. In particular, no one had ever been able to “see” the transient intermediate with ubiquitin linked at a HECT E3 catalytic cysteine, because such complexes are extremely unstable. Simona and her colleagues overcame this challenge with a very clever approach, by using an alternative, more stable bond to link the active site of the NEDD4 HECT E3 and ubiquitin.

Their study published in *Nature Structural and Molecular Biology* was a big breakthrough, and remains to date the only structure capturing an elusive HECT E3~ubiquitin intermediate, as if after ubiquitin transfer from E2!



Illuminating a ubiquitin transfer relay,
step-by-step
by Brenda A. Schulman

Their data beautifully shows a mechanism for how the E2-to-E3 relay goes forward even though the thioester bonds linking E2~ubiquitin and HECT E3~ubiquitin intermediates may be perceived as similar. In the context of the HECT E3~ubiquitin intermediate, there is a new beta sheet formed between NEDD4 and ubiquitin, which stabilizes the complex.

In terms of visualizing ubiquitin transfer cascades, our combined data suggest that NEDD4 functions as if in a children's relay. First NEDD4 faces E2 to receive ubiquitin. After ubiquitin transfer to the NEDD4 HECT domain, a new beta sheet stabilizes the intermediate. Then, the NEDD4 HECT E3 turns around to face the substrate.

The article from Simona's group also reports that all HECT E3s related to NEDD4 build K63-linked chains. These may mediate trafficking through membrane compartments, or regulate substrates through other proteasome-independent means.

The authors also found residues that when mutated completely eliminate K63 chain formation. This will serve as a very useful tool for numerous researchers trying to unravel myriad functions of HECT E3s in cells.

It also serves as tremendous motivation to understand how and why NEDD4 builds K63-linked ubiquitin chains.

On a personal note, Simona's enthusiasm is infectious, and it has been immensely inspiring for me to share data and discuss ideas with her along my own path.

Figure (page 28): X-ray crystallography



Illuminating a ubiquitin transfer relay,
step-by-step
by Brenda A. Schulman

Illuminating a ubiquitin transfer relay,
step-by-step

The author:



Brenda A. Schulman

Member, St. Jude Faculty; Investigator, Howard Hughes Medical Institute;

Co-Director, Cancer Genetics, Biochemistry & Cell Biology Program of the St. Jude Cancer Center

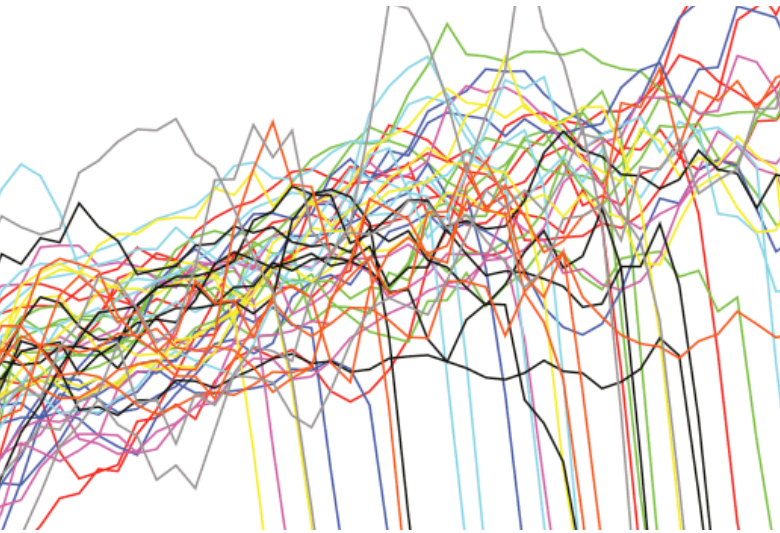
Brenda Schulman works on the mechanisms underlying protein modification by the family of ubiquitin-related proteins (UBLs). Post-translational covalent attachment of ubiquitin-like proteins (UBLs) is a predominant eukaryotic regulatory mechanism. More than a dozen UBLs - such as ubiquitin, NEDD8, ISG15, and SUMO - covalently modify myriad substrates.

Different UBLs alter the functions of their target proteins in different ways, such as by changing the target's half-life, conformation, subcellular localization, enzymatic

activity, and/or intermolecular interactions. Defects in UBL pathways have been associated with numerous diseases, including cancers, neurodegenerative disorders, and viral infections. Thus, determining mechanisms by which enzymes transfer UBLs will be of broad importance toward understanding signaling pathways and their roles in diseases. Educated at the Johns Hopkins University (BA 1989) and the Whitehead Institute/MIT (PhD 1996), Schulman held postdoctoral fellowships at MGH Cancer Center at Harvard Medical School and at

Memorial Sloan-Kettering Cancer Center. She joined the faculty of the St. Jude Children's Research Hospital in 2001.

She was elected to the National Academy of Sciences in 2013 and the American Academy of Arts and Sciences in 2012. She was joint recipient of the Dorothy Crowfoot Hodgkin Award from the Protein Society in 2011, and was honored by a Presidential Early Career Award for Scientists and Engineers in 2004, a Beckman Young Investigator Award in 2004, and a Pew Scholar in Biomedical Sciences Award in 2002.



Insights into the mechanics of adaptation to spindle assembly checkpoint

Commentary on Andrea Ciliberto's paper published on *eLife*

by Uttam Surana

Making two cells from one is a complex affair. This fundamental process of 'life in miniature' (cell division) requires a myriad of cellular processes and events that need to be coordinated and executed in a precise order. Such an overarching coordination is enforced by a class of cellular surveillance systems known as the checkpoint controls (or simply checkpoints). Checkpoints ensure that a later event is not initiated until a prior event is properly executed and completed. In the event of a malfunction, the checkpoint will impose a cell cycle arrest, preventing all subsequent events, thus allowing cells more time to complete the preceding event. There is a number of checkpoint controls operating during the cell division cycle, ensuring cells' smooth passage through various transitions. For example, DNA damage checkpoint is activated when cells incur chromosome damage; it arrests cells in G2 phase and subsequently 'allows' them to enter mitosis once the damage is repaired. Thus checkpoints play a critical role in the maintenance of genome integrity.

Like other checkpoint controls, Spindle Assembly Checkpoint (or SAC) is conserved from yeast to man and functions during mitosis (or M phase). It monitors the transition from metaphase to anaphase during which duplicated chromosomes are equally partitioned into the two daughter cells. During normal division, a number of things have to be in place before anaphase can be initiated: the master regulator kinase Cdk1 (a complex of catalytic subunit Cdk1 and the regulatory subunit cyclin) should be activated, all duplicated chromosomes have to be aligned at the metaphase plate (approximately the mid-region of the dividing cell) and the chromosomes have to be properly attached to the mitotic spindle via their kinetochores. Once these conditions are met, the cohesion between the duplicated chromosomes (due to a protein complex known as cohesins) is dissolved, an event mediated by a E3 ubiquitin ligase APC^{Cdc20} (Cdc20-activated Anaphase Promoting Complex), followed by progressive segregation of one set of chromosomes into each daughter cell by the mitotic spindle.

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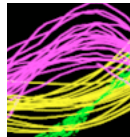
There is a functional link between APC^{Cdc20} and Cdk1 in that Cdk1 activates APC^{Cdc20} by phosphorylation in mitosis.

Central to this intricate orchestration is the attachment of duplicated chromosomes to the mitotic spindle via their kinetochores. This is the event that is monitored critically by the SAC such that a single unattached kinetochore can activate the SAC resulting in the inhibition of APC^{CDC20} and consequently, of chromosome segregation. SAC signalling that mediates inactivation of APC^{CDC20} and imposes a cell cycle arrest involves highly conserved Mad1, Mad2, Mad3, MPS1, Bub1, Bub3 and Ipl1 proteins (yeast nomenclature). During this transient arrest if all kinetochores are eventually captured by the spindle, SAC is turned off, APC^{CDC20} is activated again and cells proceed to anaphase. The presence of a single unattached kinetochore, however, keeps the SAC in the activated state and cell cycle arrest remains in place for an extended duration.

Adaptation to the spindle checkpoint is regulated by the interplay between Cdc28/Clbs and PP2A/Cdc55.

The spindle checkpoint arrests cells in metaphase until all chromosomes are properly attached to the chromosome segregation machinery. Thereafter, the anaphase promoting complex (APC/C) is activated and chromosome segregation can take place. Cells remain arrested in mitosis for hours in response to checkpoint activation, but not indefinitely. Eventually, they adapt to the checkpoint and proceed along the cell cycle. In yeast, adaptation requires the phosphorylation of APC/C. Here, we show that the protein phosphatase PP2A(Cdc55) dephosphorylates APC/C, thereby counteracting the activity of the mitotic kinase Cdc28. We also observe that the key regulator of Cdc28, the mitotic cyclin Clb2, increases before cells adapt and is then abruptly degraded at adaptation. Adaptation is highly asynchronous and takes place over a range of several hours. Our data suggest the presence of a double negative loop between PP2A(Cdc55) and APC/C(Cdc20) (i.e., a positive feedback loop) that controls APC/C(Cdc20) activity. The circuit could guarantee sustained APC/C(Cdc20) activity after Clb2 starts to be degraded.

[PMID: 23999167]



Quantitative Biology of Cell Division
Andrea Ciliberto

However, there is a twist in this neat scheme. The SAC cannot impose cell cycle arrest indefinitely. After a prolonged period of arrest, cells adapt to the activated state of SAC (i.e. become desensitized) and resume cell cycle progression despite the presence of unoccupied kinetochores. The mechanism governing this cellular response, which is clearly detrimental to the chromosome stability, is not clear. The important paper (JCB, 202:765-778) from Andrea Ciliberto's laboratory provides an insight into the mechanism underpinning this atypical cellular behaviour.



Insights into the Mechanics of Adaptation
to Spindle Assembly Checkpoint
by Uttam Surana

This study fittingly uses yeast *Saccharomyces cerevisiae* as a model system to investigate the phenomenon of adaptation, since concepts of checkpoints and ‘adaptation’ were both first defined in yeast. Using non-phosphorylatable mutants of APC subunits Cdc16 and Cdc27, and mutants lacking its activator Cdc20, Andrea and colleagues first established that adaptation to SAC requires both Cdc20 and APC phosphorylation. In these experiments Adaptation was measured in terms of a decline in the levels of the mitotic cyclin Clb2 and chromosome-segregation inhibitor Pds1, and elongation of the mitotic spindle. Intriguingly, even though Clb2 levels decline during adaptation meaning that Cdk1 activity also declines, it was found that Cdk1 activity is in fact required for adaptation. Single cell analysis of cells undergoing adaptation revealed that before adaption, Clb2 concentration increases but it rapidly declines once adaptation ‘sets-in’. There are, then, two key issues: (i) Cdk1 activity is required for adaptation and yet it declines rapidly during adaptation, and (ii) why does it take a long period before a cell initiate adaptation.

The authors reasoned that if phosphorylation of APC subunits by Cdk1 is required for adaptation then there should be a phosphatase that opposes this phosphorylation to maintain the checkpoint. Since PP2A^{Cdc55} has been reported to be required for the maintenance of the SAC, it could be the phosphatase that opposes the ‘adaptive-action’ of Cdk1. The following key observations were consistent with this notion: (i) APC subunit Cdc16 underwent enhanced phosphorylation in the absence of PP2A^{Cdc55} (ii) in contrast to *cdc55Δ* deletion cells *cdc16-6A cdc27-5A cdc55Δ* triple mutant was arrested by the checkpoint and was severely defective in its ability to adapt. These data point to a scheme where Cdk1/Clb2 phosphorylates and PP2A^{Cdc55} dephosphorylates Cdc16.

These opposing activities are what possibly determine whether a cell arrests or adapts. Since it takes some time before phosphorylation overtakes dephosphorylation by PP2A^{Cdc55}, it explains why it requires a long period for cells to

adapt to the SAC-induced arrest. Based on these central observations, Andrea and colleagues propose a dynamic model for metaphase to anaphase transition in the context of checkpoint-efficacy. According to this model, checkpoint arrest by SAC is imposed, aided by continuous dephosphorylation of APC (inactive) by PP2A^{Cdc55}. However, Clb2 continue to accumulate in the nucleus during the arrest and increasing Cdk1/Clb2 continues to phosphorylate the APC, progressively opposing the action of PP2A^{Cdc55}. At some point, the balance is tipped in the favour of net phosphorylation of APC^{Cdc20}, the process of adaptation takes hold and the levels of both Clb2 and Pds1 rapidly decline. Thus, ‘arrest/adaptation’ is proposed as a two state system in which the shifting balance between the inter-linked positive and negative control loops ultimately determines the system’s state in a given time frame.

From a teleological perspective then, the spindle assembly checkpoint control has a built-in ‘escape-route’ from a potentially unproductive prolonged arrest, allowing cells to continue with the next division cycle (even though at the cost of some degree of genetic instability) than to permanently remain arrested in metaphase and lose viability. Hence, this study by Andrea and colleagues not only provides important insights into the mechanism underlying adaptation to the spindle assembly checkpoint but is also a demonstration of how interlocking control loops determine the dynamic behaviour of cells during progression through the cell division cycle.



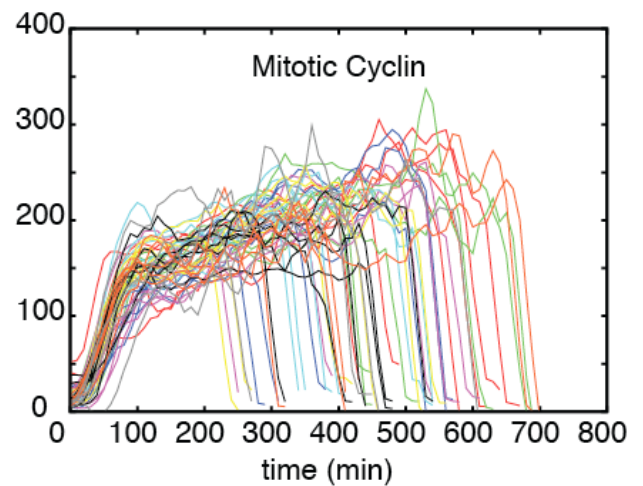


Figure: Single cell dynamics of mitotic cyclin in adapting yeast cells. When cyclin is degraded cells adapt. Each trace represents a different cell.

Insights into the Mechanics of Adaptation to Spindle Assembly Checkpoint

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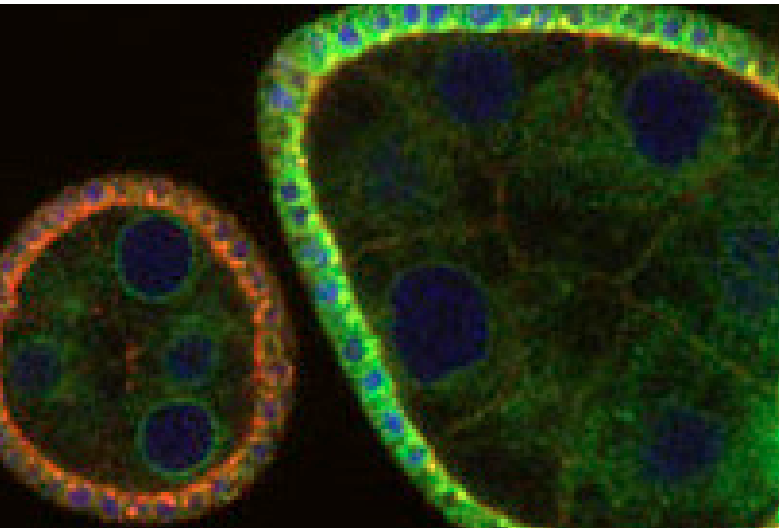


Uttam Surana

Uttam Surana undertook his graduate studies at the University of Arizona (USA) and obtained a PhD from the Dept. of Molecular and Cellular Biology. Thereafter, he moved to the Dept. of Engineering at the University of Cambridge where he spent 2 years studying the mechanical

properties of bacterial cell surface polymers and their role in cell shape determination. He spent the subsequent four years as a postdoctoral fellow at the Institute of Molecular Pathology (IMP) in Vienna, Austria investigating various aspects of cell division.

He then moved to Singapore and joined the IMCB as a Principal Investigator. For his contribution to the understanding of control circuits that regulate cell cycle, Prof Surana was awarded in 2007 Singapore's National Science Award.



Vacuolar ATPase control of signaling and tumorigenesis

Commentary on Thomas Vaccari's paper published on *Molecular oncology*

by Angelika M. Vollmar

The study of most signal transduction pathways have progressed immensely in the last years in terms of identification of ligands, receptors, transducers, and transcriptional outputs. Yet, current knowledge of signaling circuitries is still vague in terms of how the parts interact with the cell infrastructure devoted to produce, deliver and degrade them, namely the membrane compartment. A case in point of such lack of cell biological insight is that of Notch signaling. This signaling system is simple, consisting of a transmembrane receptor that doubles as transcription factor, when liberated from membrane by a rather generic protease.

The simplicity is only apparent considering that Notch signaling is used iteratively during organ development and homeostasis to instruct remarkably different cell fates such as survival, proliferation or differentiation, depending on the context. Part of context specificity is given by co-regulation with tissue-specific transcription

factors. However, another part is likely to emerge from the way the receptor is handled by the protein trafficking machinery of the cell. The elegant work of Kobia and colleagues of Dr. Vaccari's group at IFOM now shows that inhibition of a key cellular enzyme, the vacuolar- H^+ (V-) ATPase affects Notch signaling^[1].

V-ATPase is the main energized proton pump in the cell. Its function is pleiotropic and central to many cellular processes such as organelle acidification and lysosomal function^[2].

Despite more than 30 years of studies, V-ATPase has only recently implicated in regulation of major signaling pathways^[3,4]. In fact, the Vaccari lab had been one of the first groups who significantly contributed to this issue. Using *Drosophila* they showed that V-ATPase is required for activation of Notch signaling in the endo-lysosomal compartment^[5]. Their and recent work by other investigators is of utmost importance: it is bringing into focus a complex

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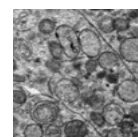
network of regulation centered around trafficking and regulation of Notch degradation by the endo-lysosomal system, a recognized nexus for signaling regulation. Given the multiple roles that V-ATPase serves in cells, a number of outstanding interesting questions remain open. How is the enzyme regulated? How does it affect Notch signaling mechanistically? As far as I can tell from my fruitful interactions with Dr. Vaccari, his group is perfectly poised and highly competent to answer those questions experimentally.

Equally interesting is the relevance of work of Kobia and colleagues to cancer. Owing to the countless uses of Notch in shaping tissues, Notch dysregulation is associated to multiple diseases. In particular, oncogenic Notch activation is a serious problem in T-cell acute lymphoblastic leukemia (T-ALL), and in certain breast and lung cancers. Kobia et al demonstrated that pharmacologic block of V-ATPase with highly-specific compounds affects Notch signaling also in cancer cells with oncogenic Notch activity. Interestingly, while proliferation was reduced by V-ATPase inhibition in all cancer cell lines tested, Notch signaling was reduced only in cell lines derived from breast cancer and not from T-ALL. Cells in which Notch signaling was not reduced tended to be those in which Akt signaling, another major tumor-associated growth pathway, is perturbed. In these, V-ATPase inhibition mimicked the effects of Akt inhibitors.

Pharmacologic inhibition of vacuolar H⁺ ATPase reduces physiologic and oncogenic Notch signaling.

Notch signaling is prominently involved in growth regulation in metazoan tissues. Because of this, Notch is often upregulated in cancer and current efforts point to developing drugs that block its activation. Notch receptor endocytosis towards acidic compartments is a recently appreciated determinant of signaling activation. Vacuolar H⁺ ATPase (V-ATPase) is responsible for acidification of endocytic organelles and mutants in V-ATPase subunit encoding genes in model organisms have been recently shown to display loss of Notch signaling. Here, we show that administration of BafilomycinA1 (BafA1), a highly specific V-ATPase inhibitor decreases Notch signaling during Drosophila and Zebrafish development, and in human cells in culture. In normal breast cells, we find that BafA1 treatment leads to accumulation of Notch in the endo-lysosomal system, and reduces its processing and signaling activity. In Notch-addicted breast cancer cells, BafA1 treatment reduces growth in cells expressing membrane tethered forms of Notch, while sparing cells expressing cytoplasmic forms. In contrast, we find that V-ATPase inhibition reduces growth of leukemia cells, without affecting Notch activatory cleavage. However, consistent with the emerging roles of V-ATPase in controlling multiple signaling pathways, in these cells Akt activation is reduced, as it is also the case in BafA1-treated breast cancer cells. Our data support V-ATPase inhibition as a novel therapeutic approach to counteract tumor growth via signaling pathways regulated at the endo-lysosomal level. [PMID 24309677]

Membrane Trafficking and Tissue Architecture
Thomas Vaccari



Vacuolar ATPase control
of signaling and tumorigenesis
by Angelika M. Vollmar

As a pharmacologist, I find inhibition of a pleiotropic enzyme a risky strategy to block oncogenes. It is indirect and one is bound to have plenty of side effects. This is why modern anticancer drugs are designed to be very specific. However, it is increasingly found that specific drugs induce resistance. Also, it is emerging that each tumor depends and is addicted to few signaling pathways acting redundantly. The work of Kobia et al and work of my group on V-ATPase regulation of HER2 signaling ^[6] suggest that one could in fact hit more than one bird with one stone, perhaps limiting the ability of the tumor to “mutate away” from inhibition of a single signaling pathway.

A final interesting aspect of the recent work of Dr. Vaccari's group is based on the fact that V-ATPase itself is found upregulated in a number of tumors. Despite previous work, whether upregulation is cause or consequence of tumorigenesis and how would V-ATPase would contribute to this is unresolved. In collaboration with a German group in Freiburg, the group of Thomas Vaccari has recently shown that overactivation of V-ATPase is sufficient for tissue transformation in *Drosophila* ^[7]. This, together with work of my group on V-ATPase and tumor cell migration ^[8], suggest that misregulation of V-ATPase might contribute to drive tissue transformation by altering multiple signaling pathways. Hopefully, we are going to learn much more of this in spring 2015 during the meeting “Vacuolar ATPase: A Novel Anti-Tumor Target” that I am co-organizing with Dr. Vaccari at IFOM.

Bibliography

1. Kobia F, Duchi S, Deflorian G and Vaccari T (2014) Pharmacologic Inhibition Of Vacuolar H⁺ ATPase Reduces Physiologic And Oncogenic Notch Signaling. *Molecular Oncology* 8: 207-220.
2. Nishi T and Forgacs M (2002) The vacuolar (H⁺)-ATPases--nature's most versatile proton pumps. *Nature Reviews Molecular Cell biology* 3: 94-103.
3. Cruciat CM, Ohkawara B, Acebron SP, Karaulanov E, Reinhard C, et al. (2010) Requirement of prorenin receptor and vacuolar H⁺-ATPase-mediated acidification for Wnt signaling. *Science* 327: 459-463.
4. Zoncu R, Bar-Peled L, Efeyan A, Wang S, Sancak Y, et al. (2011) mTORC1 senses lysosomal amino acids through an inside-out mechanism that requires the vacuolar H⁺-ATPase. *Science* 334: 678-683.
5. Vaccari T, Duchi S, Cortese K, Tacchetti C and Bilder D (2010) The vacuolar ATPase is required for physiological as well as pathological activation of the Notch receptor. *Development* 137: 1825-1832.
6. von Schwarzenberg K, Lajtos T, Simon L, Muller R, Vereb G, et al. (2014) V-ATPase inhibition overcomes trastuzumab resistance in breast cancer. *Molecular Oncology* 8: 9-19.
7. Petzoldt AG, Gleixner EM, Fumagalli A, Vaccari T and Simons M (2013) Elevated expression of the V-ATPase C subunit triggers JNK-dependent cell invasion and overgrowth in a *Drosophila* epithelium. *Disease Models & Mechanisms* 6: 689-700.
8. Wiedmann RM, von Schwarzenberg K, Palamidessi A, Schreiner L, Kubisch R, et al. (2012) The V-ATPase-inhibitor archazolid abrogates tumor metastasis via inhibition of endocytic activation of the Rho-GTPase Rac1. *Cancer Res* 72: 5976-5987

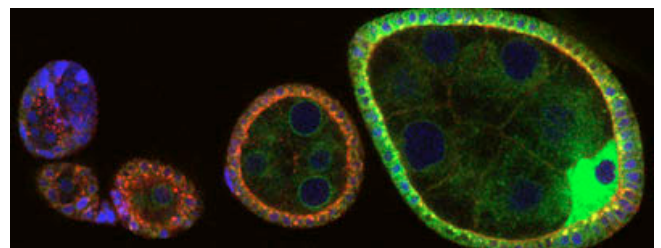


Figure: Confocal image is V-ATPase (V1 c; green), Notch (red) and DAPI (blue) in *Drosophila* egg chambers at progressive stages of development. Big cells in the center of each chamber constitute the germline, the surrounding tissue is the follicular epithelium, apical side facing the germline.



Vacuolar ATPase control of signaling and tumorigenesis

The author:



Angelika M. Vollmar

Director of the Department of Pharmacy-Center of Drug Research at the Ludwig-Maximilians-University of Munich, Germany

Angelika Vollmar was trained as a pharmacist and obtained her PhD in Pharmaceutical Biology from the Ludwig-Maximilians-University of Munich. With a fellowship from the German Research Foundation (DFG) she carried out a postdoctoral training with Dr. Harvey R. Herschmann at the Department of Biochemistry and Molecular Biology, UCLA, USA focusing on constructing "magic bullets" against cancer such as EGF-toxin conjugates. Back in Germany she expanded her scientific experiences moving to the School of Veterinary Medicine working on biogenic drugs such as natriuretic peptides and became Associate Professor for Clinical Pharmacology and Pharmacy. Receiving a Chair position and full Professorship at the Department of Pharmacy in Munich Dr. Vollmar

continued to promote natural product research as she is truly convinced that nature provides a fascinating pool of substances for drug development. The Vollmar Lab aims at deciphering the therapeutical potential of natural compounds focussing on cancer. In particular, natural compounds are characterized with respect to their effects on tumor metabolism, tumor growth and metastasis as well as tumor angiogenesis. As such Dr. Vollmar is speaker of the DFG-Research Group 1406 (<http://www.for1406.uni-muenchen.de/index.html>) concentrating on compounds of myxobacterial origin and their impact on cancer therapy. Dr. Vollmar is engaged in a number of scientific organisations: she has been member of the "Senate of the German Research

Foundation (DFG)", she is speaker of the Scientific Advisory Board of the "Robert-Bosch-Stiftung", member of the advisory board of the "Deutsche Krebshilfe" and of DECHEMA ("Small Molecule Natural Compounds with Biological Activity"). Among other awards she received the "Bundesverdienstkreuz- the order of merit of the federal republic of germany". Last but not least Dr. Vollmar shows a burning commitment in promoting the careers of young researchers being involved in a variety of mentoring programs.



Science journalism in a changing world

by Giovanni Caprara

The media is undergoing deep changes. How is it possible to communicate science well in this setting? What is the correct relationship between the researcher and the journalist today? Can the scientist perform the role of the journalist? In economic hard times, does the quality of scientific information suffer or does it improve? Several questions arise as the daily news media takes on a new dimension, a new existence, and is forced to assimilate technologies that deeply modify their work. At the basis of this transformation is the change in the measure and significance of time that affects radically any diffusion of the news.

The answer to the first question is that, thanks to the amplification of possibilities offered by new technologies, today science can be spread and reported better than in the past. But communication skills acquired by scientists are more sophisticated making the journalist's position more difficult: he/she can be overwhelmed by too much information and be influenced by the

personality of the scientist, without verifying the contents. The only way to balance the relationship is through higher knowledge on the part of the journalists, who must learn more about the topics they cover. They must do this, or risk being overwhelmed by their interviewees. In addition to more preparation, method itself needs to be strengthened and expanded. Verification, always valid and fundamental to establishing the quality of any kind of information, must be performed more rigorously, even as it becomes more difficult.

Information sources today have multiplied dramatically, thanks to the web, and it is often difficult to ascertain their level of reliability. This requires broader and more thorough verification, even though this conflicts with the need for faster diffusion of the news.

To better respond to such needs, journalists should seek opportunities to experience the professional life of scientist; not so much to "feel" more like a scientist (danger to be avoided) but

society

to get more in tune with the new area in which they operate. In addition to providing an update on practical aspects that can be integrated with theoretical considerations, this provides a more accurate perception of the speed with which the world of research is changing.

This was the aim of the initiative organized in 2013 by the UGIS (Italian Union of Science Journalists) at IFOM (FIRC Institute of Molecular Oncology). During this program, a selected group of UGIS (The Union of Italian Science Journalists) members and science journalism students from SISSA, the International School for Advanced Studies in Trieste, experienced a full week at IFOM where they followed an intensive experimental program. The aim was to update them on research methods used for cancer, a complex disease with a thousand faces and, for that reason, very difficult to understand. The participants praised the effectiveness of the experience offered by IFOM and tailored on their needs through interactive sessions with the researchers, in addition to laboratory activities. Experiencing life and research inside the Institute raised issues that would be difficult to understand from a simple visit, suggesting that similar initiatives in other scientific domains would be extremely useful.

There is no doubt that today science journalists require more preparation to properly perform their role. This is due, not only to the broader scope of the subject, but also to the use of new communication channels that allow different kinds of usage: online media requires a quicker language, while providing the possibility of links to further reading for those who need it; whereas, printed editions usually go directly into a deeper examination, integrating everything with the news headline. Moreover, any news of great scientific impact is now discussed in the popular online

channels and therefore must be addressed in all of its aspects.

The quality of scientific information in Italy may be adversely affected because online editors are still not organized to ensure high quality information within the tight deadlines that this medium imposes.

This aspect compounds another evident serious lack in the national media: public and private newspapers, television and radio news sources generally do not have science editors in their staff. Some newspapers assign occasional science stories to regular journalists, but what is missing is a stable figure that continuously covers this area, as exists for politics, economics or sports.

The absence of this kind of internal specialization, unlike what happens in other countries where science newsrooms are an established tradition, not only highlights the lack of adequate professional vision to meet the needs of the themes prevalent in today's information, but has produced another anomaly: to tackle these issues, scientists are often asked to intervene directly.

Although collaboration between researchers and the media is important, and should be strengthened, the intervention of a specialist should not replace that of the science journalist. Journalists have more appropriate communication tools for this task, thereby ensuring the kind of comprehensive discussion based on a plurality of sources that is essential for a proper analysis. The best role for scientists in the media, when appropriate, should be that of a commentator who adds value to the news provided by the science journalist.



These roles, competencies and aims are radically different and must remain so to avoid confusing the readers. The proliferation of information and sources requires more clarity. Time plays a different role in science news than it did in the past. The tempo with which news is produced and spread urges readers with a rhythm that they are not accustomed to, and scientific news is no longer seen as a fundamental path to knowledge on which to dwell, but as a relative, albeit important, step. This changes its meaning to those who receive it, and can be interpreted positively or negatively depending on one's reading capacity and background.



However, these are extraordinary measures that can be used in special situations, but cannot support the continuity and evolution of research. These new methods do show an important aspect:

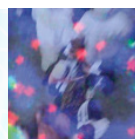
This is exactly why the role of science journalists is essential, because it is their responsibility to establish the right balance, bridging the natural limitations of the reader.

Finally, looking at the cuts to research imposed in some countries, the doubt arises that the ongoing economic crisis damages also scientific information. This doubt is legitimate because budget cuts are often followed by a reappraisal of priorities for the remaining funds. Studies in areas with direct applications may be favoured, with the aim of supporting economic recovery. Nevertheless, this legitimate need should not alter the availability of resources dedicated to basic research with more distant perspectives. To overcome the limitations imposed by budget cuts, new avenues of funding such as crowdfunding have been established.

direct involvement by the population that raises awareness of issues that would otherwise seem distant and inaccessible. This presents a new perspective for journalists, positioning them to expand their analysis and their frame of reference in order to observe, evaluate and possibly to criticize the initiatives emerging from the natural process of selection and funding.

The world of research evolves fast and this must be matched in the world of science journalism, especially in Italy, considering that it will assume a growing role in future communication.

Youscientist, IFOM Science & Society program



*Science journalism
in a changing world*

Science journalism
in a changing world

The author:



Giovanna Caprara

Science Editor at Il Corriere della Sera
President of UGIS

Giovanni Caprara, journalist and writer, is science editor at “Il Corriere della Sera”. He is the author of several publications on the history of science and space exploration, published both in Europe and the USA. Among the others: *The Space Age*, *The Adventure of Science: Challenges, Inventions and Discoveries in the Pages of “Corriere della Sera”*, *Scientists: Great Men and Discoveries from Pythagoras to the Internet*, *Italy on the Shuttle*, *A Brief History of the Great Scientific Discoveries*, *Italian Space History* and, in 2014, *Energy for Italy*.

Among his many awards, in 2000 he received the ConScientia prize for science journalist of the year, presented jointly by the universities of Milan. In the same year, the International Astronomical Union at Harvard University named after him an asteroid orbiting between Mars and Jupiter in recognition of his outreach activities in astronomy and space exploration. In 2010, he received the European Science Writers Award from the Euroscience Foundation, and in 2014 was made a Knight of the Italian Republic.

He has served as the president of the Union of Italian Scientific Journalists (UGIS) since 2011. He designed and curated the new space section in the Museum of Science and Technology in Milan, and is a member of numerous scientific committees including Bergamo Science and the Galileo Prize for science divulgation.

Publications

A snapshot of the physical and functional wiring of the Eps15 homology domain network in the nematode.

Tsushima Hanako - Malabarba Maria Grazia - Confalonieri Stefano - Senic-Matuglia Francesca - Verhoef Lisette G G C - Bartocci Cristina - D'Ario Giovanni - Cocito Andrea - Di Fiore Pier Paolo - Salcini Anna Elisabetta

PLoS One; 2013 Jan;8(2):e56383. doi: 10.1371/journal.pone.0056383

[PMID: 23424658] IF 3.730

Cell reprogramming requires silencing of a core subset of polycomb targets.

Fragola Giulia - Germain Pierre-Luc - Laise Pasquale - Cuomo Alessandro - Blasimme Alessandro - Gross Fridolin - Signaroldi Elena - Bucci Gabriele - Sommer Cesar - Pruneri Giancarlo - Mazzarol Giovanni - Bonaldi Tiziana - Mostoslavsky Gustavo - Casola Stefano - Testa Giuseppe

PLoS Genet. 2013;9(2):e1003292. doi: 10.1371/journal.pgen.1003292.

[PMID: 23468641] IF 8.517

Correlative microscopy.

Mironov Alexander A - Beznoussenko Galina V

Methods in Cell Biology; 2013 Jan;113:209-55. doi: 10.1016/B978-0-12-407239-8.00011-2

[PMID: 23317905] IF 1.444

DNA Damage in Mammalian Neural Stem Cells Leads to Astrocytic Differentiation Mediated by BMP2 Signaling through JAK-STAT.

Schneider Leonid - Pellegatta Serena - Favaro Rebecca - Pisati Federica - Roncaglia Paola - Testa Giuseppe - Nicolis Silvia K - Finocchiaro Gaetano - d'Adda di Fagnola Fabrizio

Stem Cell Reports; 2013 Jan;1(2):123-38. doi: 10.1016/j.stemcr.2013.06.004

[PMID: 24052948]

Effects of warm ischemic time on gene expression profiling in colorectal cancer tissues and normal mucosa.

Musella Valeria - Verderio Paolo - Reid James Francis - Pizzamiglio Sara - Gariboldi Manuela - Callari Maurizio - Milione Massimo - Massimo Milione - De Cecco Loris - Veneroni Silvia - Pierotti Marco Alessandro - Daidone Maria Grazia

PLoS One; 2013 Jan;8(1):e53406. doi: 10.1371/journal.pone.0053406

[PMID: 23308215] IF 3.730

Genome-wide association study in BRCA1 mutation carriers identifies novel loci associated with breast and ovarian cancer risk.

Couch Fergus J - Wang Xianshu - McGuffog Lesley - Lee Andrew - Olswold Curtis - Kuchenbaecker Karoline B - Soucy Penny - Fredericksen Zachary - Barrowdale Daniel - Dennis Joe - Gaudet Mia M - Dicks Ed - Kosel Matthew - Healey Sue - Sinilnikova Olga M - Lee Adam - Bacot François - Vincent Daniel - Hogervorst Frans B L - Peock Susan - Stoppa-Lyonnet Dominique - Jakubowska Anna - kConFab Investigators - Radice Paolo - Schmutzler Rita Katharina - SWE-BRCA - Domchek Susan M - Piedmonte Marion - Singer Christian F - Friedman Eitan - Thomassen Mads - Ontario Cancer Genetics Network - Hansen Thomas V O - Neuhausen Susan L - Szabo Csilla I - Blanco Ignacio - Greene Mark H - Karlan Beth Y - Garber Judy - Phelan Catherine M - Weitzel Jeffrey N - Montagna Marco - Olah Edith - Andrulis Irene L - Godwin Andrew K - Yannoukakos Drakoulis - Goldgar David E - Caldes Trinidad - Nevanlinna Heli - Osorio Ana - Terry Mary Beth - Daly Mary B - van Rensburg Elizabeth J - Hamann Ute - Ramus Susan J - Toland Amanda Ewart - Caligo Maria A - Olopade Olufunmilayo I - Tung Nadine - Claes Kathleen - Beattie Mary S - Southey Melissa C - Imyanitov Evgeny N - Tischkowitz Marc - Janavicius Ramunas - John Esther M - Kwong Ava - Diez Orland - Balmaña Judith - Barkardottir Rosa B - Arun Banu K - Rennert Gad - Teo Soo-Hwang - Ganz Patricia A - Campbell Ian - van der Hout Annemarie H - van Deurzen Carolien H M - Seynaeve Caroline - Gómez García Encarna B - van Leeuwen Flora E - Meijers-Heijboer Hanne E J - Gille Johannes

J P - Ausems Margreet G E M - Blok Marinus J - Ligtenberg Marjolijn J L - Rookus Matti A - Devilee Peter - Verhoef Senno - van Os Theo A M - Wijnen Juul T - HEBON - EMBRACE - Frost Debra - Ellis Steve - Fineberg Elena - Platte Radka - Evans D Gareth - Izatt Louise - Eeles Rosalind A - Adlard Julian - Eccles Diana M - Cook Jackie - Brewer Carole - Douglas Fiona - Hodgson Shirley - Morrison Patrick J - Side Lucy E - Donaldson Alan - Houghton Catherine - Rogers Mark T - Dorkins Huw - Eason Jacqueline - Gregory Helen - McCann Emma - Murray Alex - Calender Alain - Hardouin Agnès - Berthet Pascaline - Delnatte Capucine - Nogues Catherine - Lasset Christine - Houdayer Claude - Leroux Dominique - Rouleau Etienne - Prieur Fabienne - Damiola Francesca - Sobol Hagay - Coupier Isabelle - Venat-Bouvet Laurence - Castera Laurent - Gauthier-Villars Marion - Léoné Mélanie - Pujol Pascal - Mazoyer Sylvie - Bignon Yves-Jean - GEMO Study Collaborators - Z?owocka-Per?owska Elzbieta - Gronwald Jacek - Lubinski Jan - Durda Katarzyna - Jaworska Katarzyna - Huzarski Tomasz - Spurdle Amanda B - Viel Alessandra - Peissel Bernard - Bonanni Bernardo - Melloni Giulia - Ottini Laura - Papi Laura - Varesco Liliana - Tibiletti Maria Grazia - Peterlongo Paolo - Volorio Sara - Manoukian Siranoush - Pensotti Valeria - Arnold Norbert - Engel Christoph - Deissler Helmut - Gadzicki Dorothea - Gehrig Andrea - Kast Karin - Rhiem Kerstin - Meindl Alfons - Niederacher Dieter - Ditsch Nina - Plendl Hansjoerg - Preisler-Adams Sabine - Engert Stefanie - Sutter Christian - Varon-Mateeva Raymonda - Wappenschmidt Barbara - Weber Bernhard H F - Arver Brita - Stenmark-Askmal Marie - Loman Niklas - Rosenquist Richard - Einbeigi Zakaria - Nathanson Katherine L - Rebbeck Timothy R - Blank Stephanie V - Cohn David E - Rodriguez Gustavo C - Small Laurie - Friedlander Michael - Bae-Jump Victoria L - Fink-Retter Anneliese - Rappaport Christine - Gschwantler-Kaulich Daphne - Pfeiler Georg - Tea Muy-Kheng - Lindor Noralane M - Kaufman Bella - Shimon Paluch Shani - Laitman Yael - Skytte Anne-Bine - Gerdes Anne-Marie - Pedersen Inge Sokilde - Moeller Sanne Traasdahl - Kruse Torben A - Jensen Uffe Birk - Vijai Joseph - Sarrel Kara - Robson Mark - Kauff Noah - Mulligan Anna Marie - Glendon Gord - Ozelik Hilmi - Ejlersen Bent - Nielsen Finn C - Jønson Lars - Andersen Mette K - Ding Yuan Chun - Steele Linda - Foretova Lenka - Teulé Alex - Lazaro Conxi - Brunet Joan - Pujana Miquel Angel - Mai Phuong L - Loud Jennifer T - Walsh Christine - Lester Jenny - Orsulic Sandra - Narod Steven A - Herzog Josef - Sand Sharon R - Tognazzo Silvia - Agata Simona - Vaszko Tibor - Weaver Joellen - Stavropoulou Alexandra V - Buys Sandra S - Romero Atocha - de la Hoya Miguel - Aittomäki Kristiina - Muranen Taru A - Duran Mercedes - Chung Wendy K - Lasa Adriana - Dorfling Cecilia M - Miron Alexander - BCFR - Benitez Javier - Senter Leigha - Huo Dezheng - Chan Salina B - Sokolenko Anna P - Chiquette Jocelyne - Tihomirova Laima - Friebel Tara M - Agnarsson Bjarni A - Lu Karen H - Lejbkiewicz Flavio - James Paul A - Hall Per - Dunning Alison M - Tessier Daniel - Cunningham Julie - Slager Susan L - Wang Chen - Hart Steven - Stevens Kristen - Simard Jacques - Pastinen Tomi - Pankratz Vernon S - Offit Kenneth - Easton Douglas F - Chenevix-Trench Georgia - Antoniou Antonis C - CIMBA

PLoS Genetics; 2013 Jan;9(3):e1003212. doi: 10.1371/journal.pgen.1003212

[PMID: 23544013] IF 8.517

Identification of a BRCA2-specific modifier locus at 6p24 related to breast cancer risk.

Gaudet Mia M - Kuchenbaecker Karoline B - Vijai Joseph - Klein Robert J - Kirchhoff Tomas - McGuffog Lesley - Barrowdale Daniel - Dunning Alison M - Lee Andrew - Dennis Joe - Healey Sue - Dicks Ed - Soucy Penny - Sinilnikova Olga M - Pankratz Vernon S - Wang Xianshu - Eldridge Ronald C - Tessier Daniel C - Vincent Daniel - Bacot Francois - Hogervorst Frans B L - Peock Susan - Stoppa-Lyonnet Dominique - KConFab Investigators - Peterlongo Paolo - Schmutzler Rita K - Nathanson Katherine L - Piedmonte Marion - Singer Christian F - Thomassen Mads - Ontario Cancer Genetics Network - Hansen Thomas v O - Neuhausen Susan L - Blanco Ignacio - Greene Mark H - Garber Judith - Weitzel Jeffrey N - Andrulis Irene L - Goldgar David E - D'Andrea Emma - Caldes Trinidad - Nevanlinna Heli - Osorio Ana - van Rensburg Elizabeth J - Arason Adalgeir - Rennert Gad - van den Ouweland Ans M W - van der Hout Annemarie H - Kets Carolien M - Aalfs Cora M - Wijnen Juul T - Ausems Margreet G E M - HEBON - EMBRACE - Frost Debra - Ellis Steve - Fineberg Elena - Platte Radka - Evans D Gareth - Jacobs Chris - Adlard Julian - Tischkowitz Marc - Porteous Mary E - Damiola Francesca - GEMO Study Collaborators - Golmard Lisa - Barjhoux Laure - Longy Michel - Belotti Muriel - Ferrer Sandra Fert - Mazoyer Sylvie - Spurdle Amanda B - Manoukian Siranoush - Barile Monica - Genuardi Maurizio - Arnold Norbert - Meindl Alfons - Sutter Christian - Wappenschmidt Barbara - Domchek Susan M - Pfeiler Georg - Friedman Eitan - Jensen Uffe Birk - Robson Mark - Shah Sohela - Lazaro Conxi - Mai Phuong L - Benitez Javier - Southey Melissa C - Schmidt Marjanka K - Fasching Peter A - Peto Julian - Humphreys Manjeet K - Wang Qin - Michailidou Kyriaki - Sawyer Elinor J - Burwinkel Barbara - Guénel Pascal - Bojesen Stig E - Milne Roger L - Brenner Hermann - Lochmann Magdalena - GENICA Network - Aittomäki Kristiina - Dörk Thilo - Margolin Sara - Mannermaa Arto - Lambrechts Diether - Chang-Claude Jenny - Radice Paolo - Giles Graham G - Haiman Christopher A - Winqvist Robert - Devilee Peter - García-Closas Montserrat - Schoof Nils - Hooning Maartje J - Cox Angela - Pharoah Paul D P - Jakubowska Anna - Orr Nick - González-Neira Anna - Pita Guillermo - Alonso M Rosario - Hall Per - Couch Fergus J - Simard Jacques - Altshuler David - Easton Douglas F - Chenevix-Trench Georgia - Antoniou Antonis C - Offit Kenneth

PLoS Genetics; 2013 Jan;9(3):e1003173. doi: 10.1371/journal.pgen.1003173

[PMID: 23544012] IF 8.517

Meta-analysis of mismatch repair polymorphisms within the cogent consortium for colorectal cancer susceptibility.

Picelli Simone - Lorenzo Bermejo Justo - Chang-Claude Jenny - Hoffmeister Michael - Fernández-Rozadilla Ceres - Carracedo Angel - Castells Antoni - Castellví-Bel Sergi - Memembers of EPICOLON Consortium- Gastrointestinal Oncology Group of the Spanish Gastroenterological Association - Naccarati Alessio - Pardini Barbara - Vodickova Ludmila - Müller Heiko - Talseth-Palmer Bente A - Stibbard Geoffrey - Peterlongo Paolo - Nici Carmela - Veneroni Silvia - Li Li - Casey Graham - Tenesa Albert - Farrington Susan M - Tomlinson Ian - Moreno Victor - van Wezel Tom - Wijnen Juul - Dunlop Malcolm - Radice Paolo - Scott Rodney J - Vodicka Pavel - Ruiz-Ponte Clara - Brenner Hermann - Buch Stephan - Völzke Henry - Hampe Jochen - Schafmayer Clemens - Lindblom Annika

PloS One; 2013 Jan;8(9):e72091. doi: 10.1371/journal.pone.0072091

[PMID: 24039736] IF 3.730

Role of cMET in the development and progression of colorectal cancer.

Samamé Pérez-Vargas Juan Carlos - Biondani Pamela - Maggi Claudia - Gariboldi Manuela - Gloghini Annunziata - Inno Alessandro - Volpi Chiara Costanza - Gualeni Ambra Vittoria - di Bartolomeo Maria - de Braud Filippo - Castano Alessandra - Bossi Ilaria - Pietrantonio Filippo

International Journal of Molecular Sciences; 2013 Jan 14(9):18056-77. doi: 10.3390/ijms140918056

[PMID: 24005867] IF 2.464

Simultaneous in vitro characterisation of DNA deaminase function and associated DNA repair pathways.

Franchini Don-Marc - Incorvaia Elisabetta - Rangam Gopinath - Coker Heather A - Petersen-Mahrt Svend K

PloS One; 2013 Jan 9;8(12):e82097. doi: 10.1371/journal.pone.0082097

[PMID: 24349193] IF 3.730

Sox17 is indispensable for acquisition and maintenance of arterial identity.

Corada Monica - Orsenigo Fabrizio - Morini Marco Francesco - Pitulescu Mara Elena - Bhat Ganesh - Nyqvist Daniel - Breviario Ferruccio - Conti Valentina - Briot Anais - Iruela-Arispe M Luisa - Adams Ralf H - Dejana Elisabetta

Nature Communications; 2013 Jan;4:2609. doi: 10.1038/ncomms3609

[PMID: 24153254] IF 10.015

The role of VE-cadherin in vascular morphogenesis and permeability control.

Dejana Elisabetta - Vestweber Dietmar

Progress in Molecular Biology and Translational Science; 2013 Jan;116:119-44. doi: 10.1016/B978-0-12-394311-8.00006-6

[PMID: 23481193] IF 2.322

The Smc5-Smc6 complex regulates recombination at centromeric regions and affects kinetochore protein sumoylation during normal growth.

Yong-Gonzales Vladimir - Hang Lisa E - Castellucci Federica - Branzei Dana - Zhao Xiaolan

PloS One; 2013 Jan;7(12):e51540. doi: 10.1371/journal.pone.0051540

[PMID: 23284708] IF 3.730

Wnt activation of immortalized brain endothelial cells as a tool for generating a standardized model of the blood brain barrier in vitro.

Paolinelli Roberta - Corada Monica - Ferrarini Luca - Devraj Kavi - Artus Cédric - Czupalla Cathrin J - Rudini Noemi - Maddaluno Luigi - Papa Eleanna - Engelhardt Britta - Couraud Pierre Olivier - Liebner Stefan - Dejana Elisabetta

PloS One; 2013 Jan;8(8):e70233. doi: 10.1371/journal.pone.0070233

[PMID: 23940549] IF 3.730

Vascular endothelial growth factor-angiopoietin chimera with improved properties for therapeutic angiogenesis.

Anisimov Andrey - Tvorogov Denis - Alitalo Annamari - Leppänen Veli-Matti - An Yuri - Han Eun Chun - Orsenigo Fabrizio - Gaál Emilia Ilona - Holopainen Tanja - Koh Young Jun - Tammela Tuomas - Korpisalo Petra - Keskitalo Salla - Jeltsch Michael - Ylä-Herttuala Seppo - Dejana Elisabetta - Koh Gou Young - Choi Chulhee - Saharinen Pipsa - Alitalo Kari

Circulation; 2013 Jan 29;127(4):424-34. doi: 10.1161/CIRCULATIONAHA

[PMID: 23357661] IF 15.202

VE-PTP regulates VEGFR2 activity in stalk cells to establish endothelial cell polarity and lumen formation.

Hayashi Makoto - Majumdar Arindam - Li Xiujuan - Adler Jeremy - Sun Zuyue - Vertuani Simona - Hellberg Carina - Mellberg Sofie - Koch Sina - Dimberg Anna - Koh Gou Young - Dejana Elisabetta - Belting Heinz-Georg - Affolter Markus - Thurston Gavin - Holmgren Lars - Vestweber Dietmar - Claesson-Welsh Lena

Nature Communications; 2013 Jan;4:1672. doi: 10.1038/ncomms2683

[PMID: 23575676] IF 10.015

Modeling tumor progression by the sequential introduction of genetic alterations into the genome of human normal cells.

Zecchin Davide - Arena Sabrina - Martini Miriam - Sassi Francesco - Pisacane Alberto - Di Nicolantonio Federica - Bardelli Alberto

Human Mutation; 2013 Feb;34(2):330-7. doi: 10.1002/humu.22234

[PMID: 23292961] IF 5.213

SCFFbxw5 mediates transient degradation of actin remodeller Eps8 to allow proper mitotic progression.

Werner Achim - Disanza Andrea - Reifemberger Nina - Habeck Gregor - Becker Janina - Calabrese Matthew - Urlaub Henning - Lorenz Holger - Schulman Brenda - Scita Giorgio - Melchior Frauke

Nature Cell Biology; 2013 Feb;15(2):179-88. doi: 10.1038/ncb2661

[PMID: 23314863] IF 20.761

Whole exome sequencing suggests much of non-BRCA1/BRCA2 familial breast cancer is due to moderate and low penetrance susceptibility alleles.

Rots Marianne G - Petersen-Mahrt Svend K

Epigenomics; 2013 Feb;5(1):25-8. doi: 10.2217/epi.12.73

[PMID: 23414316] IF 2.433

The 2012 IMB Conference: DNA demethylation, repair and beyond. Institute of Molecular Biology, Mainz, Germany, 18-21 October 2012.

Gracia-Aznarez Francisco Javier - Fernandez Victoria - Pita Guillermo - Peterlongo Paolo - Dominguez Orlando - de la Hoya Miguel - Duran Mercedes - Osorio Ana - Moreno Leticia - Gonzalez-Neira Anna -

Rosa-Rosa Juan Manuel - Sinilnikova Olga - Mazoyer Sylvie - Hopper John - Lazaro Conchi - Southey Melissa - Odefrey Fabrice - Manoukian Siranoush - Catucci Irene - Caldes Trinidad - Lynch Henry T - Hilbers Florentine S M - van Asperen Christi J - Vasen Hans F A - Goldgar David - Radice Paolo - Devilee Peter - Benitez Javier

PloS One; 2013 Jan;8(2):e55681. doi: 10.1371/journal.pone.0055681

[PMID: 23409019] IF 3.730

Direct evidence of the importance of vitronectin and its interaction with the urokinase receptor in tumor growth.

Pirazzoli Valentina - Ferraris Gian Maria Sarra - Sidenius Nicolai

Blood; 2013 Mar 21;121(12):2316-23 ; issn 1528-0020 doi 10.1182/blood-2012-08-451187

[PMID: 23327926] IF: 9.060

Mixed lineage kinase MLK4 is activated in colorectal cancers where it synergistically cooperates with activated RAS signaling in driving tumorigenesis.

Martini Miriam - Russo Mariangela - Lamba Simona - Vitiello Elisa - Crowley Emily Hannah - Sassi Francesco - Romanelli Davide - Frattini Milo - Marchetti Antonio - Bardelli Alberto

Cancer Research; 2013 Mar 15;73(6):1912-21. doi: 10.1158/0008-5472.CAN-12-3074

[PMID: 23319808] IF: 8.650

Plasma cells require autophagy for sustainable immunoglobulin production.

Pengo Niccolò - Scolari Maria - Oliva Laura - Milan Enrico - Mainoldi Federica - Raimondi Andrea - Fagioli Claudio - Merlini Arianna - Mariani Elisabetta - Pasqualetto Elena - Orfanelli Ugo - Ponzoni Maurilio - Sitia Roberto - Casola Stefano - Cenci Simone

Nature Immunology; 2013 Mar;14(3):298-305. doi: 10.1038/ni.2524

[PMID: 23354484] IF 26.199

Analysis of the DNA-binding profile and function of TALE homeoproteins reveals their specialization and specific interactions with Hox genes/proteins.

Penkov Dmitry - Mateos San Martín Daniel - Fernandez-Díaz Luis C - Rosselló Catalina A - Torroja Carlos - Sánchez-Cabo Fátima - Warnatz H J - Sultan Marc - Yaspo Marie L - Gabrieli Arianna - Tkachuk Vsevolod - Brendolan Andrea - Blasi Francesco - Torres Miguel

Cell Reports; 2013 Apr 25;3(4):1321-33. doi: 10.1016/j.celrep.2013.03.029

[PMID: 23602564]

Association of low-penetrance alleles with male breast cancer risk and clinicopathological characteristics: results from a multicenter study in Italy.

Ottini L - Silvestri V - Saieva C - Rizzolo P - Zanna I - Falchetti M - Masala G - Navazio A S - Graziano V - Bianchi S - Manoukian S - Barile M - Peterlongo P - D'Amico C - Varesco L - Tommasi S - Russo A - Giannini G - Cortesi L - Viel A - Montagna M - Radice P - Palli D

Breast Cancer Research and Treatment; 2013 Apr;138(3):861-8. doi: 10.1007/s10549-013-2459-4

[PMID: 23468243] IF: 4.469

A review on biomarkers for prediction of treatment outcome in gastric cancer.

Pietrantonio Filippo - De Braud Filippo - Da Prat Valentina - Perrone Federica - Pierotti Marco Alessandro - Gariboldi Manuela - Fanetti Giuseppe - Biondani Pamela - Pellegrinelli Alessandro - Bossi Ilaria - Di Bartolomeo Maria

Anticancer Research; 2013 Apr;33(4); issn 1791-7530; doi 33/4/1257

[PMID: 23564763] IF: 1.713

Functional variants at the 11q13 risk locus for breast cancer regulate cyclin D1 expression through long-range enhancers.

French Juliet D - Ghossaini Maya - Edwards Stacey L - Meyer Kerstin B - Michailidou Kyriaki - Ahmed Shahana - Khan Sofia - Maranian Mel J - O'Reilly Martin - Hillman Kristine M - Betts Joshua A - Carroll Thomas - Bailey Peter J - Dicks Ed - Beesley Jonathan - Tyrer Jonathan - Maia Ana-Teresa - Beck Andrew - Knoblauch Nicholas W - Chen Constance - Kraft Peter - Barnes Daniel - González-Neira Anna - Alonso M Rosario - Herrero Daniel - Tessier Daniel C - Vincent Daniel - Bacot Francois - Luccarini Craig - Baynes Caroline - Conroy Don - Dennis Joe - Bolla Manjeet K - Wang Qin - Hopper John L - Southey Melissa C - Schmidt Marjanka K - Brooks Annegien - Verhoef Senno - Cornelissen Sten - Muir Kenneth - Lophatananon Artitaya - Stewart-Brown Sarah - Siriwanarangsarn Pornthep - Fasching Peter A - Loehberg Christian R - Ekici Arif B - Beckmann Matthias W - Peto Julian - dos Santos Silva Isabel - Johnson Nichola - Aitken Zoe - Sawyer Elinor J - Tomlinson Ian - Kerin Michael J - Miller Nicola - Marme Frederik - Schneeweiss Andreas - Sohn Christof - Burwinkel Barbara - Guénel Pascal - Truong Thérèse - Laurent-Puig Pierre - Menegaux Florence - Bojesen Stig E - Nordestgaard Børge G - Nielsen Sune F - Flyger Henrik - Milne Roger L - Zamora M Pilar - Arias Perez Jose Ignacio - Benitez Javier - Anton-Culver Hoda - Brenner Hermann - Müller Heiko - Arndt Volker - Stegmaier Christa - Meindl Alfons - Lichtner Peter - Schmutzler Rita K - Engel Christoph - Brauch Hiltrud - Hamann Ute - Justenhoven Christina - GENICA Network - Aaltonen Kirsimari - Heikkilä Päivi - Aittomäki Kristiina - Blomqvist Carl - Matsuo Keitaro - Ito Hidemi - Iwata Hiroji - Sueta Aiko - Bogdanova Natalia V - Antonenkova Natalia N - Dörk Thilo - Lindblom Annika - Margolin Sara - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - kConFab Investigators - Wu Anna H - Tseng Chiu-chen - Van Den Berg David - Stram Daniel O - Lambrechts Diether - Peeters Stephanie - Smeets Ann - Floris Giuseppe - Chang-Claude Jenny - Rudolph Anja - Nickels Stefan - Flesch-Janys Dieter - Radice Paolo - Peterlongo Paolo - Bonanni Bernardo - Sardella Domenico - Couch Fergus J - Wang Xianshu - Pankratz Vernon S - Lee Adam - Giles Graham G - Severi Gianluca - Baglietto Laura - Haiman Christopher A - Henderson Brian E - Schumacher Fredrick - Le Marchand Loic - Simard Jacques - Goldberg Mark S - Labrèche France - Dumont Martine - Teo Soo Hwang - Yip Cheng Har - Ng Char-Hong - Vithana Eranga Nishanthie - Kristensen Vessela - Zheng Wei - Deming-Halverson Sandra - Shrubsole Martha - Long Jirong - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Grip Mervi - Andrulis Irene L - Knight Julia A - Glendon Gord - Mulligan Anna Marie - Devilee Peter - Seynaeve Caroline - García-Closas Montserrat - Figueroa Jonine - Chanock Stephen J - Lissowska Jolanta - Czene Kamila - Klevebring Daniel - Schoof Nils - Hoening Maartje J - Martens John W M - Collée J Margriet - Tilanus-Linthorst Madeleine - Hall Per - Li Jingmei - Liu Jianjun - Humphreys Keith - Shu Xiao-Ou - Lu Wei - Gao Yu-Tang - Cai Hui - Cox Angela - Balasubramanian Sabapathy P - Blot William - Signorello Lisa B - Cai Qiuyin - Pharoah Paul D P - Healey Catherine S - Shah Mitul - Pooley Karen A - Kang Daehee - Yoo Keun-Young - Noh Dong-Young - Hartman Mikael - Miao Hui - Sng Jen-Hwei - Sim Xueling - Jakubowska Anna - Lubinski Jan - Jaworska-Bieniek Katarzyna - Durda Katarzyna - Sangrajrang Suleeporn - Gaborieau Valerie - McKay James - Toland Amanda E - Ambrosone Christine B - Yannoukakos Drakoulis - Godwin Andrew K - Shen Chen-Yang - Hsiung Chia-Ni - Wu Pei-Ei - Chen Shou-Tung - Swerdlow Anthony - Ashworth Alan - Orr Nick - Schoemaker Minouk J - Ponder Bruce AJ - Nevanlinna Heli - Brown Melissa A - Chenevix-Trench Georgia - Easton Douglas F - Dunning Alison M

American Journal of Human Genetics; 2013 Apr 4;92(4):489-503; doi 10.1111/ajcel.12060

[PMID: 23540573] IF: 5.705

Genome-wide association studies identify four ER negative-specific breast cancer risk loci.

Garcia-Closas Montserrat - Couch Fergus J - Lindstrom Sara - Michailidou Kyriaki - Schmidt Marjanka K - Brook Mark N - Orr Nick - Rhie Suhn Kyong - Riboli Elio - Feigelson Heather S - Le Marchand Loic - Buring Julie E - Eccles Diana - Miron Penelope - Fasching Peter A - Brauch Hiltrud - Chang-Claude Jenny - Carpenter Jane - Godwin Andrew K - Nevanlinna Heli - Giles Graham G - Cox Angela - Hopper John L - Bolla Manjeet K - Wang Qin - Dennis Joe - Dicks Ed - Howat Will J - Schoof Nils - Bojesen Stig E - Lambrechts Diether - Brooks Annegien - Andrulis Irene L - Guénel Pascal - Burwinkel Barbara - Sawyer Elinor J - Hollestelle Antoinette - Fletcher Olivia - Winqvist Robert - Brenner Hermann - Mannermaa Arto - Hamann Ute - Meindl Alfons - Lindblom Annika - Zheng Wei - Devilee Peter - Goldberg Mark S - Lubinski Jan - Kristensen Vessela - Swerdlow Anthony - Anton-Culver Hoda - Dörk Thilo - Muir Kenneth - Matsuo Keitaro - Wu Anna H - Radice Paolo - Teo Soo Hwang - Shu Xiao-Ou - Blot William - Kang Daehee - Hartman Mikael - Sangrajrang Suleeporn - Shen Chen-Yang - Southey Melissa C - Park Daniel J - Hammet Fleur - Stone Jennifer - Veer Laura J Van't - Rutgers Emiel J - Lophatananon Artitaya - Stewart-Brown Sarah - Siriwanarangsarn Pornthep - Peto Julian - Schrauder Michael G - Ekici Arif B - Beckmann Matthias W - Dos Santos Silva Isabel - Johnson Nichola - Warren Helen - Tomlinson Ian - Kerin Michael J - Miller Nicola - Marme Frederik - Schneeweiss Andreas - Sohn Christof - Truong Therese - Laurent-Puig Pierre - Kerbrat Pierre - Nordestgaard Børge G - Nielsen Sune F - Flyger Henrik - Milne Roger L - Perez Jose Ignacio

Arias - Menéndez Primitiva - Müller Heiko - Arndt Volker - Stegmaier Christa - Lichtner Peter - Lochmann Magdalena - Justenhoven Christina - Ko Yon-Dschun - Gene ENvironmental Interaction and breast Cancer (GENICA) Network - Muranen Taru A - Aittomäki Kristiina - Blomqvist Carl - Greco Dario - Heikkinen Tuomas - Ito Hidemi - Iwata Hiroji - Yatabe Yasushi - Antonenkova Natalia N - Margolin Sara - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - Balleine Rosemary - kConFab Investigators - Tseng Chiu-Chen - Berg David Van Den - Stram Daniel O - Neven Patrick - Dieudonné Anne-Sophie - Leunen Karin - Rudolph Anja - Nickels Stefan - Flesch-Janys Dieter - Peterlongo Paolo - Peissel Bernard - Bernard Loris - Olson Janet E - Wang Xianshu - Stevens Kristen - Severi Gianluca - Baglietto Laura - McLean Catriona - Coetzee Gerhard A - Feng Ye - Henderson Brian E - Schumacher Fredrick - Bogdanova Natalia V - Labrèche France - Dumont Martine - Yip Cheng Har - Taib Nur Aishah Mohd - Cheng Ching-Yu - Shrubsole Martha - Long Jirong - Pylkäs Katri - Jukkola-Vuorinen Arja - Kauppila Saila - Knight Julia A - Glendon Gord - Mulligan Anna Marie - Tollenaar Robertus A E M - Seynaeve Caroline M - Kriege Mieke - Hoening Maartje J - van den Ouweland Ans M W - van Deurzen Carolien H M - Lu Wei - Gao Yu-Tang - Cai Hui - Balasubramanian Sabapathy P - Cross Simon S - Reed Malcolm W R - Signorello Lisa - Cai Qiuyin - Shah Mitul - Miao Hui - Chan Ching Wan - Chia Kee Seng - Jakubowska Anna - Jaworska Katarzyna - Durda Katarzyna - Hsiung Chia-Ni - Wu Pei-Ei - Yu Jyh-Cherng - Ashworth Alan - Jones Michael - Tessier Daniel C - González-Neira Anna - Pita Guillermo - Alonso M Rosario - Vincent Daniel - Bacot Francois - Ambrosone Christine B - Bandera Elisa V - John Esther M - Chen Gary K - Hu Jennifer J - Rodriguez-Gil Jorge L - Bernstein Leslie - Press Michael F - Ziegler Regina G - Millikan Robert M - Deming-Halverson Sandra L - Nyante Sarah - Ingles Sue A - Waisfisz Quinten - Tsimiklis Helen - Makalic Enes - Schmidt Daniel - Bui Minh - Gibson Lorna - Müller-Myhsok Bertram - Schmutzler Rita K - Hein Rebecca - Dahmen Norbert - Beckmann Lars - Aaltonen Kirsimari - Czene Kamila - Irwanto Astrid - Liu Jianjun - Turnbull Clare - Familial Breast Cancer Study (FBCS) - Rahman Nazneen - Meijers-Heijboer Hanne - Uitterlinden Andre G - Rivadeneira Fernando - Australian Breast Cancer Tissue Bank (ABCTB) Investigators - Olswold Curtis - Slager Susan - Pilarski Robert - Ademuyiwa Foluso - Konstantopoulou Irene - Martin Nicholas G - Montgomery Grant W - Slamon Dennis J - Rauh Claudia - Lux Michael P - Jud Sebastian M - Bruning Thomas - Weaver Joellen - Sharma Priyanka - Pathak Harsh - Tapper Will - Gerty Sue - Durcan Lorraine - Trichopoulos Dimitrios - Tumino Rosario - Peeters Petra H - Kaaks Rudolf - Campa Daniele - Canzian Federico - Weiderpass Elisabete - Johansson Mattias - Khaw Kay-Tee - Travis Ruth - Clavel-Chapelon Françoise - Kolonel Laurence N - Chen Constance - Beck Andy - Hankinson Susan E - Berg Christine D - Hoover Robert N - Lissowska Jolanta - Figueroa Jonine D - Chasman Daniel I - Gaudet Mia M - Diver W Ryan - Willett Walter C - Hunter David J - Simard Jacques - Benitez Javier - Dunning Alison M - Sherman Mark E - Chenevix-Trench Georgia - Chanock Stephen J - Hall Per - Pharoah Paul D P - Vachon Celine - Easton Douglas F - Haiman Christopher A - Kraft Peter

Nature Genetics; 2013 Apr;45(4):392-8, 398e1-2. doi: 10.1038/ng.2561

[PMID: 23535733] IF 35.209

Large-scale genotyping identifies 41 new loci associated with breast cancer risk.

Michailidou Kyriaki - Hall Per - Gonzalez-Neira Anna - Ghoussaini Maya - Dennis Joe - Milne Roger L - Schmidt Marjanka K - Chang-Claude Jenny - Bojesen Stig E - Bolla Manjeet K - Wang Qin - Dicks Ed - Lee Andrew - Turnbull Clare - Rahman Nazneen - Breast and Ovarian Cancer Susceptibility Collaboration - Fletcher Olivia - Peto Julian - Gibson Lorna - Dos Santos Silva Isabel - Nevanlinna Heli - Muranen Taru A - Aittomäki Kristiina - Blomqvist Carl - Czene Kamila - Irwanto Astrid - Liu Jianjun - Waisfisz Quinten - Meijers-Heijboer Hanne - Adank Muriel - Hereditary Breast and Ovarian Cancer Research Group Netherlands (HEBON) - van der Luijt Rob B - Hein Rebecca - Dahmen Norbert - Beckman Lars - Meindl Alfons - Schmutzler Rita K - Müller-Myhsok Bertram - Lichtner Peter - Hopper John L - Southey Melissa C - Makalic Enes - Schmidt Daniel F - Uitterlinden Andre G - Hofman Albert - Hunter David J - Chanock Stephen J - Vincent Daniel - Bacot François - Tessier Daniel C - Canisius Sander - Wessels Lodewyk F A - Haiman Christopher A - Shah Mitul - Luben Robert - Brown Judith - Luccarini Craig - Schoof Nils - Humphreys Keith - Li Jingmei - Nordestgaard Børge G - Nielsen Sune F - Flyger Henrik - Couch Fergus J - Wang Xianshu - Vachon Celine - Stevens Kristen N - Lambrechts Diether - Moisse Matthieu - Paridaens Robert - Christiaens Marie-Rose - Rudolph Anja - Nickels Stefan - Flesch-Janys Dieter - Johnson Nicola - Aitken Zoe - Aaltonen Kirsimari - Heikkinen Tuomas - Broeks Annegien - Veer Laura J Van't - van der Schoot C Ellen - Guénel Pascal - Truong Thérèse - Laurent-Puig Pierre - Menegaux Florence - Marme Frederik - Schneeweiss Andreas - Sohn Christof - Burwinkel Barbara - Zamora M Pilar - Perez Jose Ignacio - Arias - Pita Guillermo - Alonso M Rosario - Cox Angela - Brock Ian W - Cross Simon S - Reed Malcolm W R - Sawyer Elinor J - Tomlinson Ian - Kerin Michael J - Miller Nicola - Henderson Brian E - Schumacher Fredrick - Le Marchand Loic - Andrulis Irene L - Knight Julia A - Glendon Gord - Mulligan Anna Marie - kConFab Investigators - Australian Ovarian Cancer Study Group - Lindblom Annika - Margolin Sara - Hoening Maartje J - Hollestelle Antoinette - van den Ouweland Ans M W - Jager Agnes - Bui Quang M - Stone Jennifer - Dite Gillian S - Apicella Carmel - Tsimiklis Helen - Giles Graham G - Severi Gianluca

- Baglietto Laura - Fasching Peter A - Haeberle Lothar - Ekici Arif B - Beckmann Matthias W - Brenner Hermann - Müller Heiko - Arndt Volker - Stegmaier Christa - Swerdlow Anthony - Ashworth Alan - Orr Nick - Jones Michael - Figueroa Jonine - Lissowska Jolanta - Brinton Louise - Goldberg Mark S - Labrèche France - Dumont Martine - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Grip Mervi - Brauch Hiltrud - Hamann Ute - Brüning Thomas - GENICA (Gene Environment Interaction and Breast Cancer in Germany) Network - Radice Paolo - Peterlongo Paolo - Manoukian Siranoush - Bonanni Bernardo - Devilee Peter - Tollenaar Rob A E M - Seynaeve Caroline - van Asperen Christi J - Jakubowska Anna - Lubinski Jan - Jaworska Katarzyna - Durda Katarzyna - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - Bogdanova Natalia V - Antonenkova Natalia N - Dörk Thilo - Kristensen Vessela N - Anton-Culver Hoda - Slager Susan - Toland Amanda E - Edge Stephen - Fostira Florentia - Kang Daehee - Yoo Keun-Young - Noh Dong-Young - Matsuo Keitaro - Ito Hidemi - Iwata Hiroji - Sueta Aiko - Wu Anna H - Tseng Chiu-Chen - Van Den Berg David - Stram Daniel O - Shu Xiao-Ou - Lu Wei - Gao Yu-Tang - Cai Hui - Teo Soo Hwang - Yip Cheng Har - Phuah Sze Yee - Cornes Belinda K - Hartman Mikael - Miao Hui - Lim Wei Yen - Sng Jen-Hwei - Muir Kenneth - Lophatananon Artitaya - Stewart-Brown Sarah - Siriwanarangsarn Pornthep - Shen Chen-Yang - Hsiung Chia-Ni - Wu Pei-Ei - Ding Shian-Ling - Sangrajrang Suleeporn - Gaborieau Valerie - Brennan Paul - McKay James - Blot William J - Signorello Lisa B - Cai Qiuyin - Zheng Wei - Deming-Halverson Sandra - Shrubsole Martha - Long Jirong - Simard Jacques - Garcia-Closas Montse - Pharoah Paul D P - Chenevix-Trench Georgia - Dunning Alison M - Benitez Javier - Easton Douglas F

Nature Genetics; 2013 Apr;45(4):353-61, 361e1-2. doi: 10.1038/ng.2563

[PMID: 23535729] IF 35.209

Multiple independent variants at the TERT locus are associated with telomere length and risks of breast and ovarian cancer.

Bojesen Stig E - Pooley Karen A - Johnatty Sharon E - Beesley Jonathan - Michailidou Kyriaki - Tyrer Jonathan P - Edwards Stacey L - Pickett Hilda A - Shen Howard C - Smart Chanel E - Hillman Kristine M - Mai Phuong L - Lawrenson Kate - Stutz Michael D - Lu Yi - Karevan Rod - Woods Nicholas - Johnston Rebecca L - French Juliet D - Chen Xiaoqing - Weischer Maren - Nielsen Sune F - Maranian Melanie J - Ghousaini Maya - Ahmed Shahana - Baynes Caroline - Bolla Manjeet K - Wang Qin - Dennis Joe - McGuffog Lesley - Barrowdale Daniel - Lee Andrew - Healey Sue - Lush Michael - Tessier Daniel C - Vincent Daniel - Bacot Francis - Australian Cancer Study - Australian Ovarian Cancer Study - Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer (kConFab) - Gene Environment Interaction and Breast Cancer (GENICA) - Swedish Breast Cancer Study (SWE-BRCA) - Hereditary Breast and Ovarian Cancer Research Group Netherlands (HEBON) - Epidemiological study of BRCA1 & BRCA2 Mutation Carriers (EMBRACE) - Genetic Modifiers of Cancer Risk in BRCA1/2 Mutation Carriers (GEMO) - Vergote Ignace - Lambrechts Sandrina - Despiere Evelyn - Risch Harvey A - González-Neira Anna - Rossing Mary Anne - Pita Guillermo - Doherty Jennifer A - Alvarez Nuria - Larson Melissa C - Fridley Brooke L - Schoof Nils - Chang-Claude Jenny - Cicek Mine S - Peto Julian - Kalli Kimberly R - Brooks Annegien - Armasu Sebastian M - Schmidt Marjanka K - Braaf Linde M - Winterhoff Boris - Nevanlinna Heli - Konecny Gottfried E - Lambrechts Diether - Rogmann Lisa - Guénel Pascal - Teoman Attila - Milne Roger L - Garcia Joaquin J - Cox Angela - Shridhar Vijayalakshmi - Burwinkel Barbara - Marme Frederik - Hein Rebecca - Sawyer Elinor J - Haiman Christopher A - Wang-Gohrke Shan - Andrulis Irene L - Moysich Kirsten B - Hopper John L - Odunsi Kunle - Lindblom Annika - Giles Graham G - Brenner Hermann - Simard Jacques - Lurie Galina - Fasching Peter A - Carney Michael E - Radice Paolo - Wilkens Lynne R - Swerdlow Anthony - Goodman Marc T - Brauch Hiltrud - Garcia-Closas Montserrat - Hillemanns Peter - Winqvist Robert - Dürst Matthias - Devilee Peter - Runnebaum Ingo - Jakubowska Anna - Lubinski Jan - Mannermaa Arto - Butzow Ralf - Bogdanova Natalia V - Dörk Thilo - Peltari Liisa M - Zheng Wei - Leminen Arto - Anton-Culver Hoda - Bunker Clareann H - Kristensen Vessela - Ness Roberta B - Muir Kenneth - Edwards Robert - Meindl Alfons - Heitz Florian - Matsuo Keitaro - du Bois Andreas - Wu Anna H - Harter Philipp - Teo Soo-Hwang - Schwaab Ira - Shu Xiao-Ou - Blot William - Hosono Satoyo - Kang Daehee - Nakanishi Toru - Hartman Mikael - Yatabe Yasushi - Hamann Ute - Karlan Beth Y - Sangrajrang Suleeporn - Kjaer Susanne Krüger - Gaborieau Valerie - Jensen Allan - Eccles Diana - Høgdall Estrid - Shen Chen-Yang - Brown Judith - Woo Yin Ling - Shah Mitul - Azmi Mat Adenan Noor - Luben Robert - Omar Siti Zawiah - Czene Kamila - Vierkant Robert A - Nordestgaard Børge G - Flyger Henrik - Vachon Celine - Olson Janet E - Wang Xianshu - Levine Douglas A - Rudolph Anja - Weber Rachel Palmieri - Flesch-Janys Dieter - Iversen Edwin - Nickels Stefan - Schildkraut Joellen M - Silva Isabel Dos Santos - Cramer Daniel W - Gibson Lorna - Terry Kathryn L - Fletcher Olivia - Vitonis Allison F - van der Schoot C Ellen - Poole Elizabeth M - Hogervorst Frans B L - Tworoger Shelley S - Liu Jianjun - Bandera Elisa V - Li Jingmei - Olson Sara H - Humphreys Keith - Orlov Irene - Blomqvist Carl - Rodriguez-Rodriguez Lorna - Aittomäki Kristiina - Salvesen Helga B - Muranen Taru A - Wik Elisabeth - Brouwers Barbara - Krakstad Camilla - Wauters Els - Halle Mari K - Wildiers Hans - Kiemeny Lambertus A - Mulot Claire - Aben Katja K -

Laurent-Puig Pierre - Altena Anne Mvan - Truong Thérèse - Massuger Leon F A G - Benitez Javier - Pejovic Tanja - Perez Jose Ignacio Arias - Hoatlin Maureen - Zamora M Pilar - Cook Linda S - Balasubramanian Sabapathy P - Kelemen Linda E - Schneeweiss Andreas - Le Nhu D - Sohn Christof - Brooks-Wilson Angela - Tomlinson Ian - Kerin Michael J - Miller Nicola - Cybulski Cezary - Henderson Brian E - Menkiszak Janusz - Schumacher Fredrick - Wentzensen Nicolas - Le Marchand Loic - Yang Hannah P - Mulligan Anna Marie - Glendon Gord - Engelholm Svend Aage - Knight Julia A - Høgdall Claus K - Apicella Carmel - Gore Martin - Tsimiklis Helen - Song Honglin - Southey Melissa C - Jager Agnes - den Ouweland Ans M Wvan - Brown Robert - Martens John W M - Flanagan James M - Kriege Mieke - Paul James - Margolin Sara - Siddiqui Nadeem - Severi Gianluca - Whittemore Alice S - Baglietto Laura - McGuire Valerie - Stegmaier Christa - Sieh Weiva - Müller Heiko - Arndt Volker - Labrèche France - Gao Yu-Tang - Goldberg Mark S - Yang Gong - Dumont Martine - McLaughlin John R - Hartmann Arndt - Ekici Arif B - Beckmann Matthias W - Phelan Catherine M - Lux Michael P - Permeth-Wey Jenny - Peissel Bernard - Sellers Thomas A - Ficarazzi Filomena - Barile Monica - Ziogas Argyrios - Ashworth Alan - Gentry-Maharaj Aleksandra - Jones Michael - Ramus Susan J - Orr Nick - Menon Usha - Pearce Celeste L - Brüning Thomas - Pike Malcolm C - Ko Yon-Dschun - Lissowska Jolanta - Figueroa Jonine - Kupryjanczyk Jolanta - Chanock Stephen J - Dansonka-Mieszkowska Agnieszka - Jukkola-Vuorinen Arja - Rzepecka Iwona K - Pylkäs Katri - Bidzinski Mariusz - Kauppila Saila - Hollestelle Antoinette - Seynaeve Caroline - Tollenaar Rob A E M - Durda Katarzyna - Jaworska Katarzyna - Hartikainen Jaana M - Kosma Veli-Matti - Kataja Vesa - Antonenkova Natalia N - Long Jirong - Shrubsole Martha - Deming-Halverson Sandra - Lophatananon Artitaya - Siriwanarangsarn Pornthep - Stewart-Brown Sarah - Ditsch Nina - Lichtner Peter - Schmutzler Rita K - Ito Hidemi - Iwata Hiroji - Tajima Kazuo - Tseng Chiu-Chen - Stram Daniel O - van den Berg David - Yip Cheng Har - Ikram M Kamran - Teh Yew-Ching - Cai Hui - Lu Wei - Signorello Lisa B - Cai Qiuyin - Noh Dong-Young - Yoo Keun-Young - Miao Hui - Iau Philip Tsau-Choong - Teo Yik Ying - McKay James - Shapiro Charles - Ademuyiwa Foluso - Fountzilas George - Hsiung Chia-Ni - Yu Jyh-Cherng - Hou Ming-Feng - Healey Catherine S - Luccarini Craig - Peock Susan - Stoppa-Lyonnet Dominique - Peterlongo Paolo - Rebbeck Timothy R - Piedmonte Marion - Singer Christian F - Friedman Eitan - Thomassen Mads - Offit Kenneth - Hansen Thomas V O - Neuhausen Susan L - Szabo Csilla I - Blanco Ignacio - Garber Judy - Narod Steven A - Weitzel Jeffrey N - Montagna Marco - Olah Edith - Godwin Andrew K - Yannoukakos Drakoulis - Goldgar David E - Caldes Trinidad - Imyanitov Evgeny N - Tihomirova Laima - Arun Banu K - Campbell Ian - Mensenkamp Arjen R - van Asperen Christi J - van Roozendaal Kees E P - Meijers-Heijboer Hanne - Collée J Margriet - Oosterwijk Jan C - Hooning Maartje J - Rookus Matti A - van der Luijt Rob B - Os Theo A Mvan - Evans D Gareth - Frost Debra - Fineberg Elena - Barwell Julian - Walker Lisa - Kennedy M John - Platte Radka - Davidson Rosemarie - Ellis Steve D - Cole Trevor - Bressac-de Paillerets Brigitte - Buecher Bruno - Damiola Francesca - Faivre Laurence - Frenay Marc - Sinilnikova Olga M - Caron Olivier - Giraud Sophie - Mazoyer Sylvie - Bonadona Valérie - Caux-Moncoutier Virginie - Toloczko-Grabarek Aleksandra - Gronwald Jacek - Byrski Tomasz - Spurdle Amanda B - Bonanni Bernardo - Zaffaroni Daniela - Giannini Giuseppe - Bernard Loris - Dolcetti Riccardo - Manoukian Siranoush - Arnold Norbert - Engel Christoph - Deissler Helmut - Rhiem Kerstin - Niederacher Dieter - Plendl Hansjoerg - Sutter Christian - Wappenschmidt Barbara - Borg Ake - Melin Beatrice - Rantala Johanna - Soller Maria - Nathanson Katherine L - Domchek Susan M - Rodriguez Gustavo C - Salani Ritu - Kaulich Daphne Gschwantler - Tea Muy-Kheng - Paluch Shani Shimon - Laitman Yael - Skytte Anne-Bine - Kruse Torben A - Jensen Uffe Birk - Robson Mark - Gerdes Anne-Marie - Ejlersen Bent - Foretova Lenka - Savage Sharon A - Lester Jenny - Soucy Penny - Kuchenbaecker Karoline B - Olswold Curtis - Cunningham Julie M - Slager Susan - Pankratz Vernon S - Dicks Ed - Lakhani Sunil R - Couch Fergus J - Hall Per - Monteiro Alvaro N A - Gayther Simon A - Pharoah Paul D P - Reddel Roger R - Goode Ellen L - Greene Mark H - Easton Douglas F - Berchuck Andrew - Antoniou Antonis C - Chenevix-Trench Georgia - Dunning Alison M

Nature Genetics; 2013 Apr;45(4):371-84, 384e1-2. doi: 10.1038/ng.2566

[PMID: 23535731] IF 35.209

Premature Cdk1/Cdc5/Mus81 pathway activation induces aberrant replication and deleterious crossover.

Szakai Barnabas - Branzei Dana

The EMBO Journal; 2013 Apr 17;1(2):123-38. doi: 10.1016/j.stemcr.2013.06.004

[PMID: 23531881] IF 9.822

Recessive cancer genes engage in negative genetic interactions with their functional paralogs.

D'Antonio Matteo - Guerra Rosalinda F - Cereda Matteo - Marchesi Stefano - Montani Francesca - Nicassio Francesco - Di Fiore Pier Paolo - Ciccarelli Francesca D

Cell Reports; 2013 Apr 25;3(4):1321-33. doi: 10.1016/j.celrep.2013.03.029

[PMID: 24360954]

Elevated expression of the V-ATPase C subunit triggers JNK-dependent cell invasion and overgrowth in a Drosophila epithelium.

Petzoldt Astrid G - Gleixner Eva Maria - Fumagalli Arianna - Vaccari Thomas - Simons Matias

Dis Model Mech; 2013 May;6(3):689-700. doi: 10.1242/dmm.010660

[PMID: 23335205] IF 4.959

Segregation of the Qb-SNAREs GS27 and GS28 into Golgi vesicles regulates intra-Golgi transport.

Fusella Aurora - Micaroni Massimo - Di Giandomenico Daniele - Mironov Alexandre A - Beznoussenko Galina V

Traffic; 2013 May;14(5):568-84. doi: 10.1111/tra.12055

[PMID: 23387339] IF 4.652

COMPLEXO: identifying the missing heritability of breast cancer via next generation collaboration.

COMPLEXO - Southey Melissa C - Park Daniel J - Nguyen-Dumont Tu - Campbell Ian - Thompson Ella - Trainer Alison H - Chenevix-Trench Georgia - Simard Jacques - Dumont Martine - Soucy Penny - Thomassen Mads - Jønson Lars - Pedersen Inge S - Hansen Thomas Vo - Nevanlinna Heli - Khan Sofia - Sinilnikova Olga - Mazoyer Sylvie - Lesueur Fabienne - Damiola Francesca - Schmutzler Rita - Meindl Alfons - Hahnen Eric - Dufault Michael R - Chris Chan Tl - Kwong Ava - Barkardóttir Rosa - Radice Paolo - Peterlongo Paolo - Devilee Peter - Hilbers Florentine - Benitez Javier - Kvist Anders - Törngren Therese - Easton Douglas - Hunter David - Lindstrom Sara - Kraft Peter - Zheng Wei - Gao Yu-Tang - Long Jirong - Ramus Susan - Feng Bing-Jian - Weitzel Jeffrey N - Nathanson Katherine - Offit Kenneth - Joseph Vijai - Robson Mark - Schrader Kasmintan - Wang San Ming - Kim Yeong C - Lynch Henry - Snyder Carrie - Tavtigian Sean - Neuhausen Susan - Couch Fergus J - Goldgar David E

Breast Cancer Research; 2013 Jun 21;15(3):402; issn 1465-542X doi 10.1186/bcr3434

[PMID: 23809231] IF: 5.872

CIP4 controls CCL19-driven cell steering and chemotaxis in chronic lymphocytic leukemia.

Malet-Engra Gema - Viaud Julien - Ysebaert Loïc - Farcé Manon - Lafouresse Fanny - Laurent Guy - Gaits-Iacovoni Frédérique - Scita Giorgio - Dupré Loïc

Cancer Research; 2013 Jun 1;73(11):3412-24. doi: 10.1158/0008-5472.CAN-12-3564

[PMID: 23644527] IF: 8.650

EndMT contributes to the onset and progression of cerebral cavernous malformations.

Maddaluno Luigi - Rudini Noemi - Cuttano Roberto - Bravi Luca - Giampietro Costanza - Corada Monica - Ferrarini Luca - Orsenigo Fabrizio - Papa Eleanna - Boulday Gwenola - Tournier-Lasserre Elisabeth - Chapon Françoise - Richichi Cristina - Retta Saverio Francesco - Lampugnani Maria Grazia - Dejana Elisabetta

Nature; 2013 Jun 27;498(7455):492-6. doi: 10.1038/nature12207

[PMID: 23748444] IF 38.597

Endothelial adherens junctions at a glance.

Dejana Elisabetta - Orsenigo Fabrizio

Journal of Cell Science; 2013 Jun 15;126(Pt 12):2545-9. doi: 10.1242/jcs.124529

[PMID: 23781019] IF 5.877

Gold-nanoparticle-based colorimetric discrimination of cancer-related point mutations with picomolar sensitivity.

Valentini Paola - Fiammengo Roberto - Sabella Stefania - Gariboldi Manuela - Maiorano Gabriele - Cingolani Roberto - Pompa Pier Paolo

ACS Nano; 2013, Jun, 25; vol.7, issue 6; doi 10.1021/nn401757w;

[PMID: 23697628] IF: 12.062

Oxidative stress activates a specific p53 transcriptional response that regulates cellular senescence and aging.

Gambino Valentina - De Michele Giulia - Venezia Oriella - Migliaccio Pierluigi - Dall'Olio Valentina - Bernard Loris - Minardi Simone Paolo - Della Fazia Maria Agnese - Bartoli Daniela - Servillo Giuseppe - Alcalay Myriam - Luzi Lucilla - Giorgio Marco - Scrable Heidi - Pelicci Pier Giuseppe - Migliaccio Enrica

Aging Cell, 2013 Jun; 12(3); doi 10.1111/accel.12060;

[PMID: 23448364] IF: 5.705

Silencing of mammalian Sar1 isoforms reveals COPII-independent protein sorting and transport.

Cutrona Meritxell B - Beznoussenko Galina V - Fusella Aurora - Martella Oliviano - Moral Pedro - Mironov Alexander A

Traffic; 2013 Jun;14(6):691-708. doi: 10.1111/tra.12060

[PMID: 23433038] IF 4.652

Structure of a ubiquitin-loaded HECT ligase reveals the molecular basis for catalytic priming.

Maspero Elena - Valentini Eleonora - Mari Sara - Cecatiello Valentina - Soffientini Paolo - Pasqualato Sebastiano - Polo Simona

Nature Structural & Molecular Biology; 2013 Jun;20(6):696-701. doi: 10.1038/nsmb.2566

[PMID: 23644597] IF 11.902

Ubiquitination dynamics in the early-branching eukaryote *Giardia intestinalis*.

Niño Carlos A - Chaparro Jenny - Soffientini Paolo - Polo Simona - Wasserman Moises

Microbiology Open; 2013 Jun;2(3):525-39. doi: 10.1002/mbo3.88

[PMID: 23613346]

Urokinase plasminogen activator receptor: a functional integrator of extracellular proteolysis, cell adhesion, and signal transduction.

Ferraris Gian Maria Sarra - Sidenius Nicolai

Seminars in Thrombosis and Hemostasis; 2013 Jun;39(4):347-55. doi: 10.1055/s-0033-1334485

[PMID: 23532573] IF 4.216

Threshold-controlled ubiquitination of the EGFR directs receptor fate.

Sigismund Sara - Algisi Veronica - Nappo Gilda - Conte Alexia - Pascolutti Roberta - Cuomo Alessandro - Bonaldi Tiziana - Argenzio Elisabetta - Verhoef Lisette G G C - Maspero Elena - Bianchi Fabrizio - Capuani Fabrizio - Ciliberto Andrea - Polo Simona - Di Fiore Pier Paolo

The EMBO Journal; 2013 Jul 31;32(15):2140-57. doi: 10.1038/emboj.2013.149

[PMID: 23799367] IF 9.822

DNA damage checkpoint and recombinational repair differentially affect the replication stress tolerance of Smc6 mutants.

Chen Yu-Hung - Szakal Barnabas - Castellucci Federica - Branzei Dana - Zhao Xiaolan

Molecular Biology of the Cell; 2013 Aug;24(15):2431-41. doi: 10.1091/mbc.E12-11-0836

[PMID: 23783034] IF 4.604

Progressive hearing loss and gradual deterioration of sensory hair bundles in the ears of mice lacking the actin-binding protein Eps8L2.

Furness David N - Johnson Stuart L - Manor Uri - Rüttiger Lukas - Tocchetti Arianna - Offenhauser Nina - Olt Jennifer - Goodyear Richard J - Vijayakumar Sarath - Dai Yuhai - Hackney Carole M - Franz Christoph - Di Fiore Pier Paolo - Masetto Sergio - Jones Sherri M - Knipper Marlies - Holley Matthew C - Richardson Guy P - Kachar Bechara - Marcotti Walter

Proceedings of the National Academy of Sciences of U.S.A.; 2013 Aug 20;110(34):13898-903. doi: 10.1073/pnas.1304644110

[PMID: 23918390] IF 9.737

The LXR-IDOL axis defines a clathrin-, caveolae-, and dynamin-independent endocytic route for LDLR internalization and lysosomal degradation.

Sorrentino Vincenzo - Nelson Jessica K - Maspero Elena - Marques André R A - Scheer Lilith - Polo Simona - Zelcer Noam

Journal of Lipid Research; 2013 Aug;54(8):2174-84. doi: 10.1194/jlr.M037713

[PMID: 23733886] IF 4.386

Adaptation to the spindle checkpoint is regulated by the interplay between Cdc28/Clbs and PP2A^{Cdc55}.

Vernieri Claudio - Chioli Elena - Francia Valentina - Gross Fridolin - Ciliberto Andrea

The Journal of Cell Biology; 2013 Sep 2;202(5):765-78. doi: 10.1083/jcb.201303033

[PMID: 23999167] IF 10.822

KRAS gene amplification in colorectal cancer and impact on response to EGFR-targeted therapy.

Valtorta Emanuele - Misale Sandra - Sartore-Bianchi Andrea - Nagtegaal Iris D - Paraf François - Lauricella Calogero - Dimartino Valentina - Hobor Sebastijan - Jacobs Bart - Ercolani Cristiana - Lamba Simona - Scala Elisa - Veronese Silvio - Laurent-Puig Pierre - Siena Salvatore - Tejpar Sabine - Mottolese Marcella - Punt Cornelis J A - Gambacorta Marcello - Bardelli Alberto - Di Nicolantonio Federica

International Journal of Cancer; 2013 Sep 1;133(5):1259-65. doi: 10.1002/ijc.28106

[PMID: 23404247] IF 6.198

T cell-derived IL-17 mediates epithelial changes in the airway and drives pulmonary neutrophilia.

Fogli Laura K - Sundrud Mark S - Goel Swati - Bajwa Sofia - Jensen Kari - Derudder Emmanuel - Sun Amy - Coffre Maryaline - Uyttenhove Catherine - Van Snick Jacques - Schmidt-Supprian Marc - Rao Anjana - Grunig Gabriele - Durbin Joan - Casola Stefano - Casola Stefano S - Rajewsky Klaus - Koralov Sergei B

Journal of Immunology; 2013 Sep 15;191(6):3100-11. doi: 10.4049/jimmunol.1301360

[PMID: 23966625] IF 5.520

VE-cadherin and endothelial adherens junctions: active guardians of vascular integrity.

Giannotta Monica - Trani Marianna - Dejana Elisabetta

Developmental Cell; 2013 Sep 16;26(5):441-54. doi: 10.1016/j.devcel.2013.08.020

[PMID: 24044891] IF 12.861

A direct role for small non-coding RNAs in DNA damage response.

d'Adda di Fagagna Fabrizio

Trends in Cell Biology; 2013 Oct; doi: 10.1016/j.tcb.2013.09.008

[PMID: 24156824] IF 11.721

A normalization strategy for the analysis of plasma microRNA qPCR data in colorectal cancer.

Pizzamiglio Sara - Bottelli Stefano - Ciniselli Chiara Maura - Zanutto Susanna - Bertan Claudia - Gariboldi Manuela - Pierotti Marco Alessandro - Verderio Paolo

International Journal of Cancer; 2013 oct 8;1 doi: 10.1002/ijc.28530

[PMID: 24150995] IF 6.198

Golgi's way: a long path toward the new paradigm of the intra-Golgi transport.

Mironov Alexander A - Sesorova Irina V - Beznoussenko Galina V

Histochemistry and Cell Biology; 2013 Oct;140(4):383-93. doi: 10.1007/s00418-013-1141-6

[PMID: 24068461] IF 2.613

Membrane and actin dynamics interplay at lamellipodia leading edge.

Bisi Sara - Disanza Andrea - Malinverno Chiara - Frittoli Emanuela - Palamidessi Andrea - Scita Giorgio

Current Opinion in Cell Biology; 2013 Oct;25(5):565-73. doi: 10.1016/j.ceb.2013.04.001

[PMID: 23639310] IF 11.410

A large-scale assessment of two-way SNP interactions in breast cancer susceptibility using 46 450 cases and 42 461 controls from the breast cancer association consortium.

Milne Roger L - Herranz Jesús - Michailidou Kyriaki - Dennis Joe - Tyrer Jonathan P - Zamora M Pilar - Arias-Perez José Ignacio - González-Neira Anna - Pita Guillermo - Alonso M Rosario - Wang Qin -

Bolla Manjeet K - Czene Kamila - Eriksson Mikael - Humphreys Keith - Darabi Hatf - Li Jingmei - Anton-Culver Hoda - Neuhausen Susan L - Ziogas Argyrios - Clarke Christina A - Hopper John L - Dite Gillian S - Apicella Carmel - Southey Melissa C - Chenevix-Trench Georgia - !kConFab Investigators - Australian Ovarian Cancer Study Group - Swerdlow Anthony - Ashworth Alan - Orr Nicholas - Schoemaker Minouk - Jakubowska Anna - Lubinski Jan - Jaworska-Bieniek Katarzyna - Durda Katarzyna - Andrulis Irene L - Knight Julia A - Glendon Gord - Mulligan Anna Marie - Bojesen Stig E - Nordestgaard Børge G - Flyger Henrik - Nevanlinna Heli - Muranen Taru A - Aittomäki Kristiina - Blomqvist Carl - Chang-Claude Jenny - Rudolph Anja - Seibold Petra - Flesch-Janys Dieter - Wang Xianshu - Olson Janet E - Vachon Celine - Purrington Kristen - Winqvist Robert - Pylkäs Katri - Jukkola-Vuorinen Arja - Grip Mervi - Dunning Alison M - Shah Mitul - Guénel Pascal - Truong Thérèse - Sanchez Marie - Mulot Claire - Brenner Hermann - Dieffenbach Aida Karina - Arndt Volker - Stegmaier Christa - Lindblom Annika - Margolin Sara - Hooning

Maartje J - Hollestelle Antoinette - Collée J Margriet - Jager Agnes - Cox Angela - Brock Ian W - Reed Malcolm W R - Devilee Peter - Tollenaar Robert A E M - Seynaeve Caroline - Haiman Christopher A - Henderson Brian E - Schumacher Fredrick - Le Marchand Loic - Simard Jacques - Dumont Martine - Soucy Penny - Dörk Thilo - Bogdanova Natalia V - Hamann Ute - Försti Asta - Rüdiger Thomas - Ulmer Hans-Ulrich - Fasching Peter A - Häberle Lothar - Ekici Arif B - Beckmann Matthias W - Fletcher Olivia - Johnson Nichola - Dos Santos Silva Isabel - Peto Julian - Radice Paolo - Peterlongo Paolo - Peissel Bernard - Mariani Paolo - Giles Graham G - Severi Gianluca - Baglietto Laura - Sawyer Elinor - Tomlinson Ian - Kerin Michael - Miller Nicola - Marme Federik - Burwinkel Barbara - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - Lambrechts Diether - Yesilyurt Betül T - Floris Giuseppe - Leunen Karin - Alnæs Grethe Grenaker - Kristensen Vessela - Børresen-Dale Anne-Lise - García-Closas Montserrat - Chanock Stephen J - Lissowska Jolanta - Figueroa Jonine D - Schmidt Marjanka K - Broeks Annegien - Verhoef Senno - Rutgers Emiel J - Brauch Hiltrud - Brüning Thomas - Ko Yon-Dschun - The GENICA Network - Couch Fergus J - Toland Amanda E - The TNBCC - Yannoukakos Drakoulis - Pharoah Paul D P - Hall Per - Benítez Javier - Malats Núria - Easton Douglas F

Human Molecular Genetics; 2013 Nov; doi: 10.1093/hmg/ddt581

[PMID: 24242184] IF 7.692

Functional characterization of a novel FGFR1OP-RET rearrangement in hematopoietic malignancies.

Bossi Daniela - Carlomagno Francesca - Pallavicini Isabella - Pruneri Giancarlo - Trubia Maurizio - Raviele Paola Rafaniello - Marinelli Alessandra - Anaganti Suresh - Cox Maria Christina - Viale Giuseppe - Santoro Massimo - Di Fiore Pier Paolo - Minucci Saverio

Molecular Oncology; 2013 Nov; doi: 10.1016/j.molonc.2013.11.004

[PMID: 24315414] IF 6.701

Pharmacologic inhibition of vacuolar H⁺ ATPase reduces physiologic and oncogenic Notch signaling.

Kobia Francis - Duchi Serena - Deflorian Gianluca - Vaccari Thomas

Molecular Oncology; 2013 Nov; doi: 10.1016/j.molonc.2013.11.002

[PMID: 24309677] IF 6.701

Pknox1/Prep1 regulates mitochondrial oxidative phosphorylation components in skeletal muscle.

Kanzleiter Timo - Rath Michaela - Penkov Dmitry - Puchkov Dmytro - Schulz Nadja - Blasi Francesco - Schürmann Annette

Molecular and Cellular Biology; 2013 Jan;34(2):290-8. doi: 10.1128/MCB.01232-13

[PMID: 24216763] IF 5.372

Fine-scale mapping of the FGFR2 breast cancer risk locus: putative functional variants differentially bind FOXA1 and E2F1.

Meyer Kerstin B - O'Reilly Martin - Michailidou Kyriaki - Carlebur Saskia - Edwards Stacey L - French Juliet D - Prathalingham Radhika - Dennis Joe - Bolla Manjeet K - Wang Qin - de Santiago Ines - Hopper John L - Tsimiklis Helen - Apicella Carmel - Southey Melissa C - Schmidt Marjanka K - Broeks Annegien - Van 't Veer Laura J - Hogervorst Frans B - Muir Kenneth - Lophatananon Artitaya - Stewart-Brown Sarah - Siriwanarangsarn Pornthep - Fasching Peter A - Lux Michael P - Ekici Arif B - Beckmann Matthias W - Peto Julian - Dos Santos Silva Isabel - Fletcher Olivia - Johnson Nichola - Sawyer Elinor J - Tomlinson Ian - Kerin Michael J - Miller Nicola - Marme Federik - Schneeweiss Andreas - Sohn Christof - Burwinkel Barbara - Guénel Pascal - Truong Thérèse - Laurent-Puig Pierre - Menegaux Florence - Bojesen Stig E - Nordestgaard Børge G - Nielsen Sune F - Flyger Henrik - Milne Roger L - Zamora M Pilar - Arias Jose I - Benitez Javier - Neuhausen Susan - Anton-Culver Hoda - Ziogas Argyrios - Dur Christina C - Brenner Hermann - Müller Heiko - Arndt Volker - Stegmaier Christa - Meindl Alfons - Schmutzler Rita K - Engel Christoph - Ditsch Nina - Brauch Hiltrud - Brüning Thomas - Ko Yon-Dschun - GENICA Network - Nevanlinna Heli - Muranen Taru A - Aittomäki Kristiina - Blomqvist Carl - Matsuo Keitaro - Ito Hidemi - Iwata Hiroji - Yatabe Yasushi - Dörk Thilo - Helbig Sonja - Bogdanova Natalia V - Lindblom Annika - Margolin Sara - Mannermaa Arto - Kataja Vesa - Kosma Veli-Matti - Hartikainen Jaana M - Chenevix-

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American Journal of Human Genetics; 2013 Dec 5;93(6); doi 10.1016/j.ajhg.2013.10.026

[PMID: 24290378] IF: 11.202

Germinal center dysregulation by histone methyltransferase EZH2 promotes lymphomagenesis.

Caganova Marieta - Carrisi Chiara - Varano Gabriele - Mainoldi Federica - Zanardi Federica - Germain Pierre-Luc - George Laura - Alberghini Federica - Ferrarini Luca - Talukder Asoke K - Ponzoni Maurilio - Testa Giuseppe - Nojima Takuya - Doglioni Claudio - Kitamura Daisuke - Toellner Kai-M - Su I-hsin - Casola Stefano

the Journal of Clinical Investigation; 2013 Dec 2;123(12):5009-22. doi: 10.1172/JCI70626

[PMID: 24200695] IF 12.812

PREP1 deficiency downregulates hepatic lipogenesis and attenuates steatohepatitis in mice.

Oriente Francesco - Cabaro Serena - Liotti Antonietta - Longo Michele - Parrillo Luca - Pagano Teresa Bruna - Raciti Gregory Alexander - Penkov Dmitry - Paciello Orlando - Miele Claudia - Formisano Pietro - Blasi Francesco - Beguinot Francesco

Diabetologia; 2013 Dec;56(12):2713-22. doi: 10.1007/s00125-013-3053-3

[PMID: 24052111] IF 6.487

Proteomics strategies to identify SUMO targets and acceptor sites: a survey of RNA-binding proteins SUMOylation.

Filosa Giuseppe - Barabino Silvia M L - Bachi Angela

Neuromolecular Med; 2013 Dec;15(4):661-76. doi: 10.1007/s12017-013-8256-8

[PMID: 23979992] IF 4.492

Signaling and mechanical roles of E-cadherin.

Bhatt Tanay - Rizvi Abrar - Batta Surya Prakash Rao - Kataria Sunny - Jamora Colin

Cell Communication & Adhesion; 2013 Dec;20(6):189-99. doi: 10.3109/15419061.2013.854778

[PMID: 24205986] IF: 1.048

Skewed B cell differentiation affects lymphoid organogenesis but not T-cell mediated autoimmunity.

Colombo Emanuela - Tentorio Paolo - Musio Silvia - Rajewsky Klaus - Pedotti Rosetta - Casola Stefano - Farina Cinthia

Clinical and Experimental Immunology; 2013 Dic 11; doi: 10.1111/cei.12250

[PMID: 24325711] IF 3.409

The GTPase-activating protein RN-tre controls focal adhesion turnover and cell migration.

Palamidessi Andrea - Frittoli Emanuela - Ducano Nadia - Offenhauser Nina - Sigismund Sara - Kajiho Hiroaki - Parazzoli Dario - Oldani Amanda - Gobbi Marco - Serini Guido - Di Fiore Pier Paolo - Scita Giorgio - Lanzetti Letizia

Current Biology; 2013 Dec 2;23(23):2355-64. doi: 10.1016/j.cub.2013.09.060

[PMID: 24239119] IF 9.494



Corporate profile

IFOM, the FIRC Institute of Molecular Oncology, is an Italian highly technology, non-profit research centre supported by FIRC, the Italian Foundation for Cancer Research. Research conducted at IFOM aims to understand the molecular processes responsible for the onset and development of cancer.

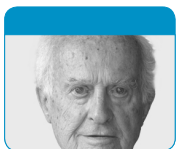
To meet the demands of modern-day science, IFOM created a research environment where scientists from the major national scientific institutions in the Milan area could collaborate and pool their organisational, economical and cultural resources. The creation of a research institute “network” was the first of its kind in Italy and has made IFOM an internationally competitive research centre in molecular oncology and functional genomics.

IFOM has been recognised as a Centre of Excellence for Research by the Lombardy Regional Council, which also contributed to IFOM’s development.

Having established a solid base in basic research, IFOM is now concentrating its efforts on translational research for the rapid transfer of scientific findings from the laboratory to diagnostic and therapeutic clinical practice. IFOM has adopted a strong international approach, fostering partnerships with world-class research institutes in Singapore and India. Thanks to these agreements, IFOM is becoming an important player in the global landscape of cancer research institutions.

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