ARTÍCULO DE MAYOR FACTOR DE IMPACTO OCTUBRE 2015

AMPK and PFKFB3 mediate glycolysis and survival in response to mitophagy during mitotic arrest

Elena Domènech, Carolina Maestre, Lorena Esteban-Martínez, David Partida,Rosa Pascual, Gonzalo Fernández-Miranda, Esther Seco, Ramón Campos-Olivas, Manuel Pérez, Diego Megias, Katherine Allen, Miguel López, Asishį K. Saha, Guillermo Velasco, Eduardo Rial, Raúl Méndez, Patricia Boya, María Salazar-Roa & Marcos Malumbres

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NATURE CELL BIOLOGY | ARTICLE

AMPK and PFKFB3 mediate glycolysis and survival in response to mitophagy during mitotic arrest

Elena Domènech, Carolina Maestre, Lorena Esteban-Martínez, David Partida, Rosa Pascual, Gonzalo Fernández-Miranda, Esther Seco, Ramón Campos-Olivas, Manuel Pérez, Diego Megias, Katherine Allen, Miguel López, Asish K. Saha, Guillermo Velasco, Eduardo Rial, Raúl Méndez, Patricia Boya, María Salazar-Roa & Marcos Malumbres

Nature Cell Biology 17, 1304–1316 (2015) doi:10.1038/ncb3231
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Abstract

Blocking mitotic progression has been proposed as an attractive therapeutic strategy to impair proliferation of tumour cells. However, how cells survive during prolonged mitotic arrest is not well understood. We show here that survival during mitotic arrest is affected by the special energetic requirements of mitotic cells. Prolonged mitotic arrest results in mitophagy-dependent loss of mitochondria, accompanied by reduced ATP levels and the activation of AMPK. Oxidative respiration is replaced by glycolysis owing to AMPK-dependent phosphorylation of PFKFB3 and increased production of this protein as a consequence of mitotic-specific translational activation of its mRNA. Induction of autophagy or inhibition of AMPK or PFKFB3 results in enhanced cell death in mitosis and improves the anti-tumoral efficiency of microtubule poisons in breast cancer cells. Thus, survival of mitotic-arrested cells is limited by their metabolic requirements, a feature with potential implications in cancer therapies aimed to impair mitosis or metabolism in tumour cells.

Subject terms: Apoptosis Cell signalling Energy metabolism Mitosis

ARTÍCULO DE MAYOR FACTOR DE IMPACTO NOVIEMBRE 2015

The consensus molecular subtypes of colorectal cancer.

Justin Guinney, Rodrigo Dienstmann, Xin Wang, Aurélien de Reyniès, Andreas Schlicker, Charlotte Soneson, Laetitia Marisa, Paul Roepman, Gift Nyamundanda, Paolo Angelino, Brian M Bot, Jeffrey S Morris, Iris M Simon, Sarah Gerster, Evelyn Fessler, Felipe De Sousa E Melo, Edoardo Missiaglia, Hena Ramay, David Barras, Krisztian Homicsko, Dipen Maru, Ganiraju C Manyam, Bradley Broom, Valerie Boige, Beatriz Perez-Villamil et al.

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The consensus molecular subtypes of colorectal cancer

Justin Guinney, Rodrigo Dienstmann, Xin Wang, Aurélien de Reyniès, Andreas Schlicker, Charlotte Soneson, Laetitia Marisa, Paul Roepman, Gift Nyamundanda, Paolo Angelino, Brian M Bot, Jeffrey S Morris, Iris M Simon, Sarah Gerster, Evelyn Fessler, Felipe De Sousa E Melo, Edoardo Missiaglia, Hena Ramay, David Barras, Krisztian Homicsko, Dipen Maru, Ganiraju C Manyam, Bradley Broom, Valerie Boige, Beatriz Perez-Villamil *et al.*

Nature Medicine (2015) doi:10.1038/nm.3967
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Abstract

Colorectal cancer (CRC) is a frequently lethal disease with heterogeneous outcomes and drug responses. To resolve inconsistencies among the reported gene expression–based CRC classifications and facilitate clinical translation, we formed an international consortium dedicated to large-scale data sharing and analytics across expert groups. We show marked interconnectivity between six independent classification systems coalescing into four consensus molecular subtypes (CMSs) with distinguishing features: CMS1 (microsatellite instability immune, 14%), hypermutated, microsatellite unstable and strong immune activation; CMS2 (canonical, 37%), epithelial, marked WNT and MYC signaling activation; CMS3 (metabolic, 13%), epithelial and evident metabolic dysregulation; and CMS4 (mesenchymal, 23%), prominent transforming growth factor–β activation, stromal invasion and angiogenesis. Samples with mixed features (13%) possibly represent a transition phenotype or intratumoral heterogeneity. We consider the CMS groups the most robust classification system currently available for CRC—with clear biological interpretability—and the basis for future clinical stratification and subtype-based targeted interventions.

Subject terms: Cancer genomics Colorectal cancer

ARTÍCULOS DE MAYOR FACTOR DE IMPACTO DICIEMBRE 2015

Coronary vascular regulation, remodelling, and collateralization: mechanisms and clinical implications on behalf of the working group on coronary pathophysiology and microcirculation

Axel R. Pries, Lina Badimon, Raffaele Bugiardini3, Paolo G. Camici, Maria Dorobantu5, Dirk J. Duncker, Javier Escaned, Akos Koller, Jan J. Piek, and Cor deWit.

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European Heart Journal
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CURRENT OPINION

Coronary vascular regulation, remodelling, and collateralization: mechanisms and clinical implications on behalf of the working group on coronary pathophysiology and microcirculation

Axel R. Pries[1]*, Lina Badimon[2], Raffaele Bugiardini[3], Paolo G. Camici[4], Maria Dorobantu[5], Dirk J. Duncker[6], Javier Escaned[7], Akos Koller[8], Jan J. Piek[9], and Cor de Wit[10]*

[1]Department of Physiology, Charitè-University Medicine Berlin, Thielallee 71, D-14195 Berlin, Germany; [2]Cardiovascular Research Center, CSIC-ICCC, Hospital de la Santa Creu i Sant Pau, CIBERObn-Institute Carlos III, Barcelona, Spain; [3]Department of Internal Medicine, Section of Cardiology, Policlinico S. Orsola, 40138 Bologna, Italy; [4]Department of Cardio-Thoracic-Vascular Medicine, San Raffaele Scientific Institute and Vita-Salute University San Raffaele, Milan, Italy; [5]University of Medicine and Pharmacy "Carol Davila" of Bucharest, Emergency Clinical Hospital of Bucharest, Cardiology Department, Bucureşti, Romania; [6]Experimental Cardiology, Thoraxcenter, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands; [7]Cardiovascular Institute, Hospital Clínico San Carlos, 28040 Madrid, Spain; [8]Department of Pathophysiology and Gerontology, University of Physical Education, Budapest, Hungary and Department of Physiology NYMC, Valhalla, USA; [9]AMC Heart Center, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands; and [10]Institut für Physiologie, Universität zu Lübeck and Deutsches Zentrumfür Herz-Kreislauf-Forschung (DZHK) e.V., partner site: Hamburg/Kiel/Lübeck, Lübeck, Germany

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Deferral vs. performance of percutaneous coronary intervention of functionallynon-significant coronary stenosis: 15-yearfollow-up of the DEFER trial

Frederik M. Zimmermann, Angela Ferrara, Nils P. Johnson, Lokien X. van Nunen, Javier Escaned, Per Albertsson, Raimund Erbel, Victor Legrand,Hyeong-Cheol Gwon, Wouter S. Remkes, Pieter R. Stella, Pepijn van Schaardenburgh, G. JanWillemBech, Bernard De Bruyne, and Nico H.J. Pijls.

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CLINICAL RESEARCH
Coronary artery disease

Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial

Frederik M. Zimmermann[1], Angela Ferrara[2], Nils P. Johnson[3], Lokien X. van Nunen[1,4], Javier Escaned[5], Per Albertsson[6], Raimund Erbel[7], Victor Legrand[8], Hyeong-Cheol Gwon[9], Wouter S. Remkes[10], Pieter R. Stella[11], Pepijn van Schaardenburgh[12], G. Jan Willem Bech[13,14], Bernard De Bruyne[2], and Nico H.J. Pijls[1,4]*

[1]Department of Cardiology, Catharina Hospital Eindhoven, Michelangelolaan 2, Eindhoven 5623 EJ, The Netherlands; [2]Cardiovascular Center, Aalst, Belgium; [3]Weatherhead PET Center For Preventing and Reversing Atherosclerosis, Division of Cardiology, Department of Medicine, University of Texas Medical School and Memorial Hermann Hospital, Houston, TX, USA; [4]Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands; [5]Hospital Clínico San Carlos/Faculty of Medicine, Complutense University of Madrid, and Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain; [6]Department of Cardiology, Sahlgrenska University Hospital Gothenburg, Sweden; [7]Department of Cardiology, West-German Heart and Vascular Centre, University Hospital of Essen, Essen, Germany; [8]Department of Cardiology, University Hospital of Liège, Liège, Belgium; [9]Division of Cardiology, Cardiac and Vascular Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [10]Department of Cardiology, Isala Klinieken, Zwolle, The Netherlands; [11]Department of Interventional Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands; [12]Department of Cardiology, VieCuri, Venlo, The Netherlands; [13]Department of Cardiology, HagaZiekenhuis, The Hague, The Netherlands; and [14]Reinier de Graaf Groep, Delft, The Netherlands

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