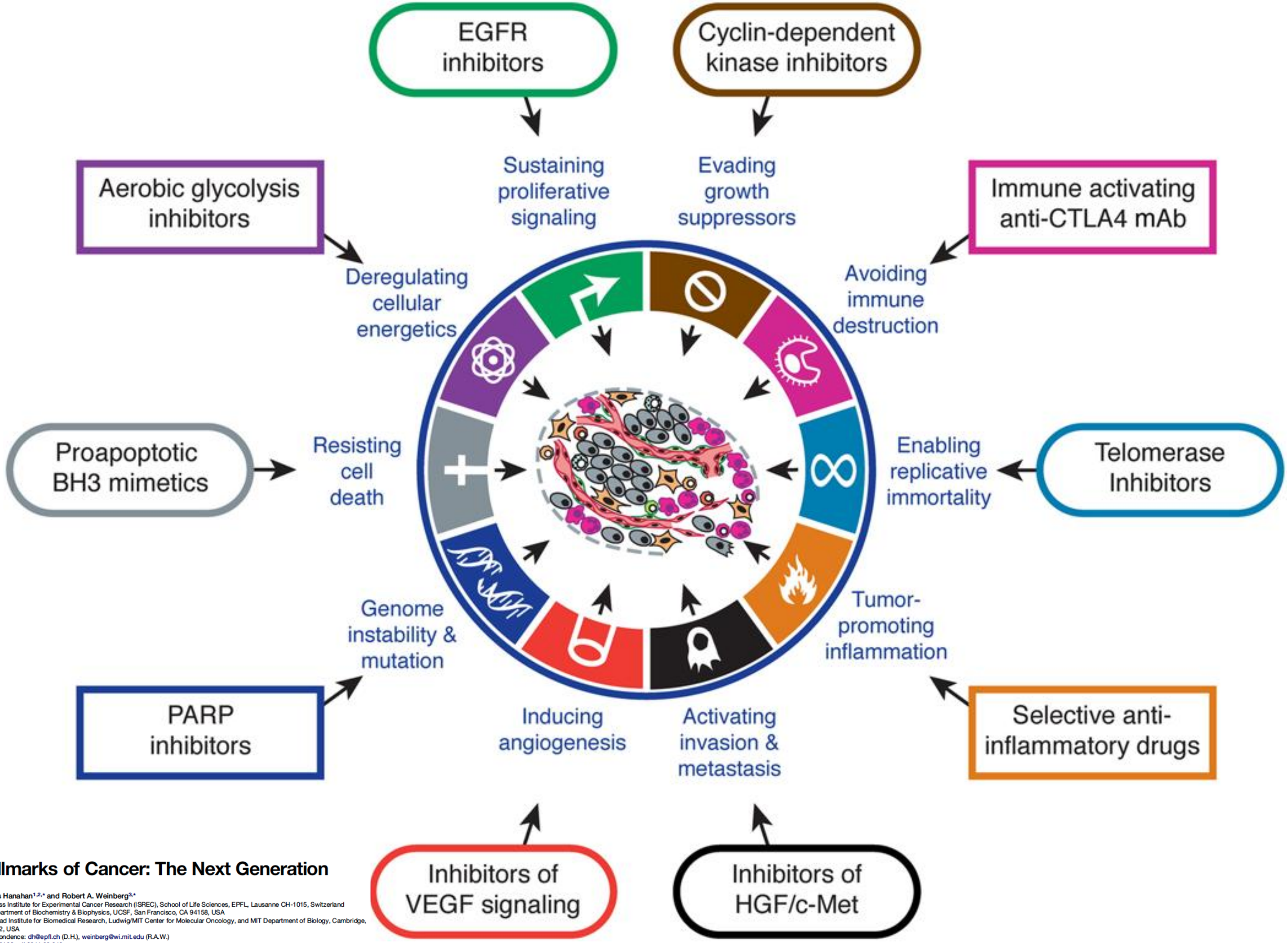
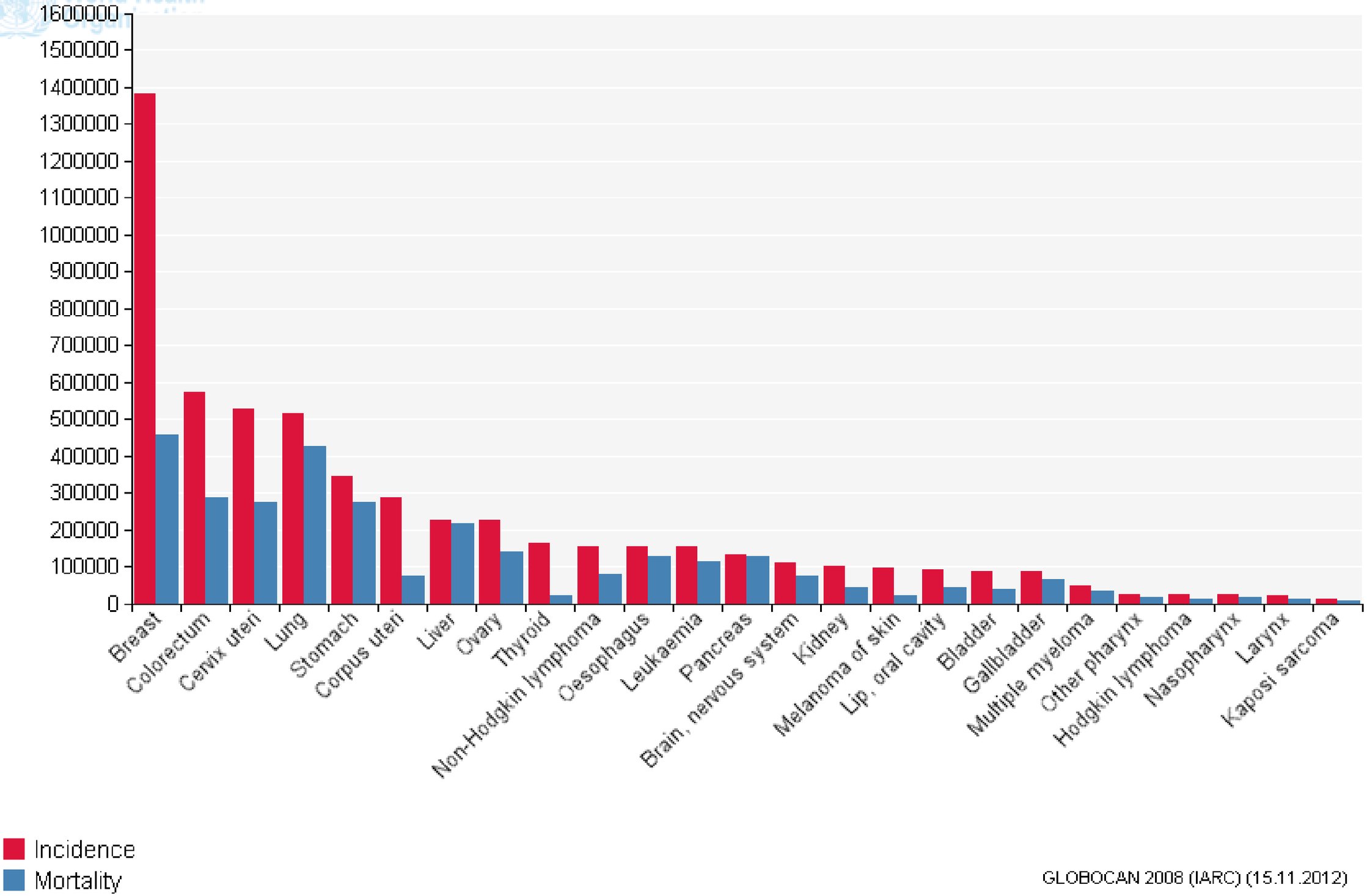
- Declaro não ter qualquer conflito de interesse



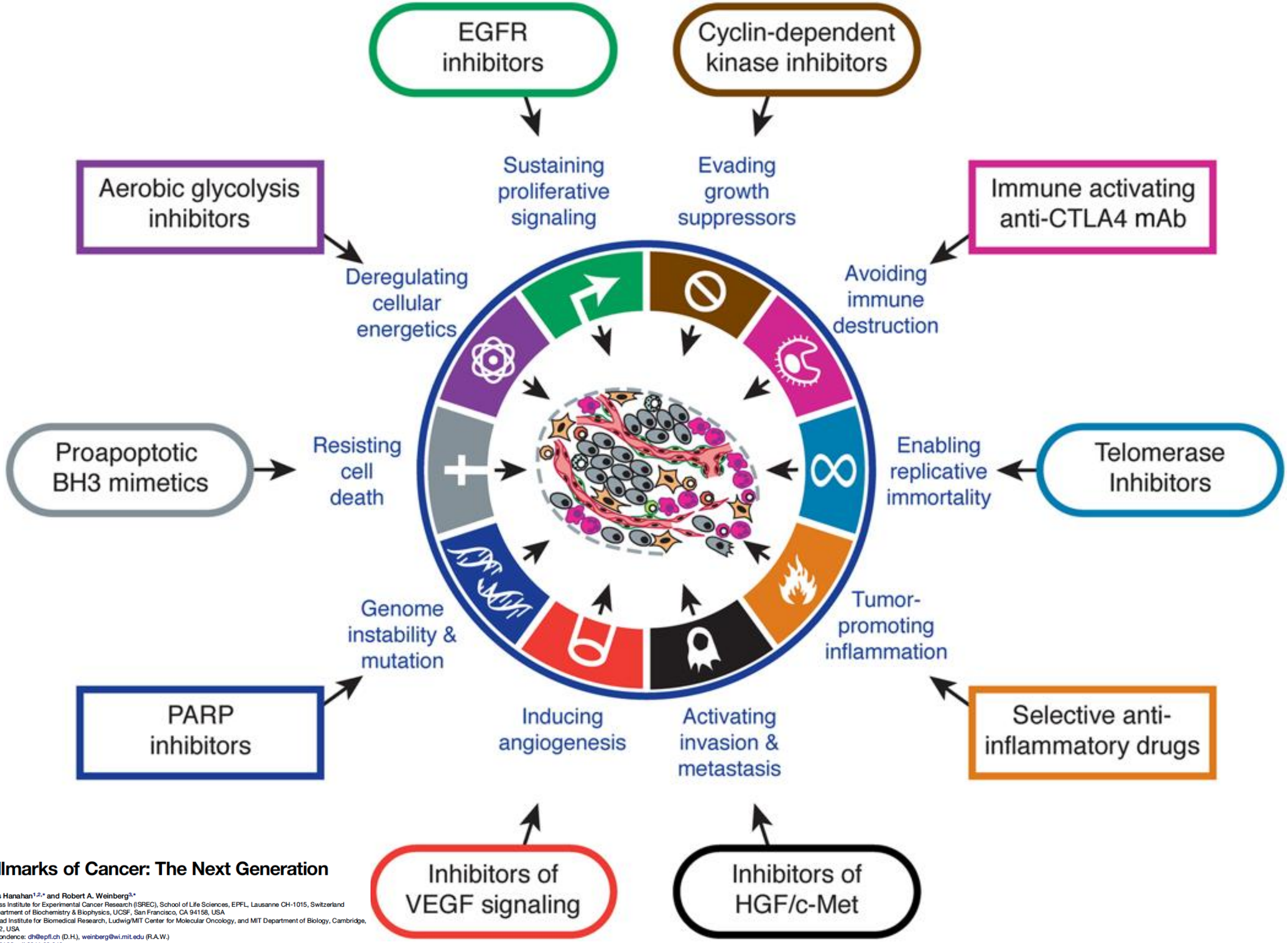
Hallmarks of Cancer: The Next Generation

Douglas Hanahan[1,2,*] and Robert A. Weinberg[3,*]
[1]The Swiss Institute for Experimental Cancer Research (ISREC), School of Life Sciences, EPFL, Lausanne CH-1015, Switzerland
[2]The Department of Biochemistry & Biophysics, UCSF, San Francisco, CA 94158, USA
[3]Whitehead Institute for Biomedical Research, Ludwig/MIT Center for Molecular Oncology, and MIT Department of Biology, Cambridge, MA 02142, USA
*Correspondence: dh@epfl.ch (D.H.), weinberg@wi.mit.edu (R.A.W.)
DOI 10.1016/j.cell.2011.02.013

World: Women, all ages



GLOBOCAN 2008 (IARC) (15.11.2012)



Hallmarks of Cancer: The Next Generation

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*Correspondence: dh@epfl.ch (D.H.), weinberg@wi.mit.edu (R.A.W.)
DOI 10.1016/j.cell.2011.02.013

Influência da hipoxia tumoral na manutenção do fenótipo tronco-celular e resistência a quimioterapia

Prof. Dr. Daniel G Tiezzi
Setor de Mastologia e Oncologia Ginecológica
Faculdade de Medicina de Ribeirão Preto
Universidade de São Paulo

Departamento Ginecologia e Obstetrícia
Faculdade de Medicina de Ribeirão Preto - FMRP/USP

FAPESP
FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE SÃO PAULO

FACULDADE de MEDICINA de RIBEIRÃO PRETO
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Hipóxia tecidual e câncer

- Thomlinson e Gray (1955) - resistência à radioterap

- Hipóxia - influência na ação de drogas citotóxicas

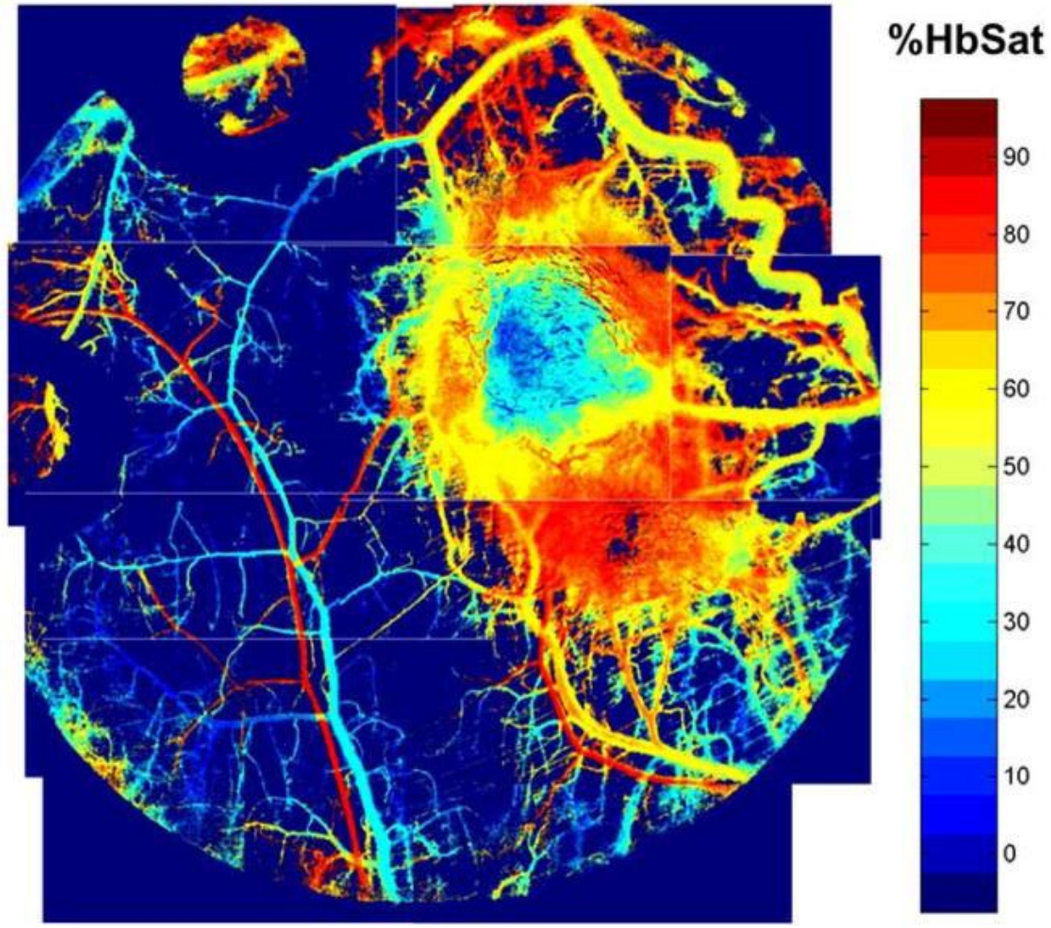
- Hipóxia e prognóstico em neoplasias sólidas

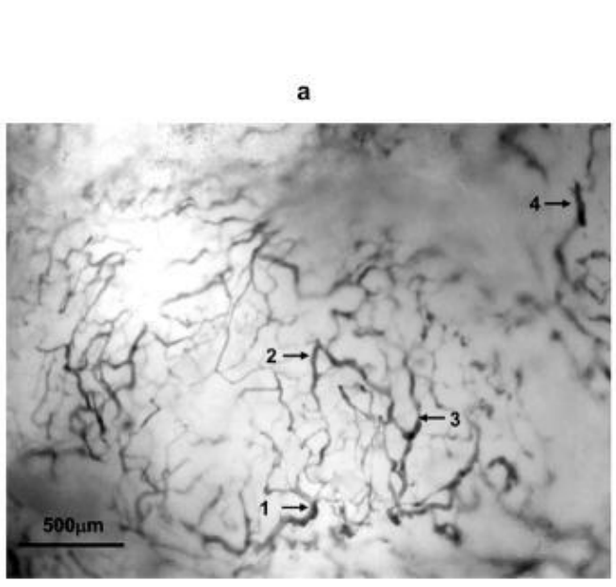
Hipóxia tecidual e câncer

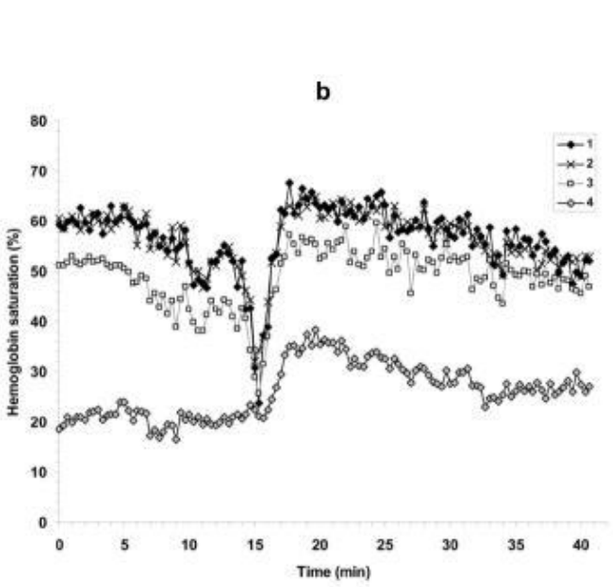
Published in final edited form as:
Curr Mol Med. 2009 May ; 9(4): 435–441.

Novel Imaging Provides New Insights into Mechanisms of Oxygen Transport in Tumors

Matthew E. Hardee[1], **Mark W. Dewhirst**[*,2], **Nikita Agarwal**[3], and **Brian S. Sorg**[3]







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Hipóxia tecidual e câncer

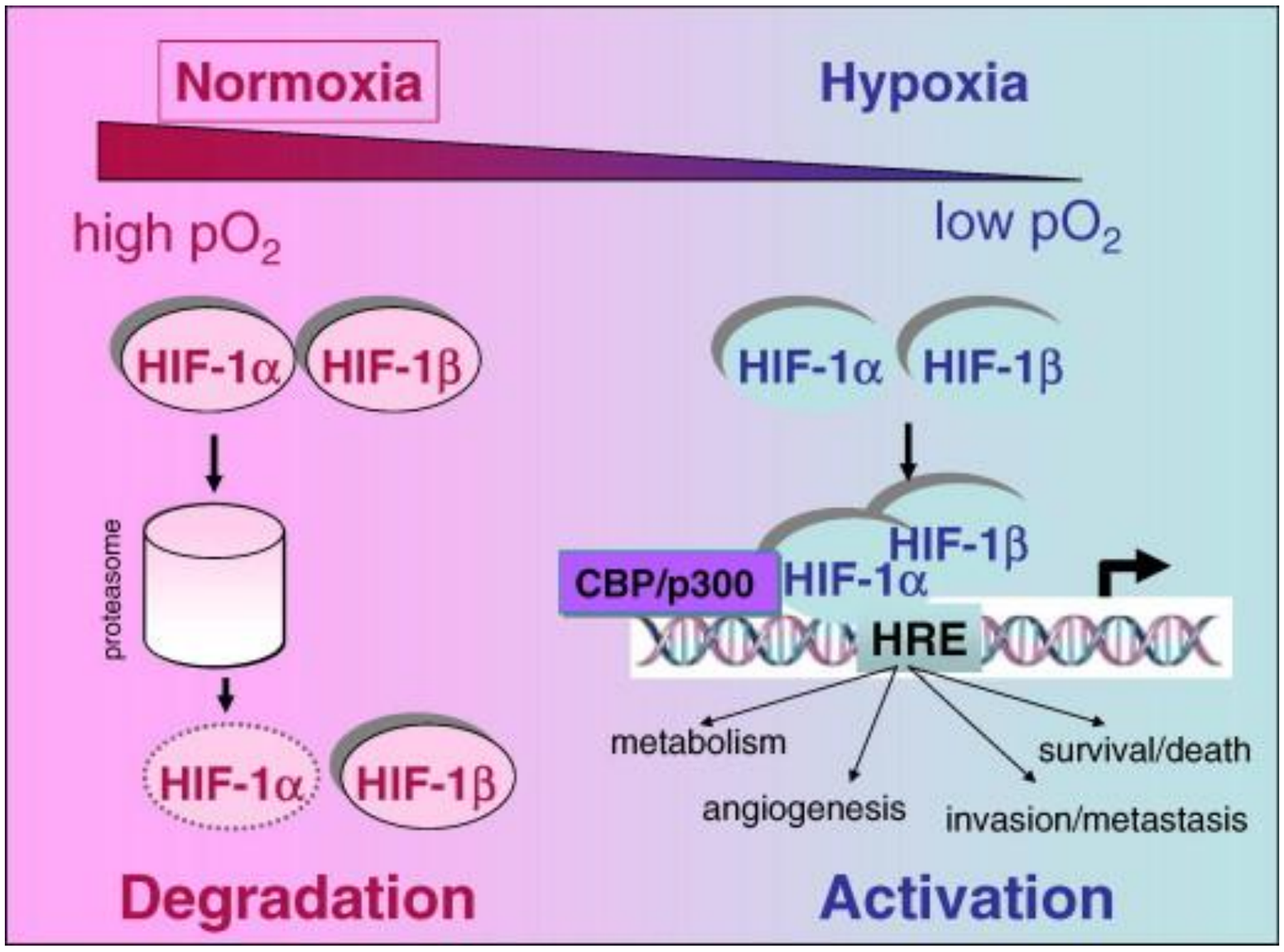
FEBS Letters 581 (2007) 3582–3591

Minireview

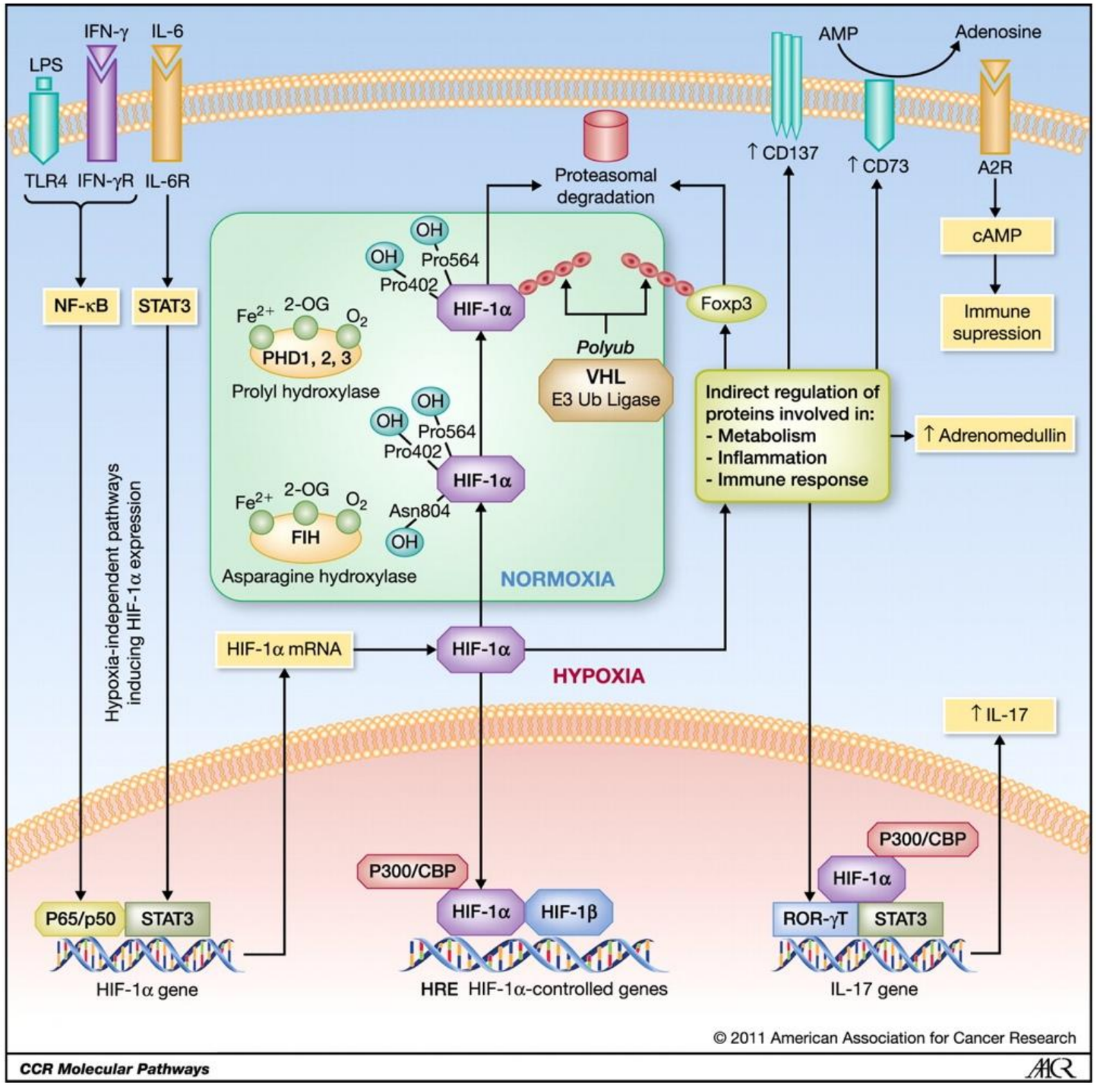
Oxygen, a source of life and stress

M. Christiane Brahimi-Horn*, Jacques Pouysségur

Institute of Signaling, Developmental Biology and Cancer Research, University of Nice, CNRS UMR 6543, Centre A. Lacassagne, 33 Avenue Valombrose, 06189 Nice, France



Hipóxia tecidual e câncer



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Minireview

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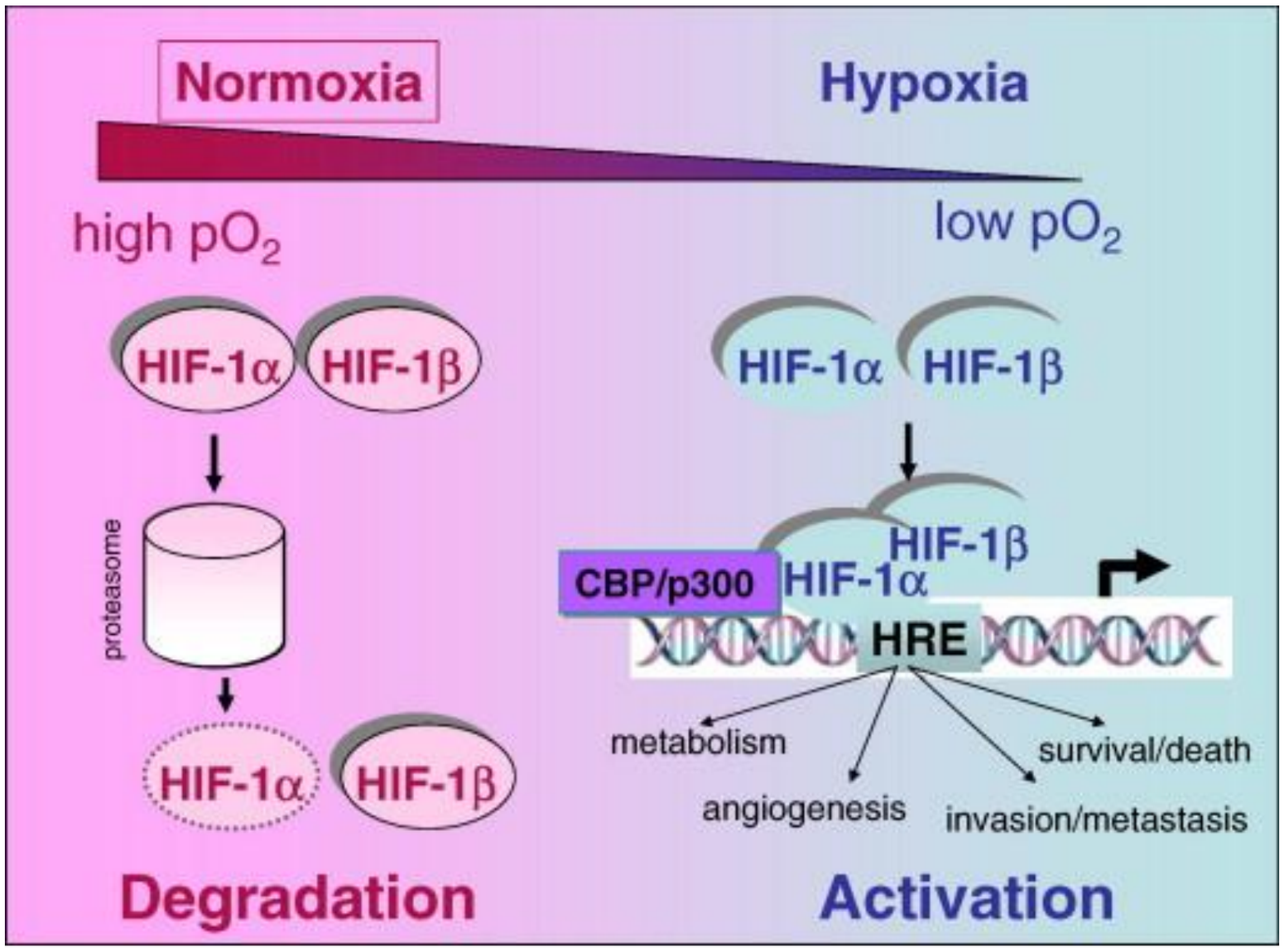
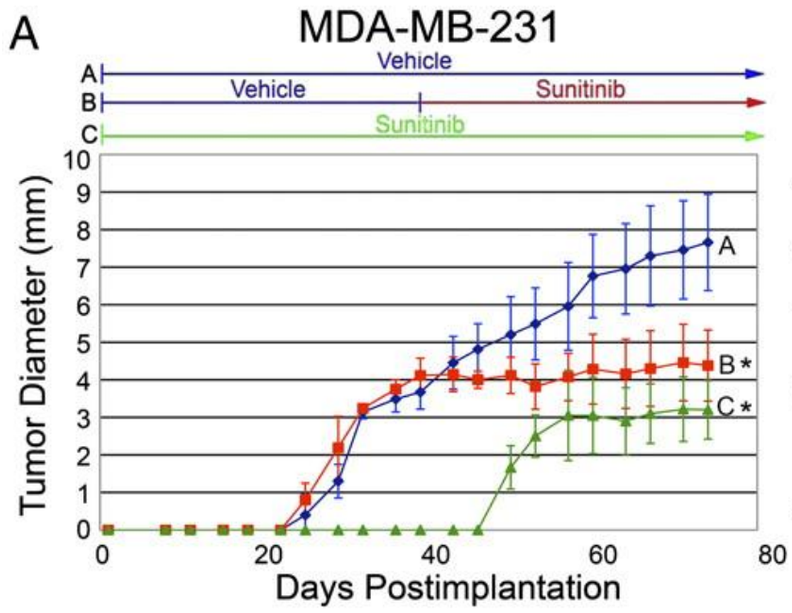


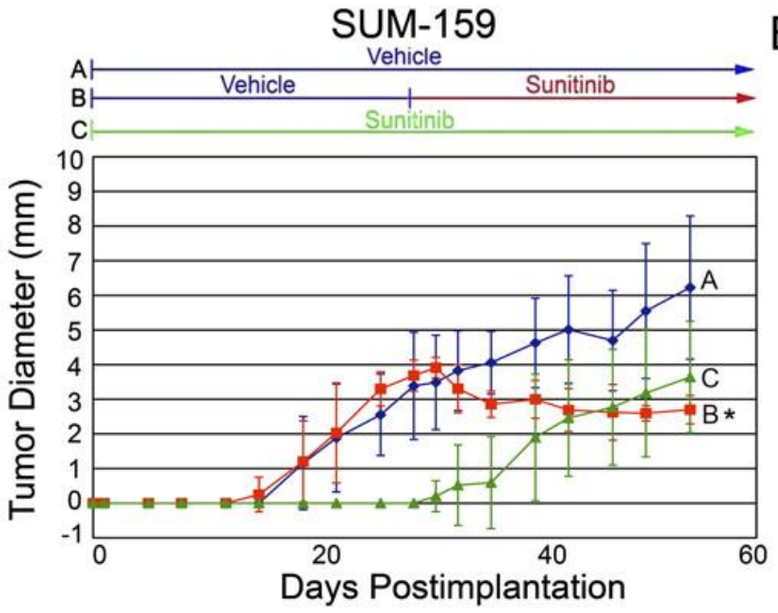
Antiangiogenic agents increase breast cancer stem cells via the generation of tumor hypoxia

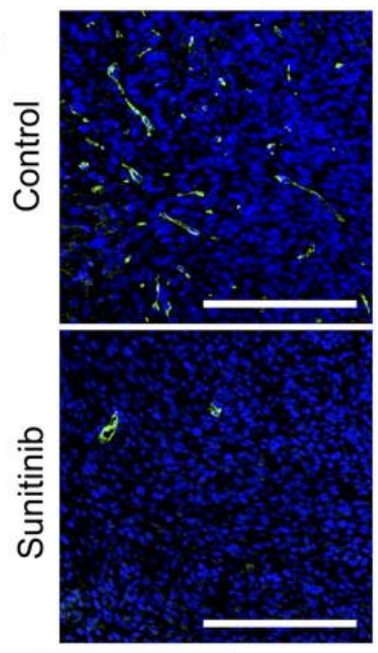
Sarah J. Conley, Elizabeth Gheordunescu, Pramod Kakarala, Bryan Newman, Hasan Korkaya, Amber N. Heath, Shawn G. Clouthier, and Max S. Wicha[1]

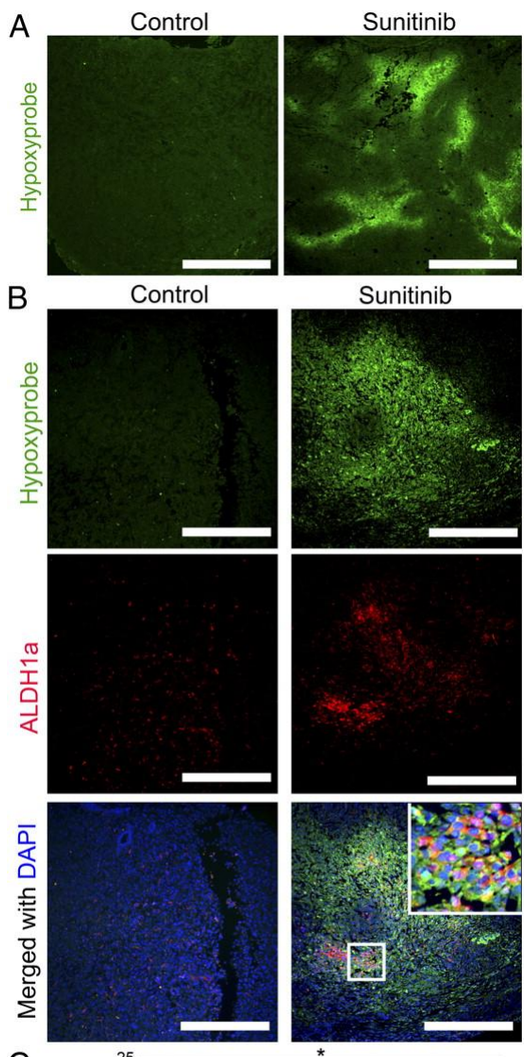
Comprehensive Cancer Center, Department of Internal Medicine, University of Michigan, Ann Arbor, MI 48109

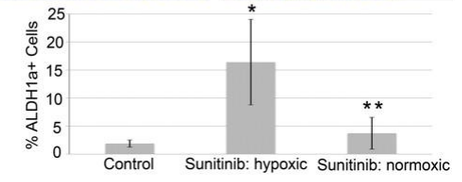
PNAS | February 21, 2012 | vol. 109 | no. 8 | 2785

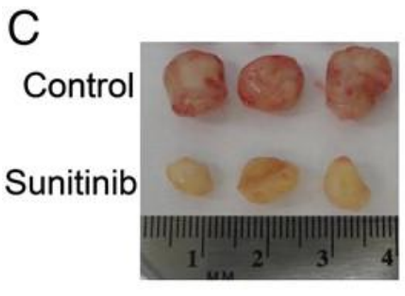


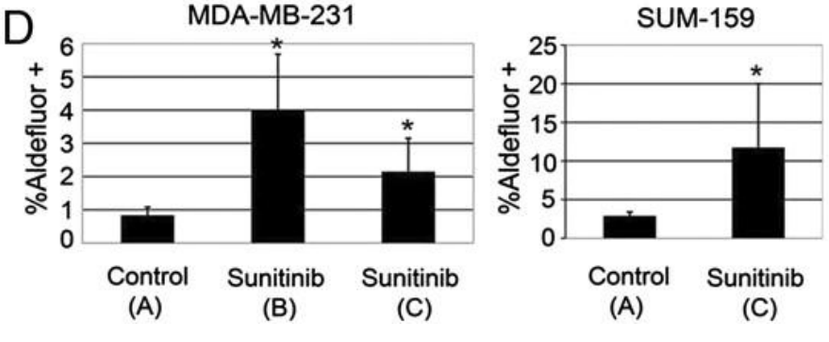


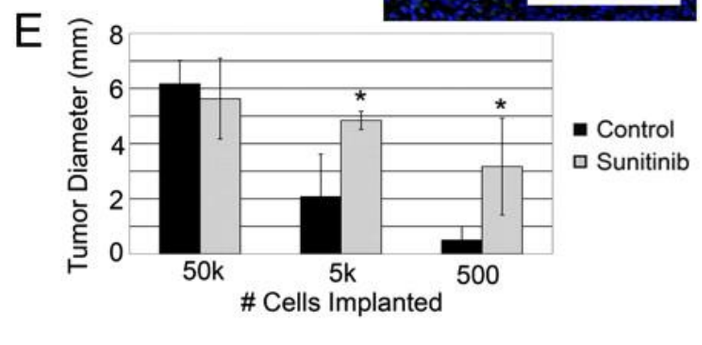












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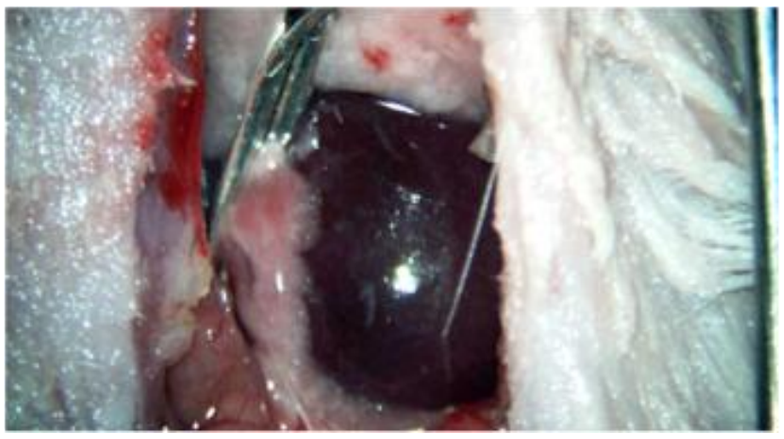
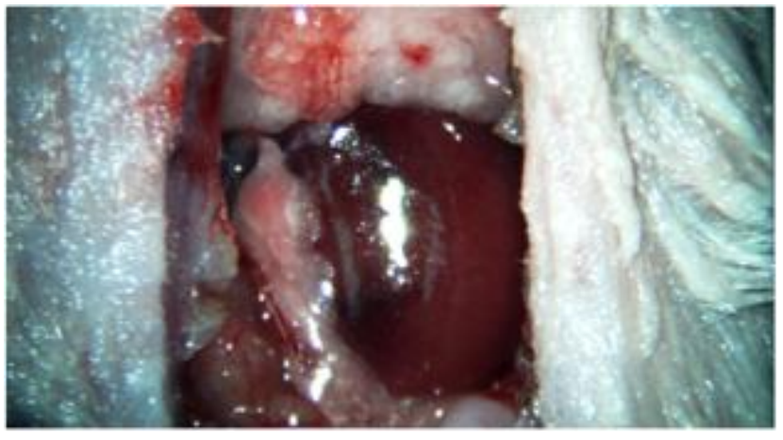
Mouse renal 4T1 cell engraftment as a model to study the influence of hypoxia in breast cancer progression[1]

Heriton Marcelo Ribeiro Antonio[I], Larissa Raquel Mouro Mandarano[I], Alan Augusto Coelho[II], Marcelo Guimarães Tiezzi[III], Jurandyr Moreira de Andrade[IV], Daniel Guimarães Tiezzi[V]

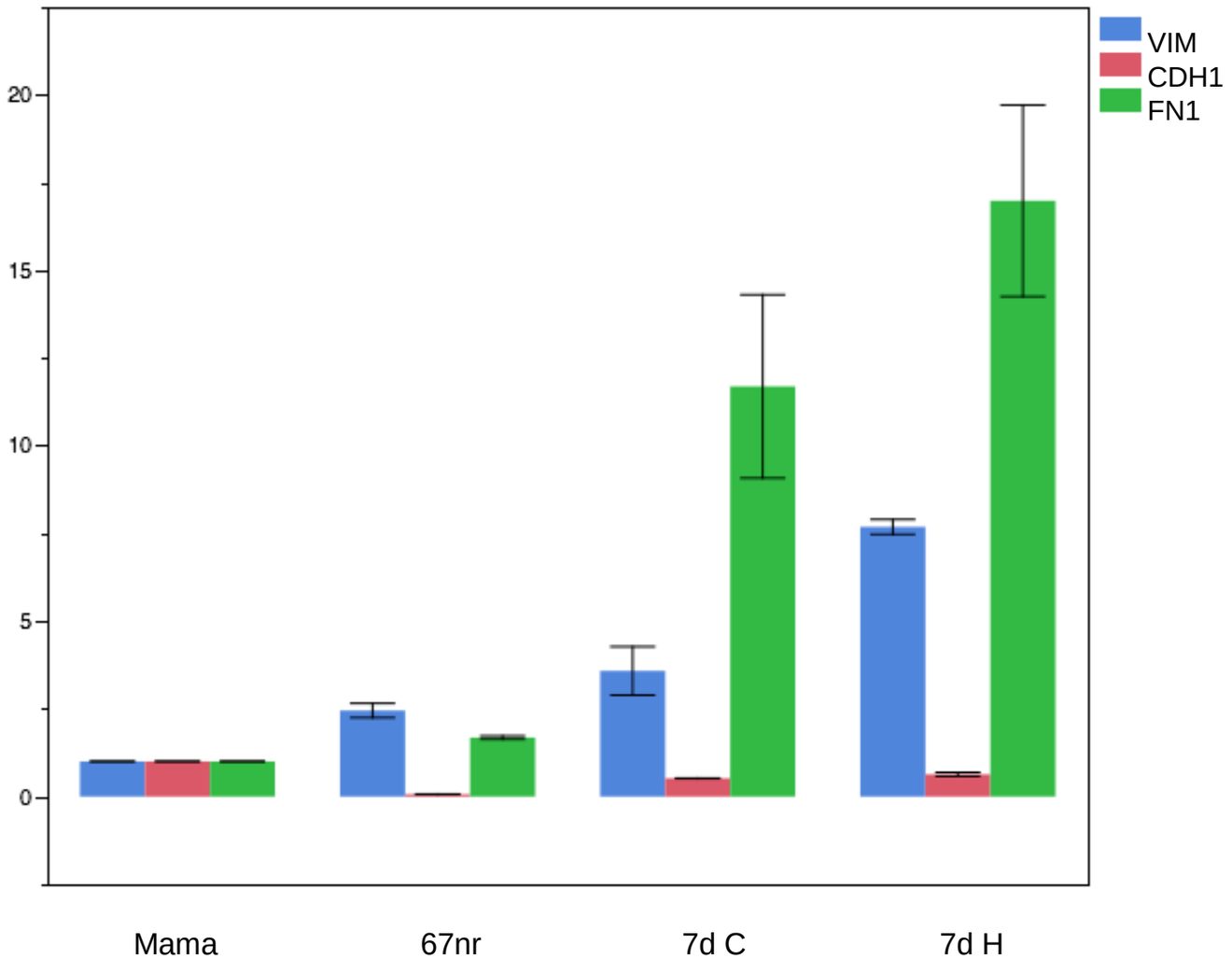




	C 14 days	H 14 days	C 21 days	H 21 days
Presence of lung metastases (n)	0/4	2/4	4/4	4/4
Number of metastases				
Mouse 1	0	4	4	14
Mouse 2	0	0	3	1
Mouse 3	0	0	6	2
Mouse 4	0	1	1	15
Total area of lung metastases (mm^2)				
Mouse 1	0	0.55	0.13	1.75
Mouse 2	0	0	0.12	0.005
Mouse 3	0	0	1.83	0.59
Mouse 4	0	0.004	0.006	2.7
Mean area of lung metastases (mm^2)	0	0.13 ± 0.27	0.52 ± 0.87	1.26 ± 1.2

67nr - transplante renal BALB/c

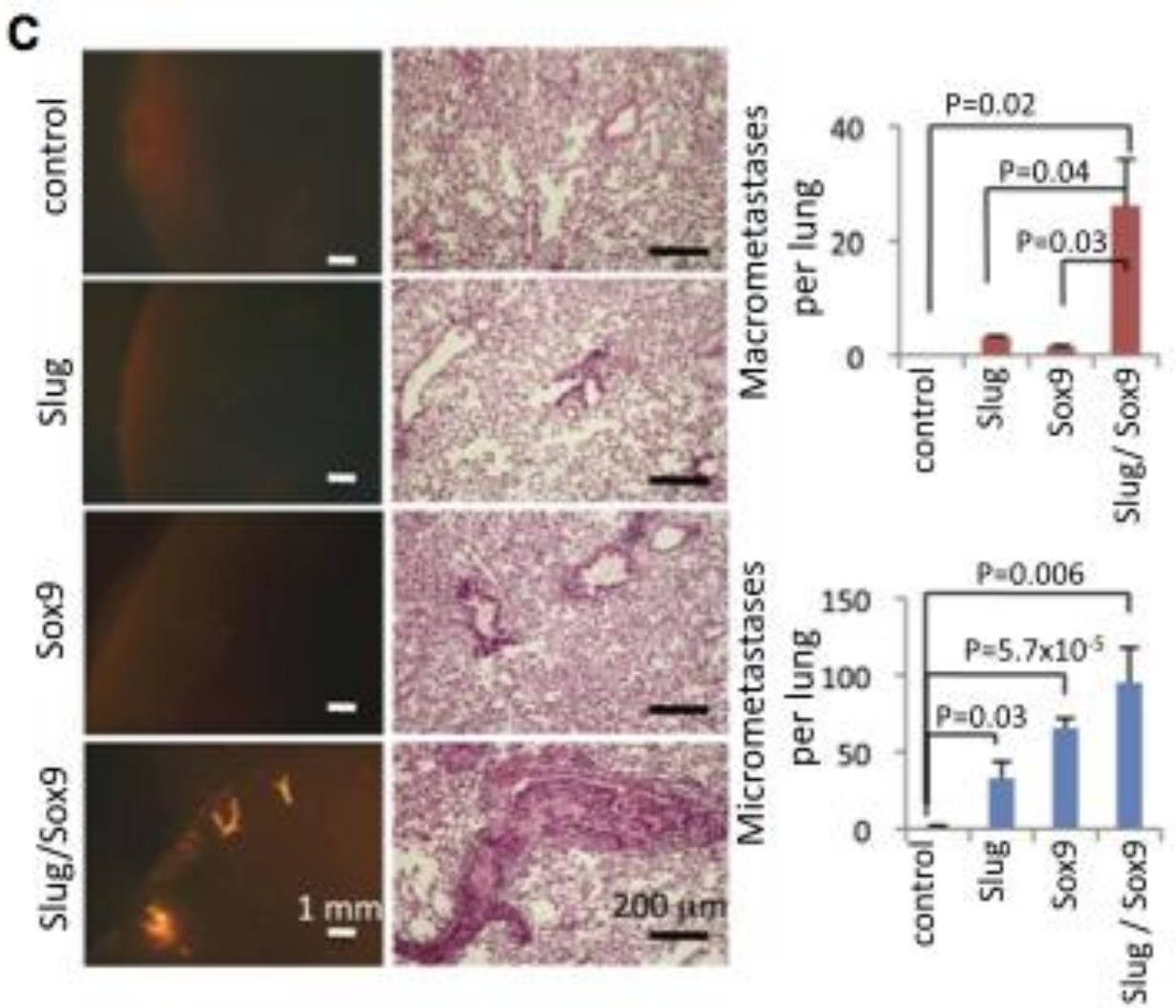
Presença de meta pulmonar		
Linhagem	Grupos	
67nr	Controle	Hipóxia
7 dias	1/6	3/6
21 dias	2/6	5/6

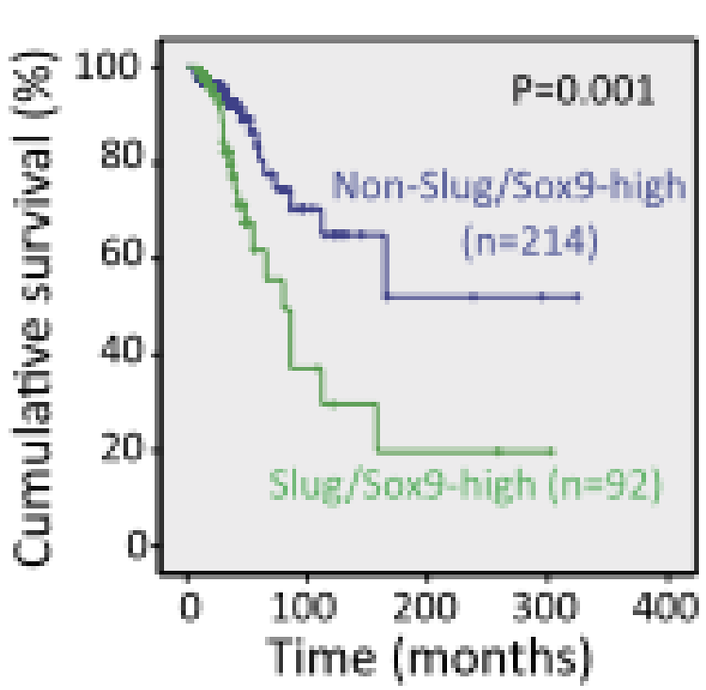


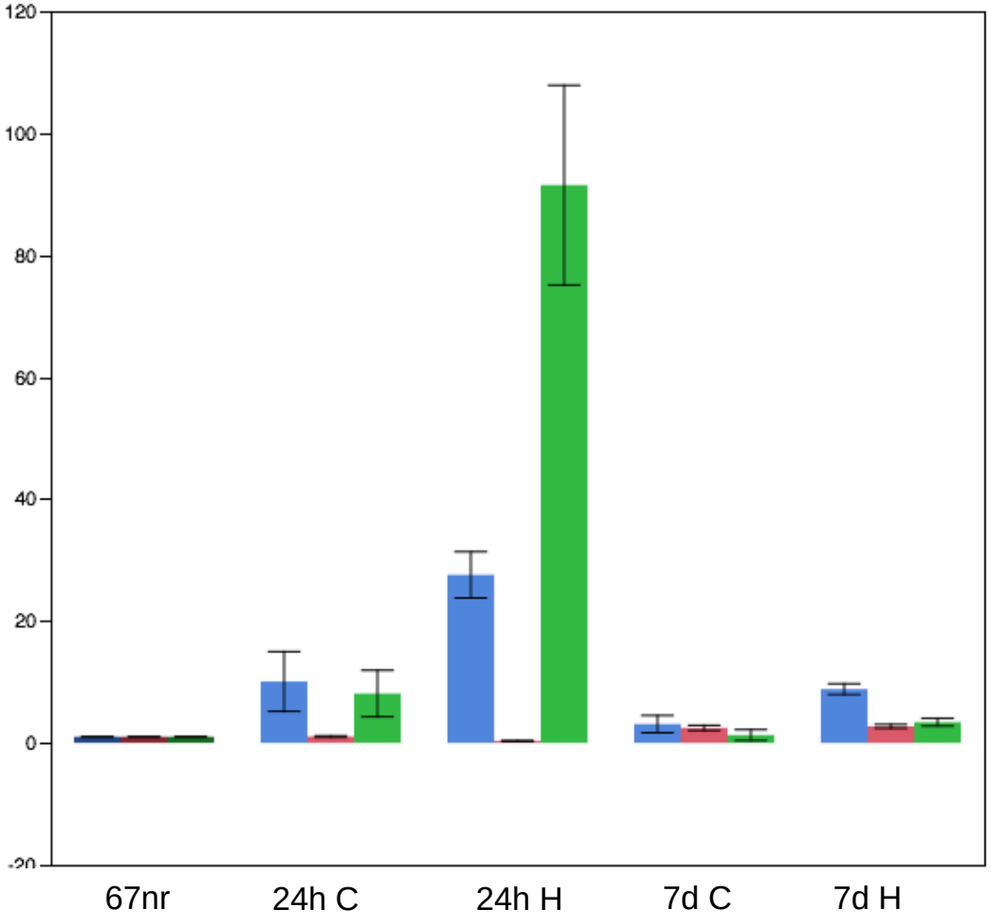
Slug and Sox9 Cooperatively Determine the Mammary Stem Cell State

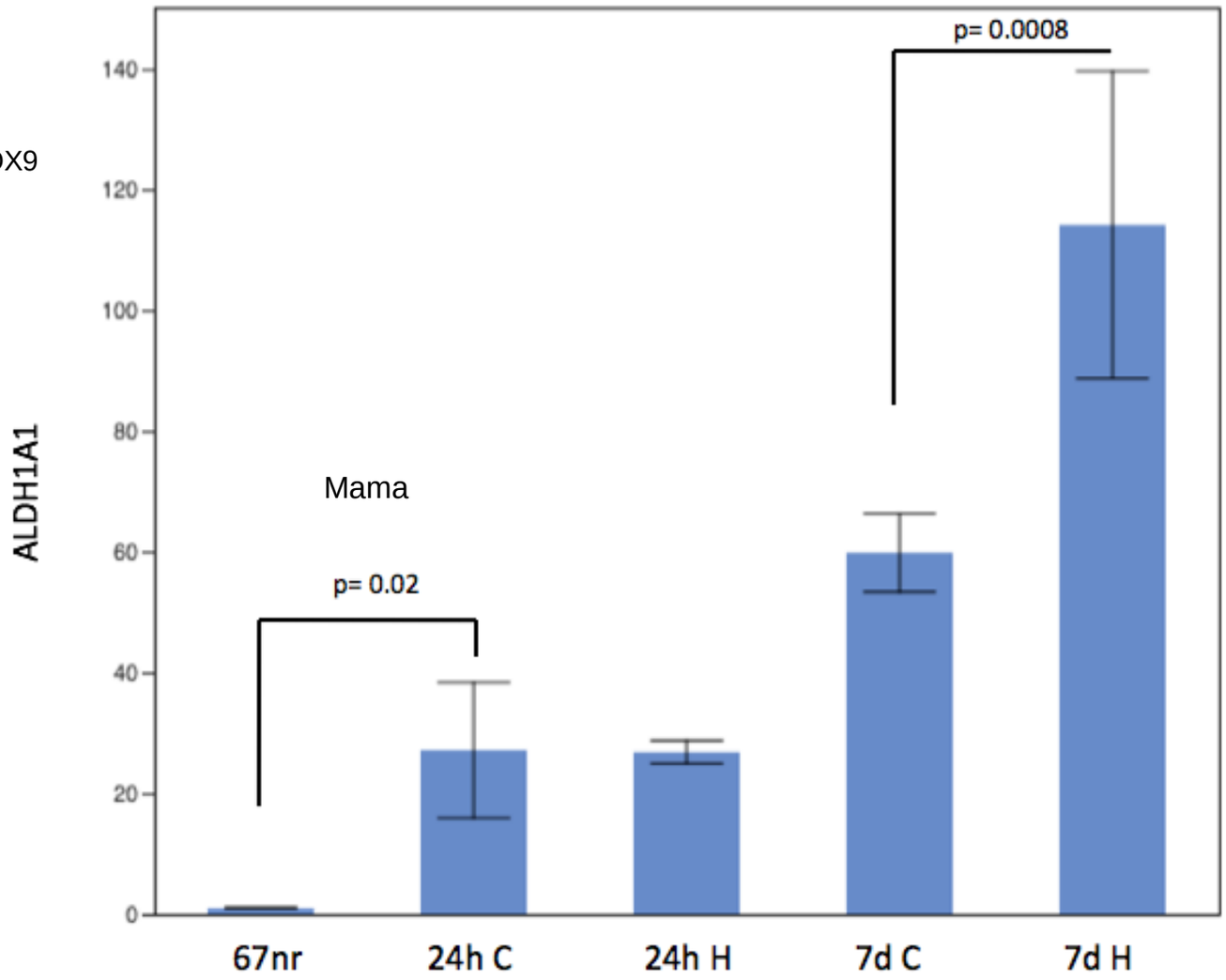
Wenjun Guo,[1,7] Zuzana Keckesova,[1] Joana Liu Donaher,[1] Tsukasa Shibue,[1] Verena Tischler,[2] Ferenc Reinhardt,[1] Shalev Itzkovitz,[3,4] Aurelia Noske,[2] Ursina Zürrer-Härdi,[2] George Bell,[1] Wai Leong Tam,[1] Sendurai A. Mani,[6] Alexander van Oudenaarden,[3,4] and Robert A. Weinberg[1,3,5,*]

[1]Whitehead Institute for Biomedical Research, 9 Cambridge Center, Cambridge, MA 02142, USA
[2]Institute of Surgical Pathology, University Hospital Zurich, 8091 Zurich, Switzerland
[3]Department of Biology
[4]Department of Physics
[5]Ludwig Center for Molecular Oncology
Massachusetts Institute of Technology, Cambridge, MA 02139, USA
[6]Department of Molecular Pathology, University of Texas M.D. Anderson Cancer Center, Houston, TX 77054, USA

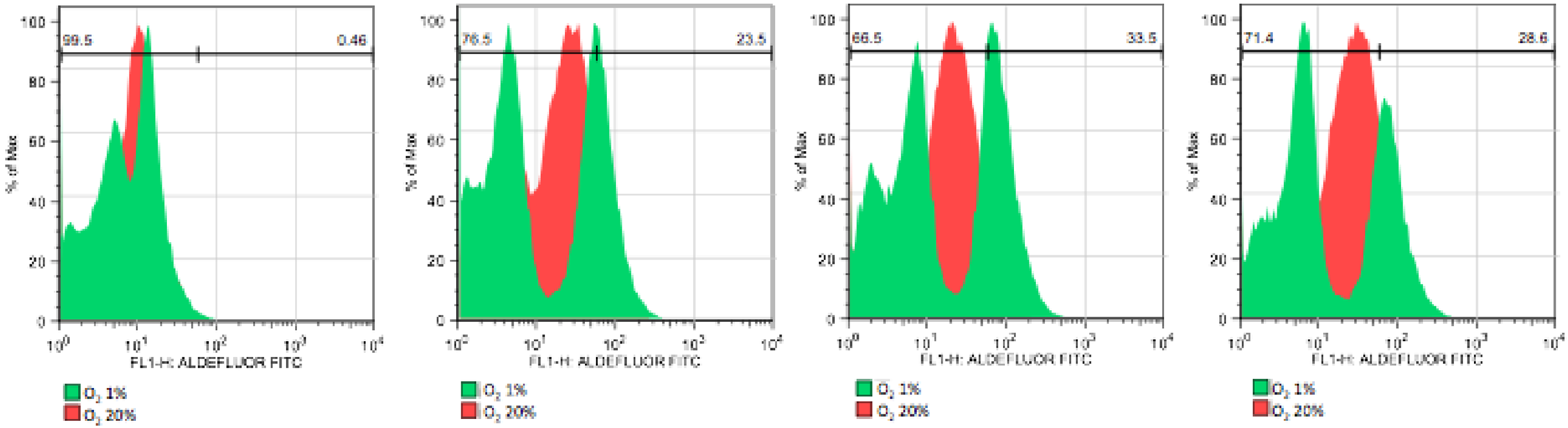





SLUG
SOX9
SLUG/SOX9
120
100
80
60
40
20
0
-20
67nr
24h C
24h H
7d C
7d H


ALDH1A1
Mama
p= 0.0008
p= 0.02
140
120
100
80
60
40
20
0
67nr
24h C
24h H
7d C
7d H

67nr - ALDEFLUOR®



Mean ALDEFLUOR^{High}= 28.5 ± 5.0

Mean ALDEFLUOR^{High}= 6.4 ± 2.4

p= 0.007

CLINICS

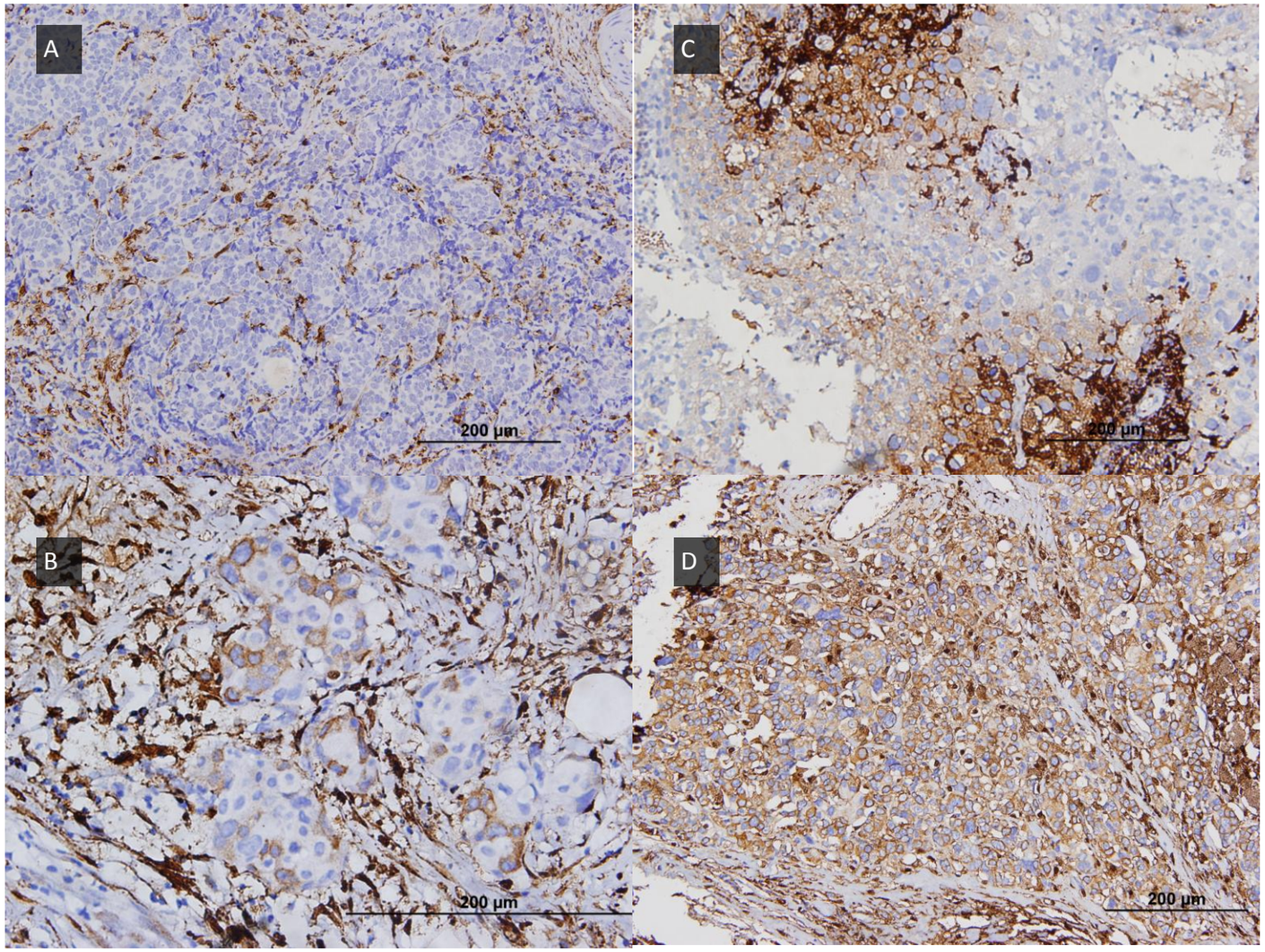
CLINICAL SCIENCE

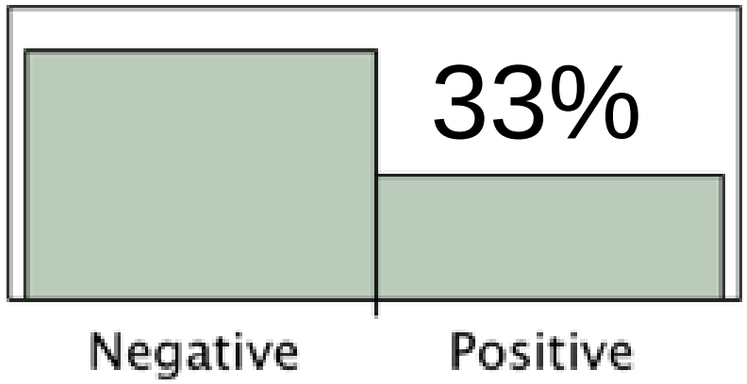
Expression of aldehyde dehydrogenase after neoadjuvant chemotherapy is associated with expression of hypoxia-inducible factors 1 and 2 alpha and predicts prognosis in locally advanced breast cancer

Daniel Guimarães Tiezzi,[I] Willian Simões Clagnan,[I] Larissa Raquel Mouro Mandarano,[I] Christiani Bisinoto de Sousa,[I] Heitor Ricardo Cosiski Marana,[I] Marcelo Guimarães Tiezzi,[II] Jurandyr Moreira de Andrade[I]

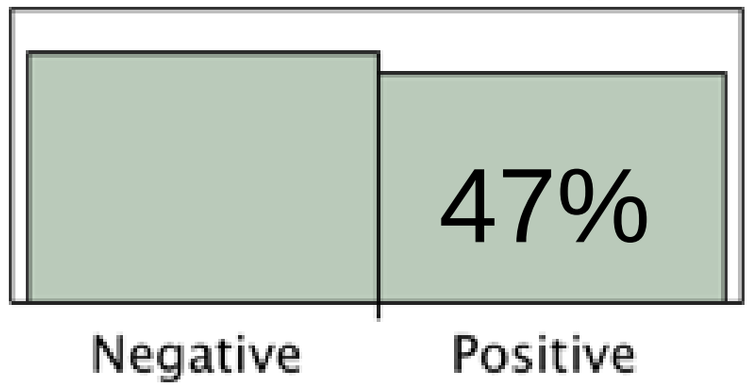
[I]Universidade de São Paulo, Hospital das Clínicas of the Ribeirão Preto School of Medicine, Breast Disease Division Department of Gynecology and Obstetrics, Ribeirão Preto/SP, Brazil. [II]Laboratório de Anatomia Patológica e Citopatologia de Presidente Prudente, São Paulo/SP, Brazil.

Expressão da ALDH-1 em carcinoma de mama localmente avançado



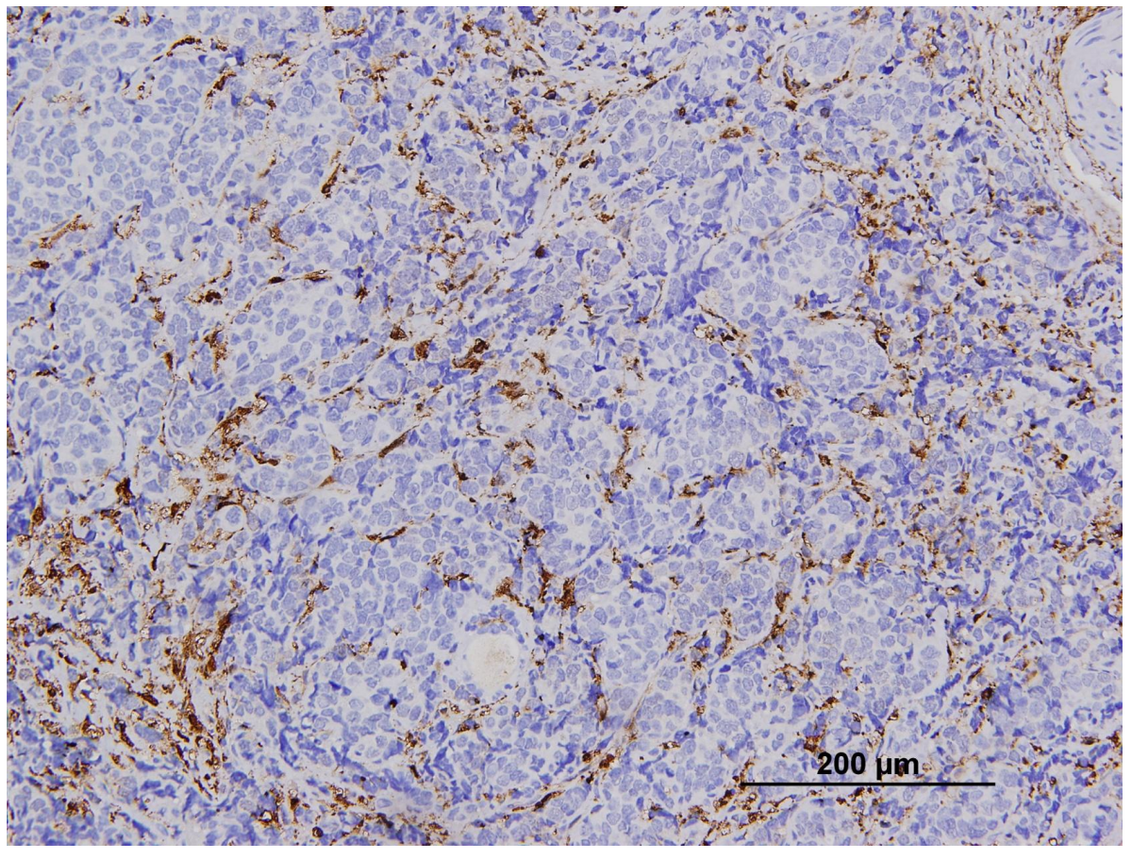


Antes da QT

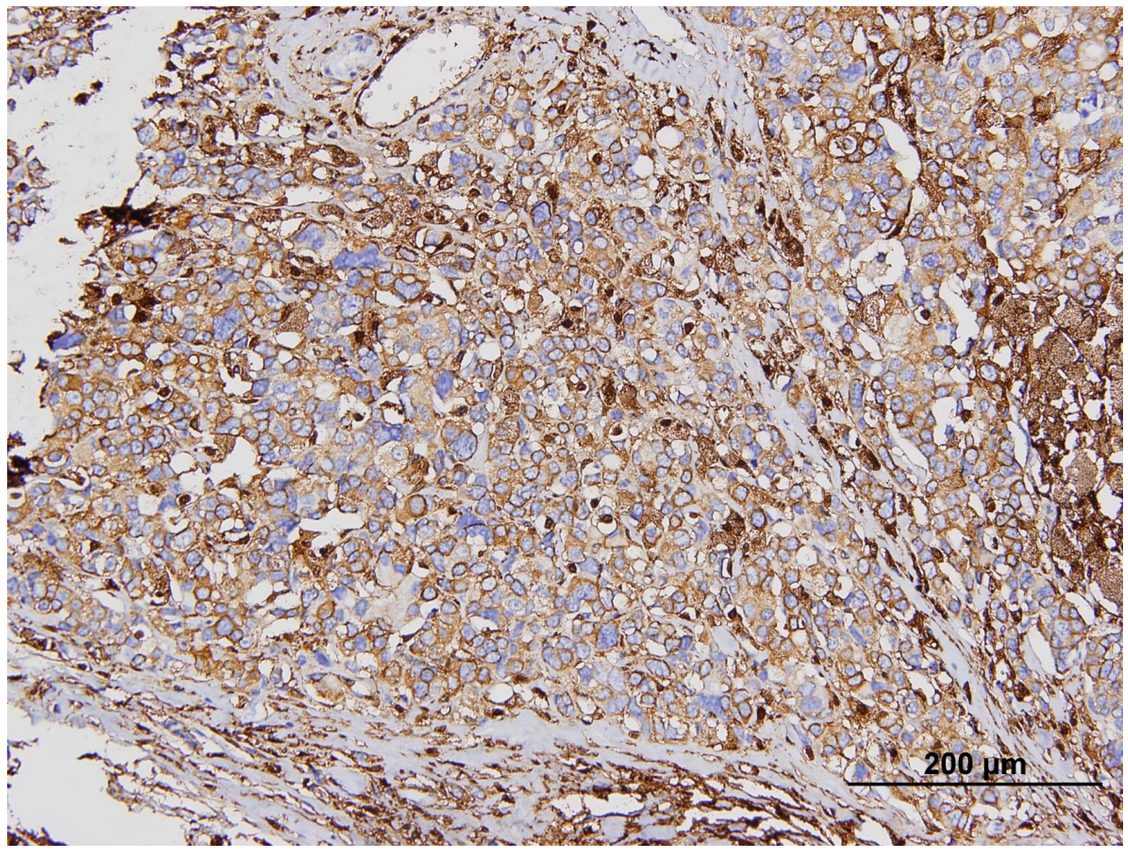


Após a QT

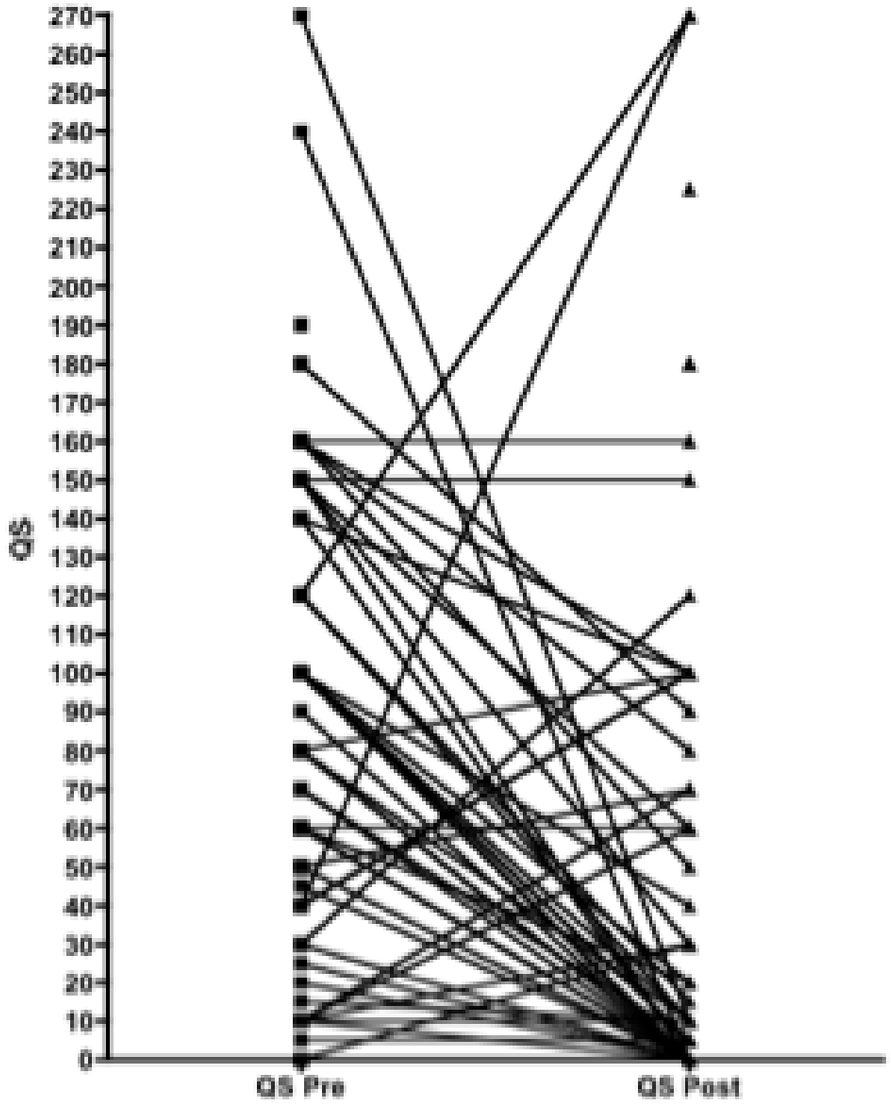
Expressão da ALDH-1 em carcinoma de mama localmente avançado

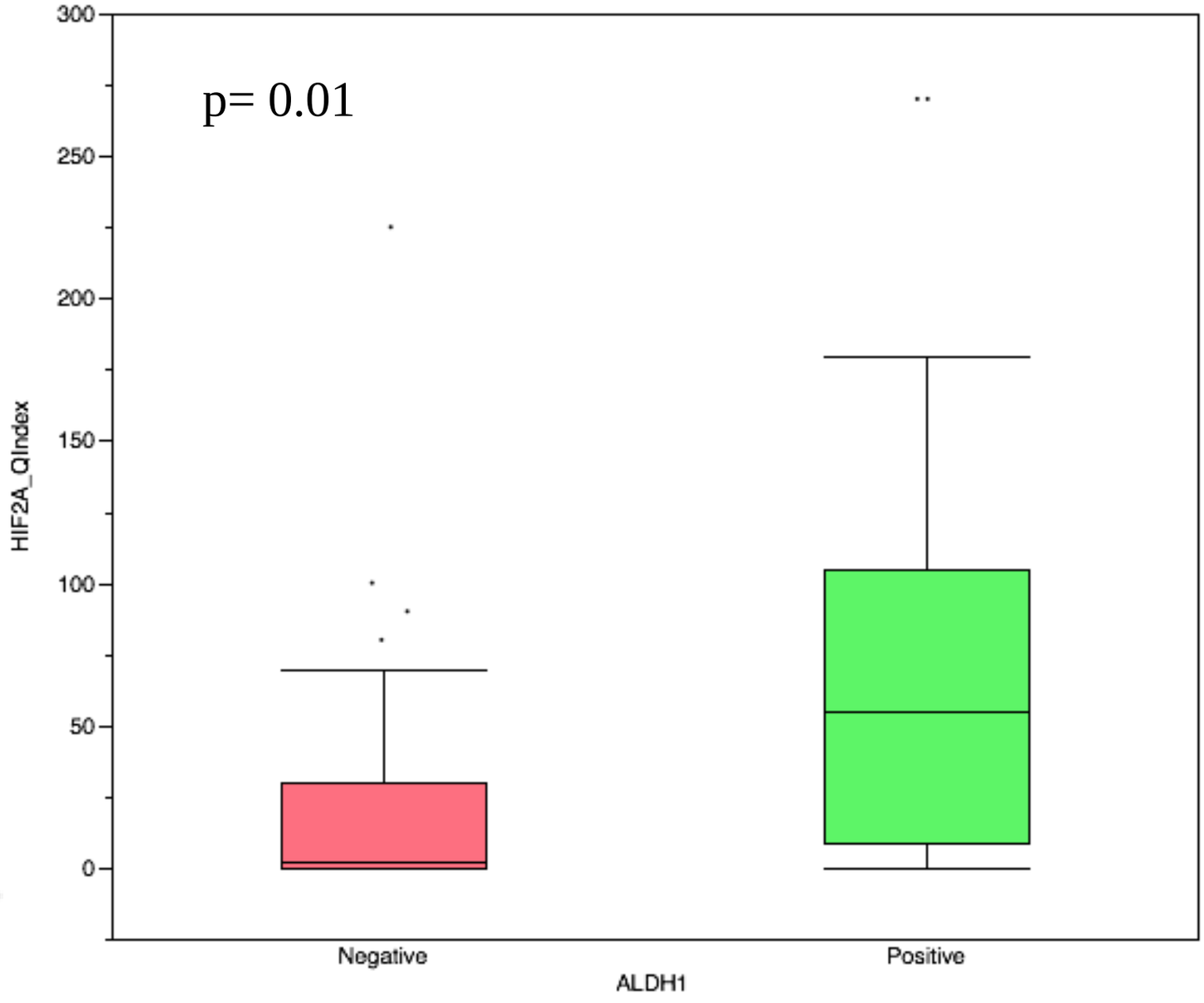


Antes da QT



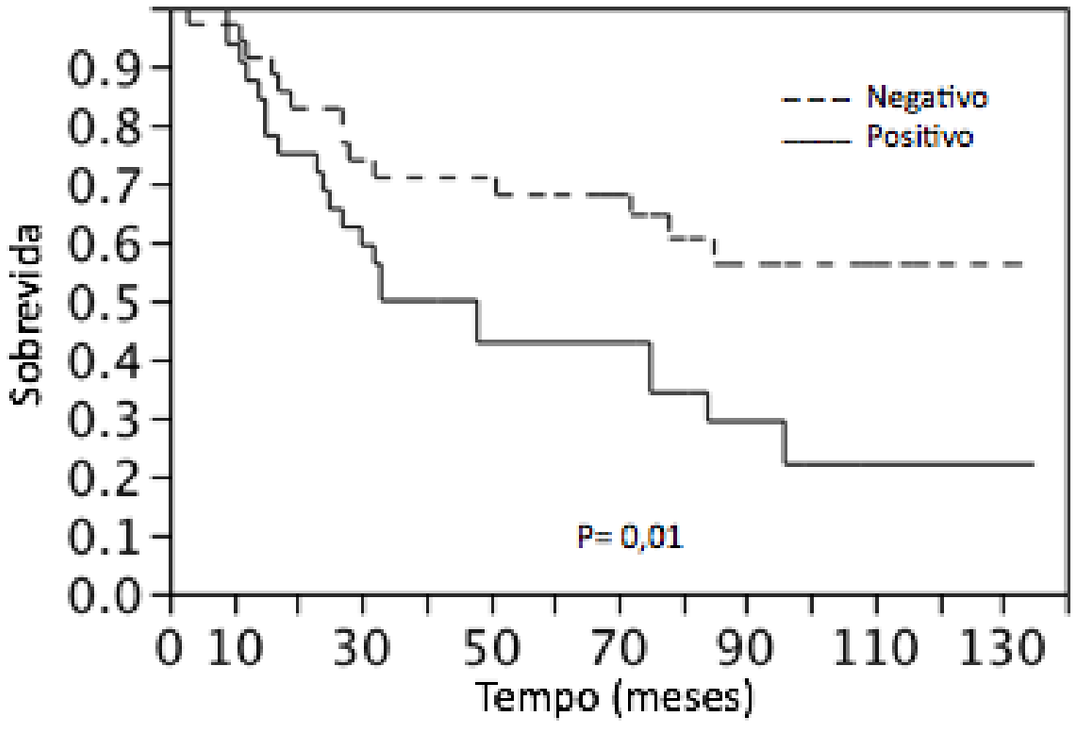
Após a QT


QS
270
260
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
QS Pre
QS Post

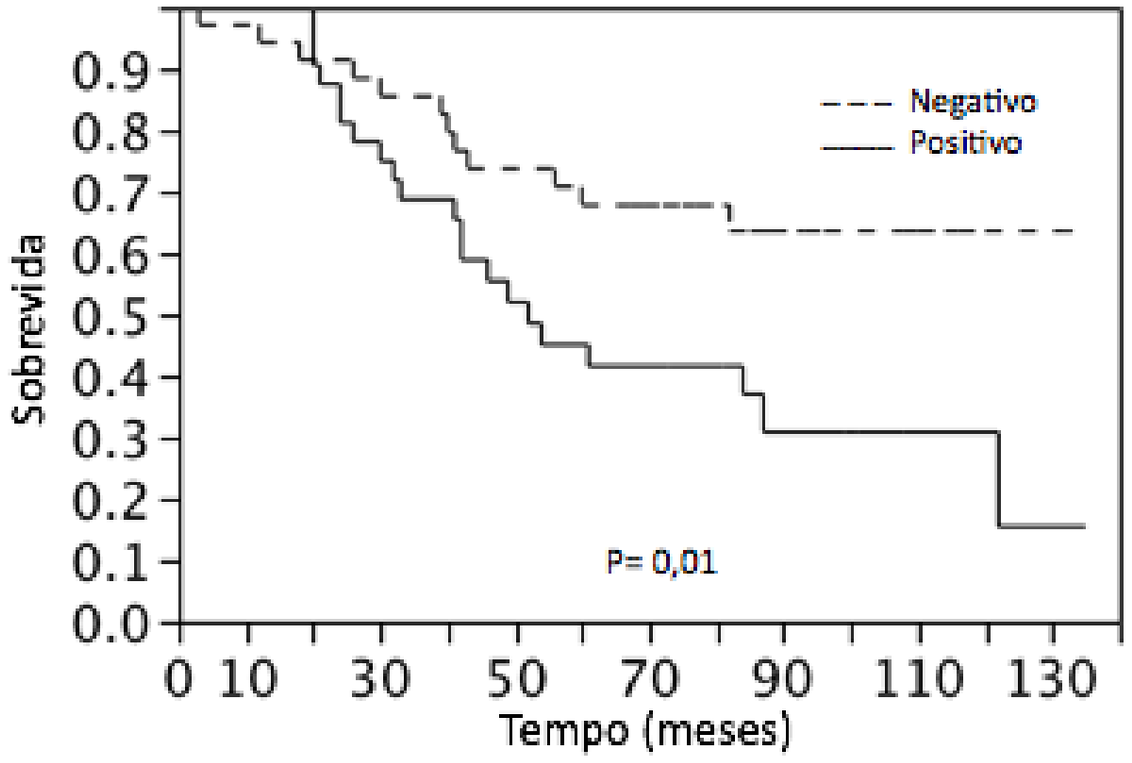

p= 0.01
HIF2A_QIndex
300
250
200
150
100
50
0
Negative
Positive
ALDH1

HIF2A

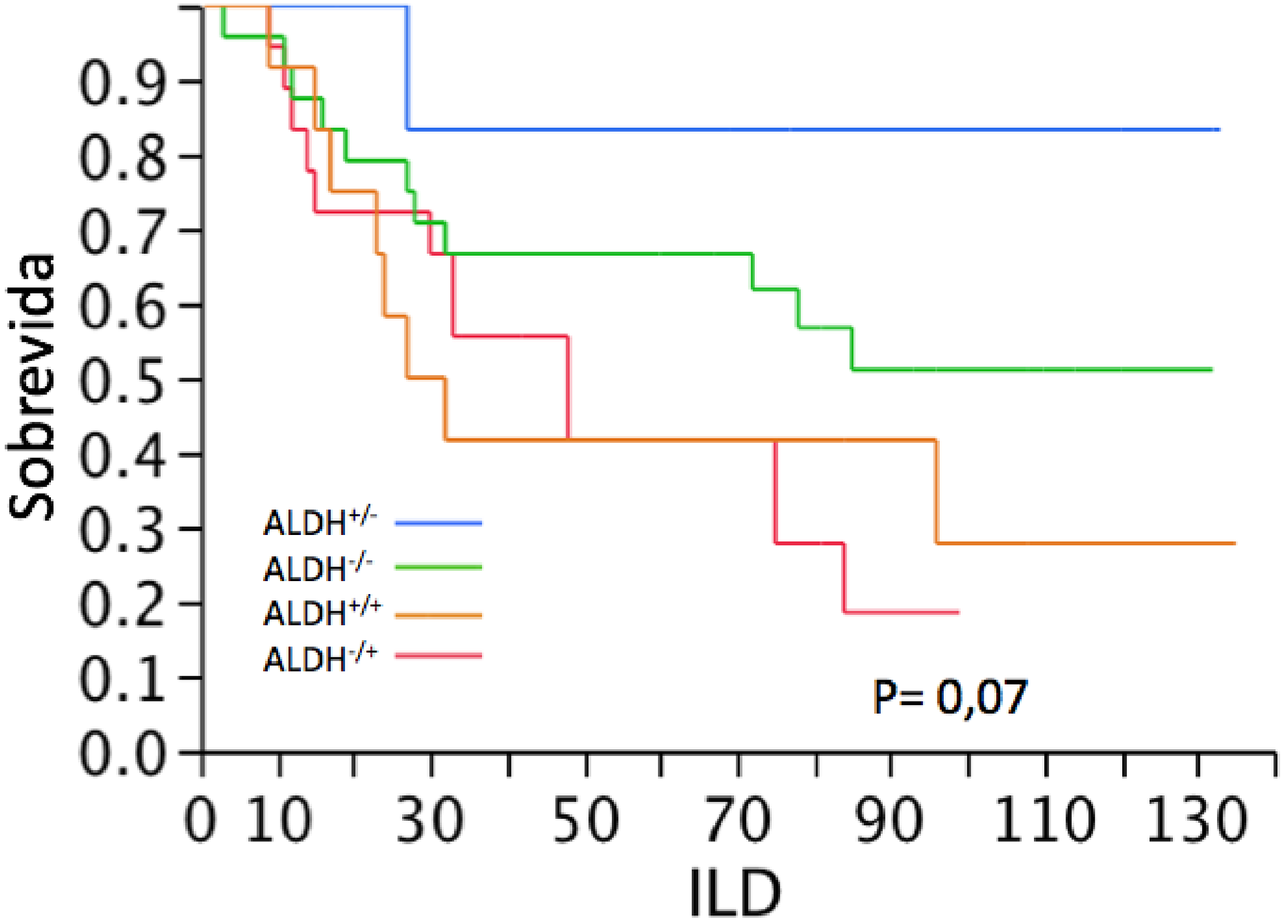
Expressão da ALDH-1 em carcinoma de mama localmente avançado

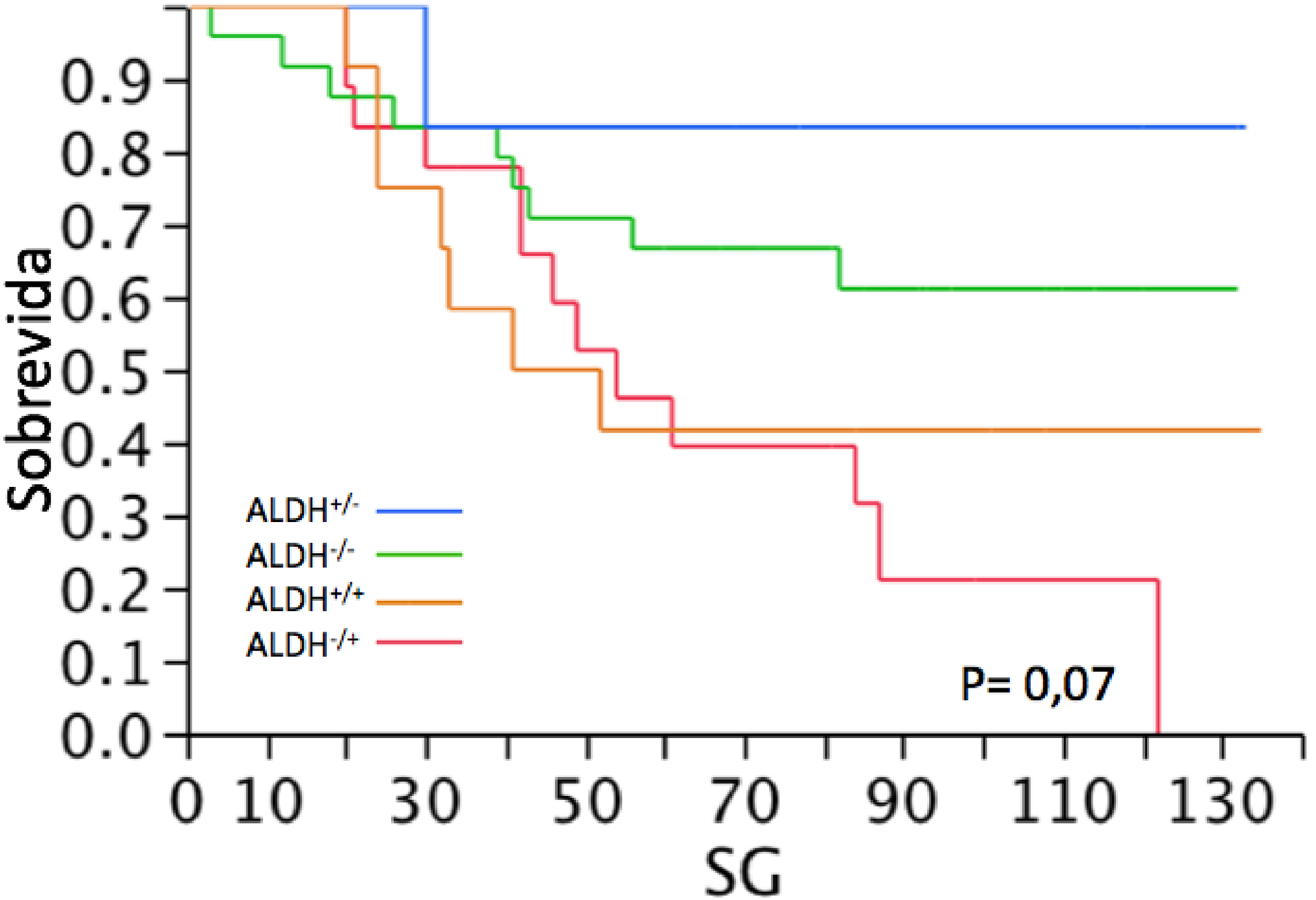


SLD



SG


Sobrevida
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
ALDH+/-
ALDH-/-
ALDH+/+
ALDH-/+
P= 0,07
0
10
30
50
70
90
110
130
ILD


Sobrevida
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
ALDH+/-
ALDH-/-
ALDH+/+
ALDH-/+
P= 0,07
0
10
30
50
70
90
110
130
SG

Expressão da ALDH-1 em carcinoma de mama localmente avançado

Fator	***HR***	**IC 95%**	**p**
Idade	0.94	0.91 - 0.98	0.01
Axila	0.68	0.25 - 1.8	0.44
pRC	0.52	0.09 - 2.77	0.45
HER2	2.25	0.93 - 5.47	0.07
ALDH1	2.54	1.04 - 6.23	0.04

Translational up-regulation of the EGFR by tumor hypoxia provides a nonmutational explanation for its overexpression in human cancer

Aleksandra Franovic, Lakshman Gunaratnam, Karlene Smith, Isabelle Robert, David Patten, and Stephen Lee*

MOLECULAR AND CELLULAR BIOLOGY, Aug. 2011, p. 3339–3350 Vol. 31, No. 16
0270-7306/11/$12.00 doi:10.1128/MCB.01121-10

Hypoxia-Induced Epigenetic Regulation and Silencing of the *BRCA1* Promoter[▽]

Yuhong Lu,[1] Adrian Chu,[2] Mitchell S. Turker,[2] and Peter M. Glazer[1]*

Departments of Therapeutic Radiology and Genetics, Yale University School of Medicine, New Haven, Connecticut 06510,[1] and Department of Molecular and Medical Genetics, Oregon Health and Science University, Portland, Oregon[2]

RESEARCH ARTICLE

Neoplasia • Vol. 7, No. 4, April 2005, pp. 324–330 324
www.neoplasia.com

Hypoxia-Inducible Factor-1α and the Glycolytic Phenotype in Tumors[1]

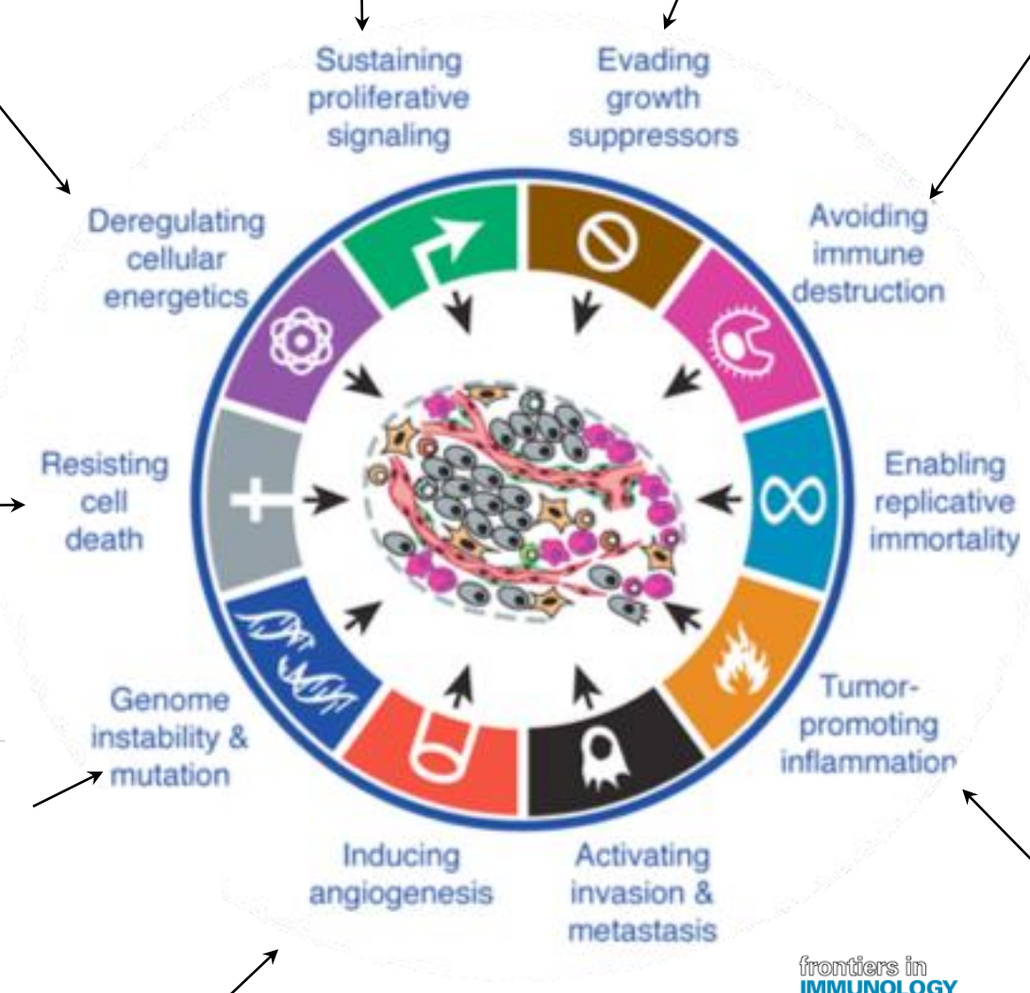
Ian F. Robey, Anthony D. Lien, Sarah J. Welsh, Brenda K. Baggett and Robert J. Gillies

Clinical Cancer Research

Molecular Pathways

Molecular Pathways: Hypoxia Response in Immune Cells Fighting or Promoting Cancer

Asis Palazón[1,2], Julián Aragonés[3], Aizea Morales-Kastresana[1,2], Manuel Ortiz de Landázuri[3], and Ignacio Melero[1,2]



American Journal of Pathology, Vol. 163, No. 2, August 2003

Apoptosis-Resistance of Hypoxic Cells

Multiple Factors Involved and a Role for IAP-2

Published OnlineFirst December 22, 2009; DOI:10.1158/1078-0432.CCR-09-1630

Clinical Cancer Research

Human Cancer Biology

Aldehyde Dehydrogenase 1–Positive Cancer Stem Cells Mediate Metastasis and Poor Clinical Outcome in Inflammatory Breast Cancer

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Hypoxia Causes Downregulation of Mismatch Repair System and Genomic Instability in Stem Cells

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nature medicine

Regulation of angiogenesis by hypoxia: role of the HIF system

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frontiers in IMMUNOLOGY

REVIEW ARTICLE
published: 23 February 2012
doi: 10.3389/fimmu.2012.00021

Hypoxia promotes tumor growth in linking angiogenesis to immune escape

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