PROGRAMA DE PÓS-GRADUAÇÃO
STRICTO SENSU – EDUCAÇÃO FÍSICA

Universidade Católica de Brasília

CÂNCER E EXERCÍCIO

PROF. DR. JONATO PRESTES

CÂNCER

Desequilíbrios na regulação celular podem resultar em uma massa denominada TUMOR ou NEOPLASIA

“CRESCIMENTO NOVO OU ANORMAL”:

- **Tumores benignos**
- **Tumores malignos**

Courneya, Mackey e Rhodes, 2006

Desequilíbrios na regulação celular podem resultar em uma massa denominada TUMOR ou NEOPLASIA

TUMORES MALIGNOS x TUMORES BENIGNOS

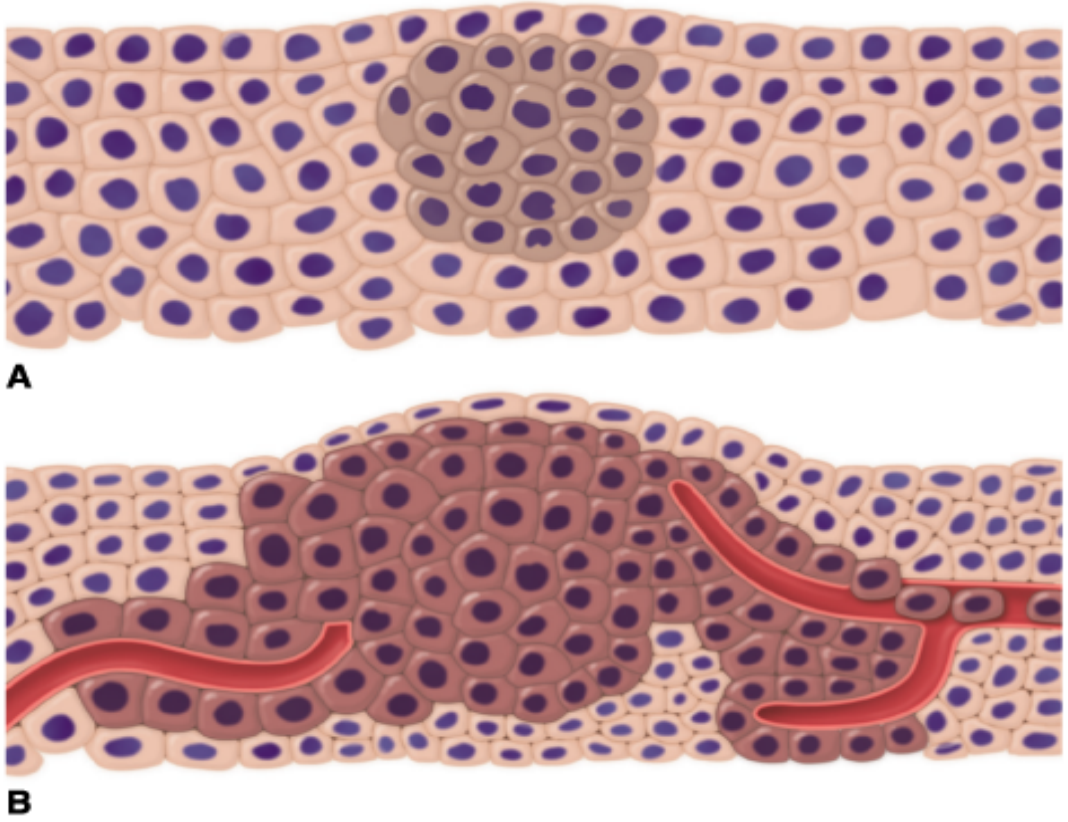
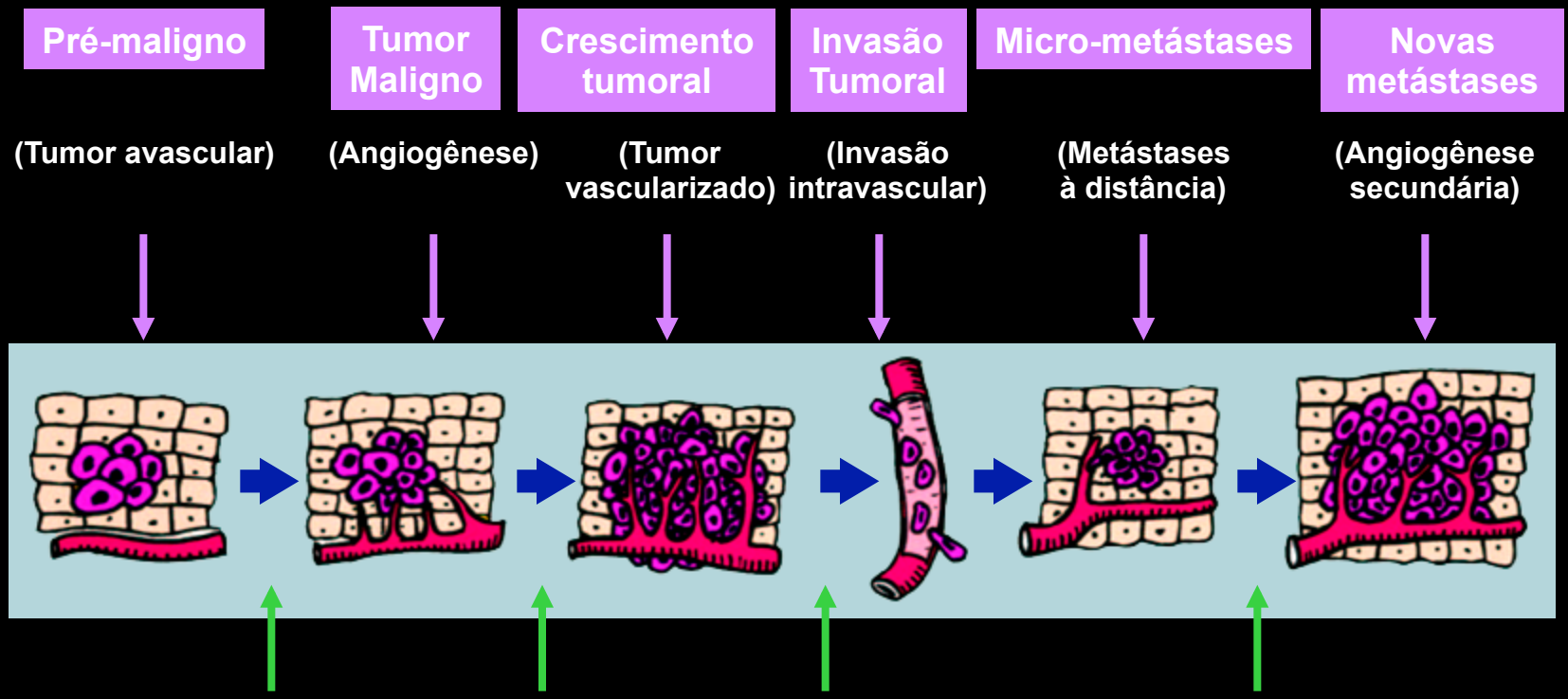


FIGURA 7.6 Tumores benignos *versus* tumores malignos. **A.** O tumor benigno é representado pelo crescimento lento de uma massa celular que ainda não invadiu tecidos adjacentes. **B**. O tumor maligno é representado pelo crescimento celular agressivo e pela invasão de tecidos vizinhos e vasos sanguíneos.

Courneya, Mackey e Rhodes, 2006

Angiogênese no desenvolvimento tumoral



Poon RT, et al. J Clin Oncol 19:1207–25; 2001

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Mais de 100 doenças que podem ocorrer em qualquer tecido ou órgão. 4 CLASSIFICAÇÕES (tipo de célula que lhes dá origem):

- Carcinoma (células epiteliais, glândulas e órgãos internos);

Cerca de 80 a 90% dos cânceres (ex:. próstata, cólon, pulmão, cervical e mama)

Abbas et al., 2003

CÂNCER

- Leucemia (origem nas células do sangue);
- Linfoma (origem no sistema imune);
- Sarcoma (tecidos conjuntivos, como ossos, tendões, cartilagem, gordura e músculos).

Abbas et al., 2003

Fisiopatologia do câncer

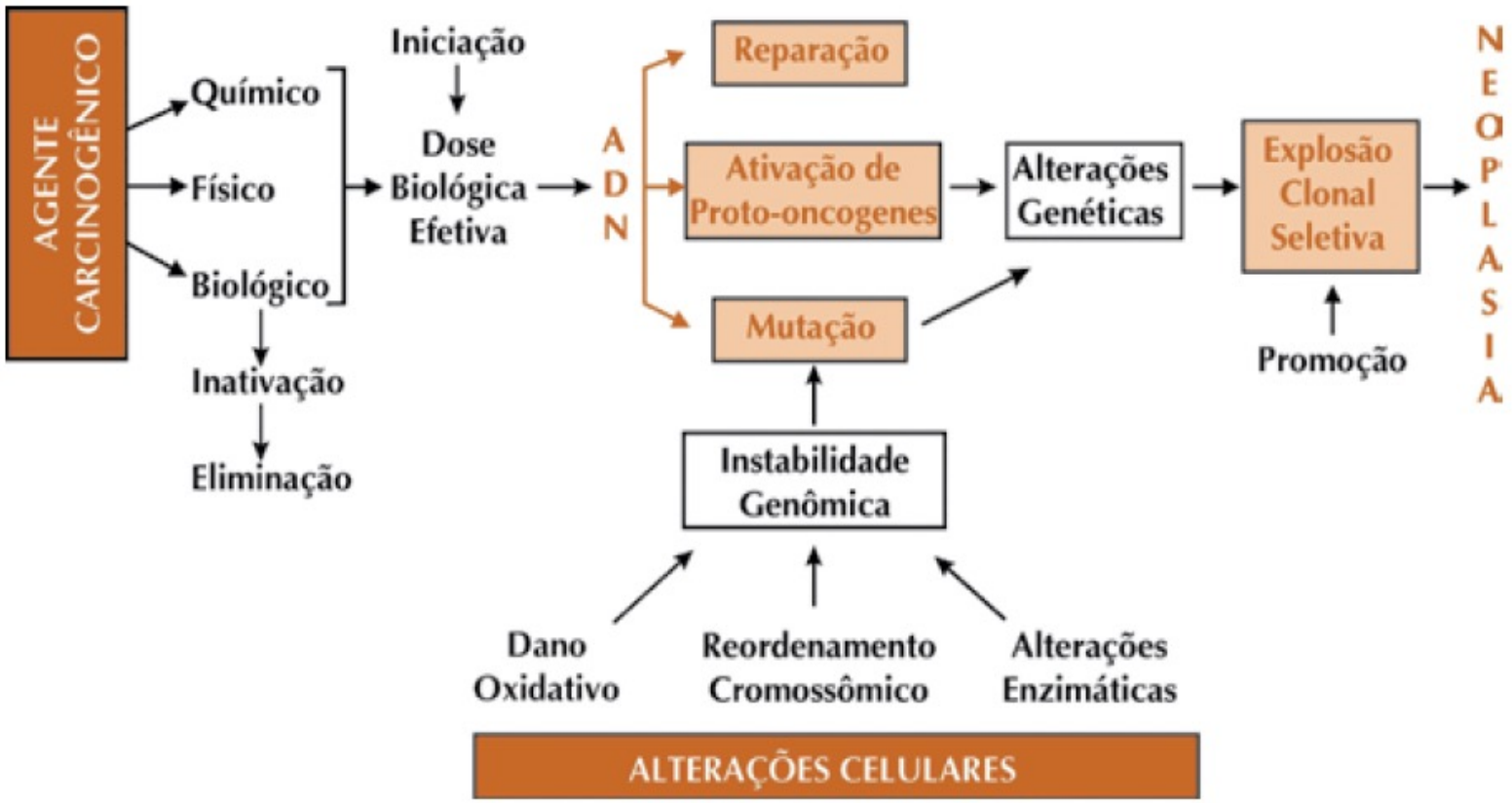


Figura 29 - As etapas da carcinogênese

Fonte: INCA (2002, p. 58)

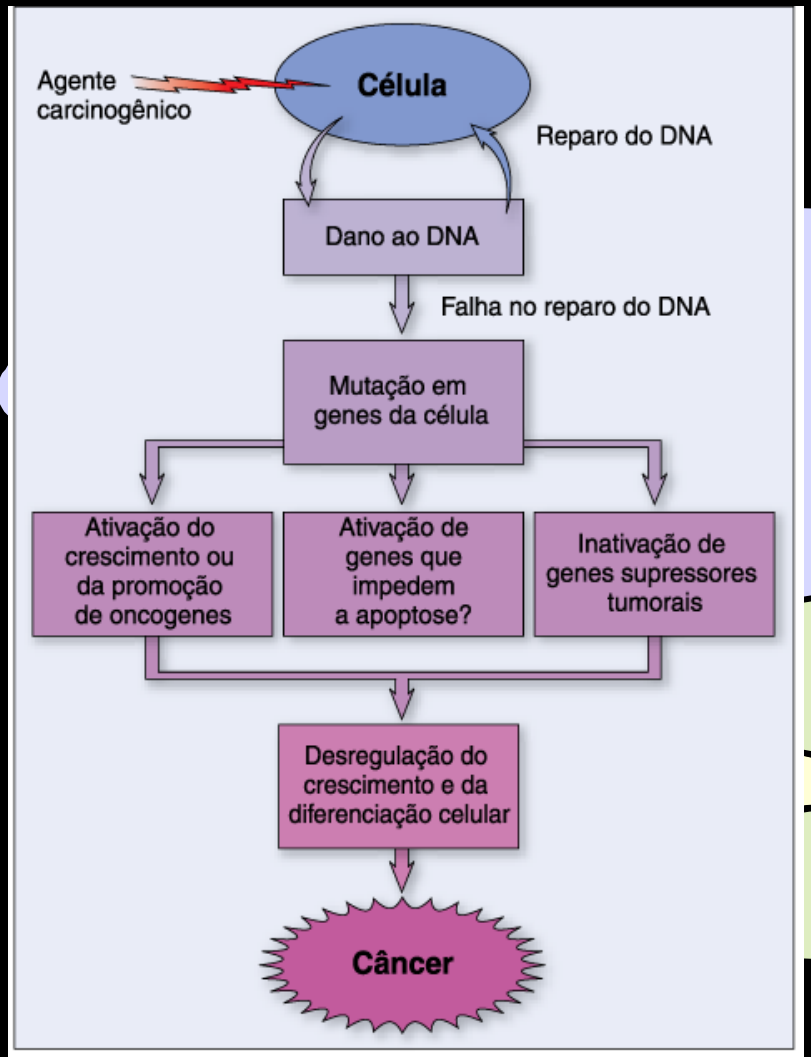
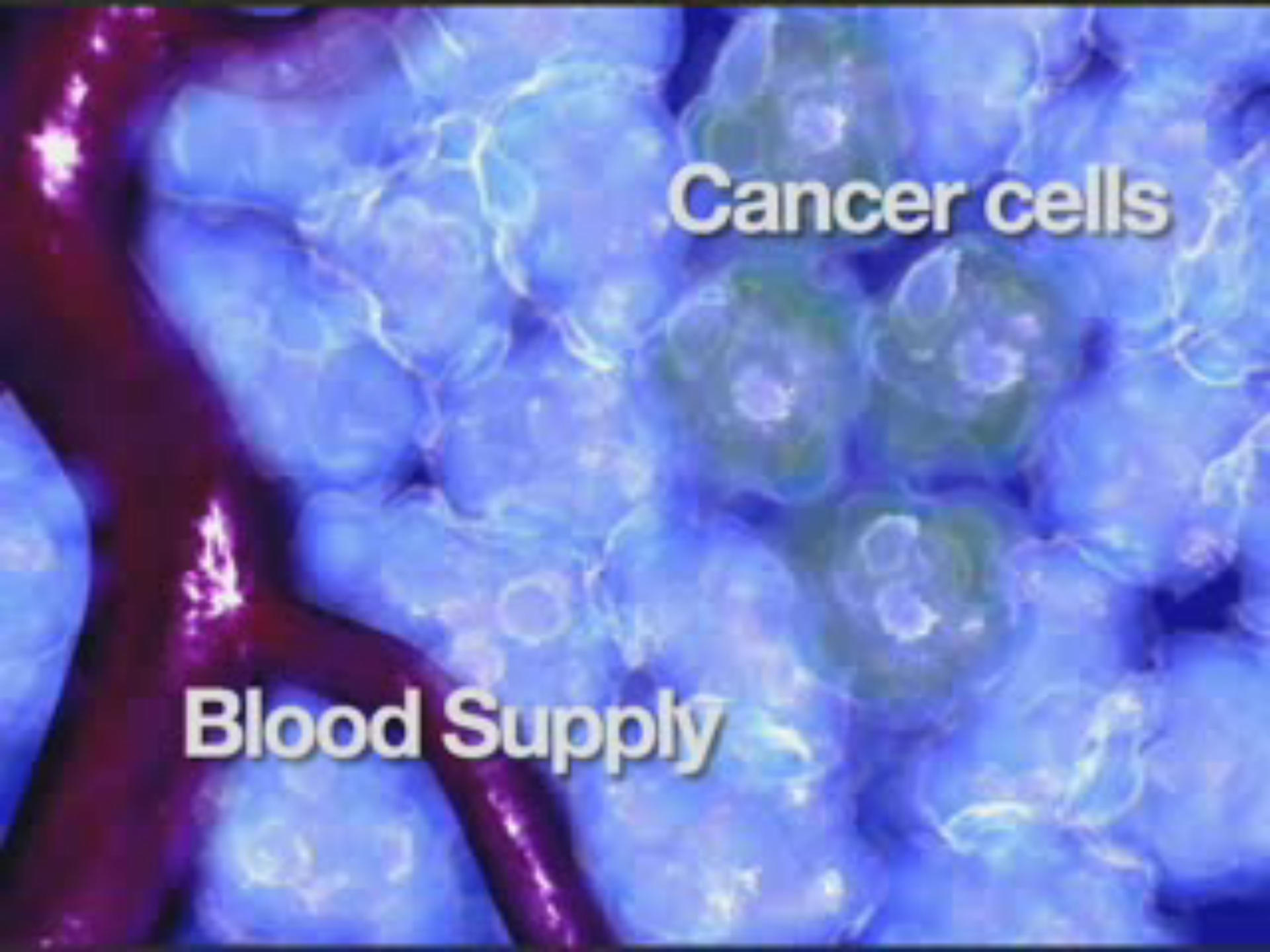


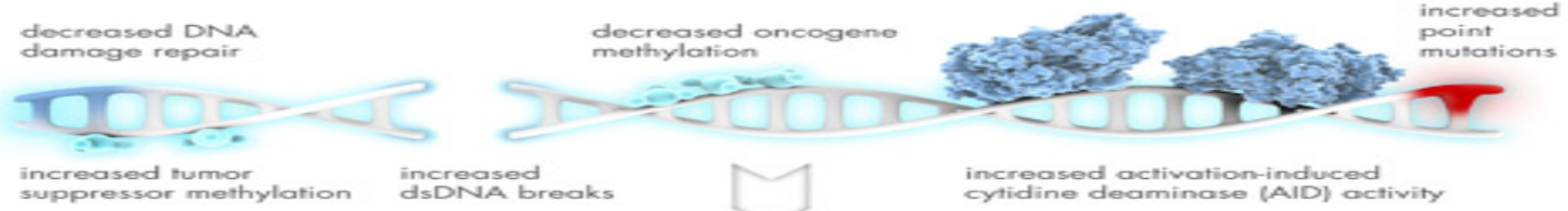
FIGURA 7.3 Mapa conceitual. Mecanismos genômicos do câncer. (Imagem modificada a partir de Porth CM. Essentials of Pathophysiology: Concepts of Altered Health States. Philadelphia: Lippincott Williams & Wilkins, 2003.)

- Falha nos processos que induzem a divisão celular


Cancer cells
Blood Supply

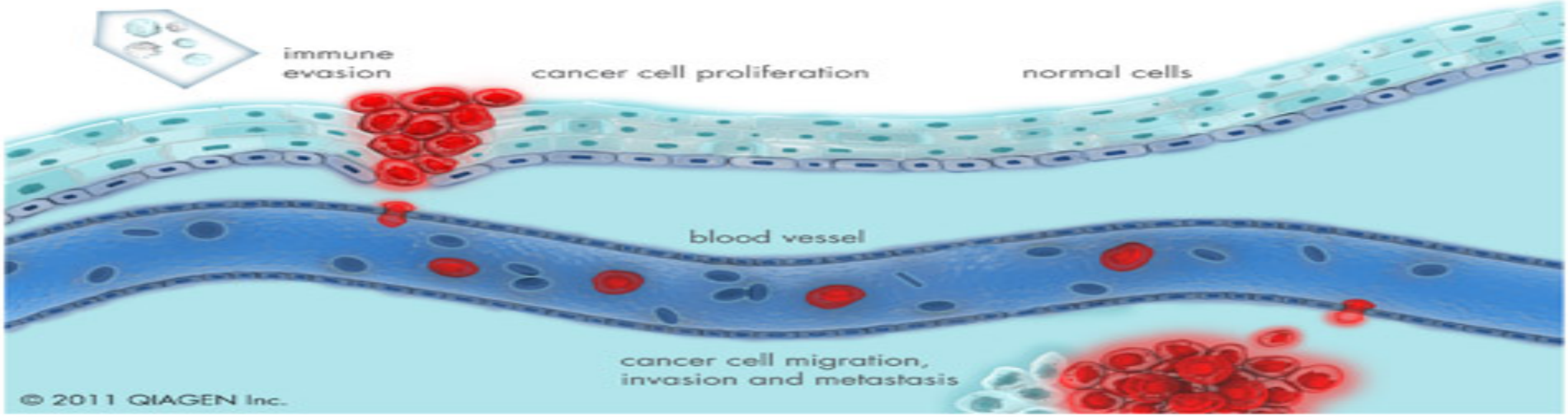
Extrinsic pathway

Genomic and epigenetic instability



Inflammatory mediators

Transformation and metastasis

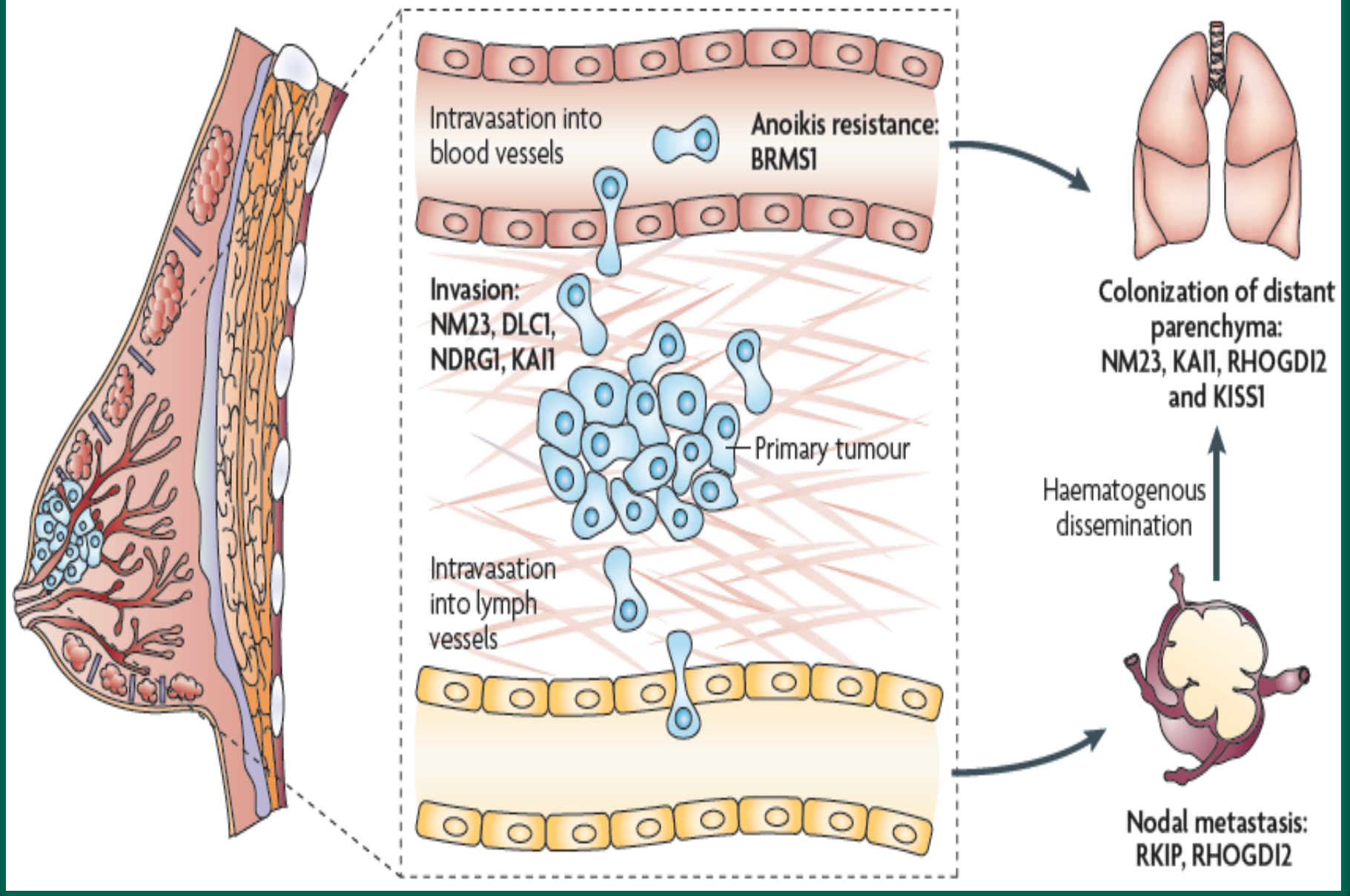


Learning therapeutic lessons from metastasis suppressor proteins

Steven Christopher Smith and Dan Theodorescu

NATURE REVIEWS | CANCER

VOLUME 9 | APRIL 2009 |


Intravasation into blood vessels
Anoikis resistance: BRMS1
Invasion: NM23, DLC1, NDRG1, KAI1
Primary tumour
Intravasation into lymph vessels
Colonization of distant parenchyma: NM23, KAI1, RHOGDI2 and KISS1
Haematogenous dissemination
Nodal metastasis: RKIP, RHOGDI2

Annals of Oncology

Annals of Oncology 23: 298–304, 2012
doi:10.1093/annonc/mdr306
Published online 27 June 2011

Cancer of unknown primary: progress in the search for improved and rapid diagnosis leading toward superior patient outcomes

F. A. Greco[1]*, K. Oien[2], M. Erlander[3], R. Osborne[4], G. Varadhachary[5], J. Bridgewater[6], D. Cohen[7] & H. Wasan[8]

Table 1. Favorable prognostic subsets of patients with unknown primary cancer recognized by clinical and pathologic features in the last three decades

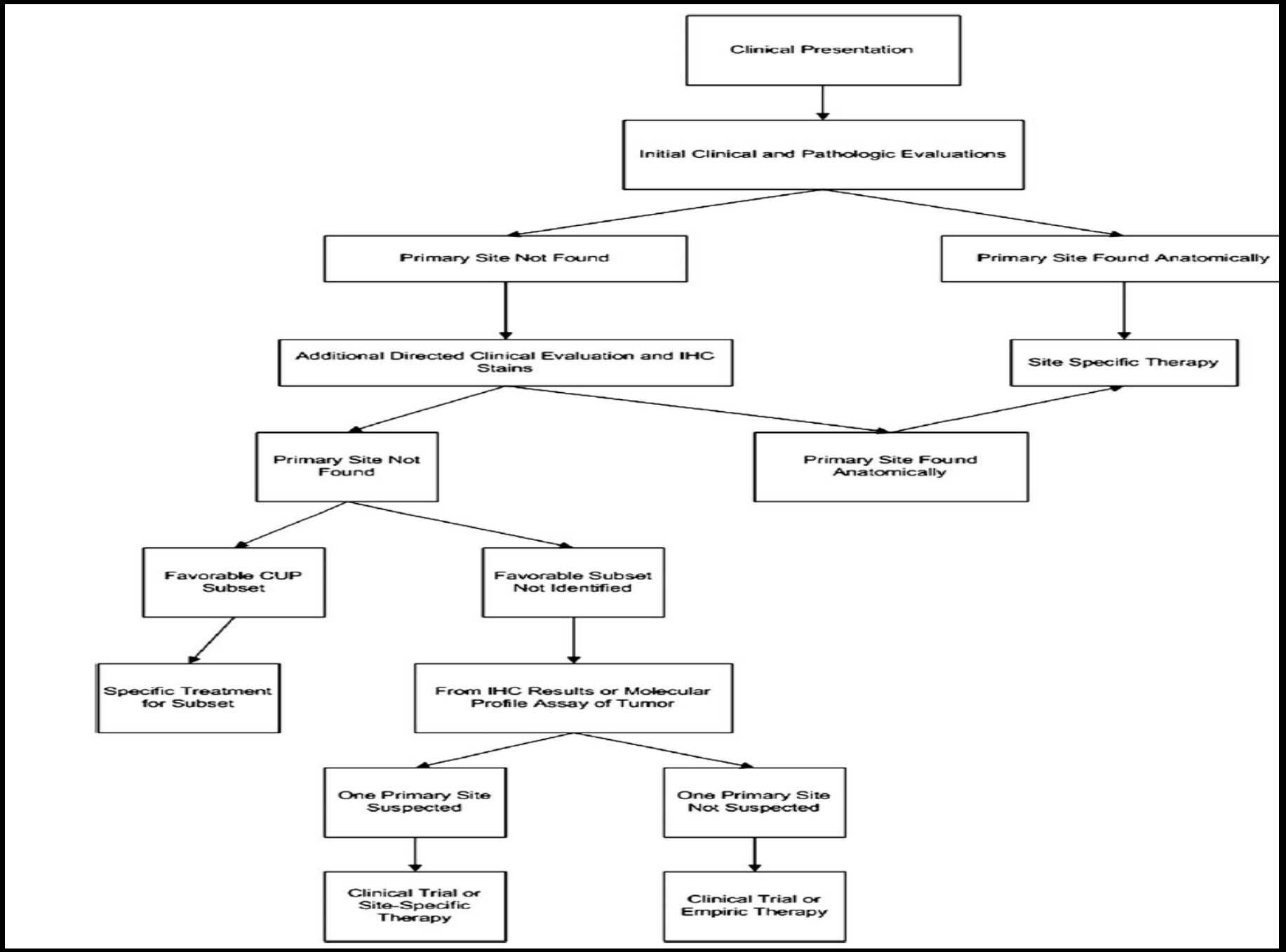
1.	Extragonadal germ cell tumor
2.	Poorly differentiated malignant neoplasms (60%= lymphoma)
3.	Retroperitoneal, mediastinal and/or peripheral lymph node involvement
4.	Squamous cell carcinoma (head/neck or inguinal area)
5.	Isolated axillary carcinoma (women, rare in men)
6.	Peritoneal carcinoma (women, rare in men)
7.	Blastic bone METS or increased PSA in serum or tumor (men)
8.	Neuroendocrine carcinoma (low-grade or well differentiated-carcinoid /islet cell type)
9.	Neuroendocrine carcinoma (high-grade or poorly differentiated-small cell, large cell, others)
10.	Single site of involvement (one lesion)

Table 2. Commercially available molecular assays using gene expression profiling for CUP

	Test	Platform	Material	No. of genes profiled	No. of tumor classes	Strategy	Claimed % sensitivity
bioTheranostics	CancerTYPE ID®	RT-PCR	FFPE	92	54	Nearest Neighbor	87
Pathworks	Pathwork® Tissue Of Origin Test	Oligonucleotide microarray	Fresh/frozen	>1500	15	'Similarity Score' to rule in or rule out certain tumor types	84
Rosetta Genomics–Prometheus	miRview™ mets (ProOnc Tumour SourceDxT)	RT-PCR for microRNA	FFPE	48	25; 42[a]	Binary decision tree combined with *K* nearest neighbors	90% for majority of cases

[a]Forty-two tumor classes in second-generation test of Rosetta Genomics.

CUP, cancer of unknown primary; FFPE, formalin-fixed paraffin-embedded.


Clinical Presentation
Initial Clinical and Pathologic Evaluations
Primary Site Not Found
Primary Site Found Anatomically
Additional Directed Clinical Evaluation and IHC Stains
Site Specific Therapy
Primary Site Not Found
Primary Site Found Anatomically
Favorable CUP Subset
Favorable Subset Not Identified
Specific Treatment for Subset
From IHC Results or Molecular Profile Assay of Tumor
One Primary Site Suspected
One Primary Site Not Suspected
Clinical Trial or Site-Specific Therapy
Clinical Trial or Empiric Therapy

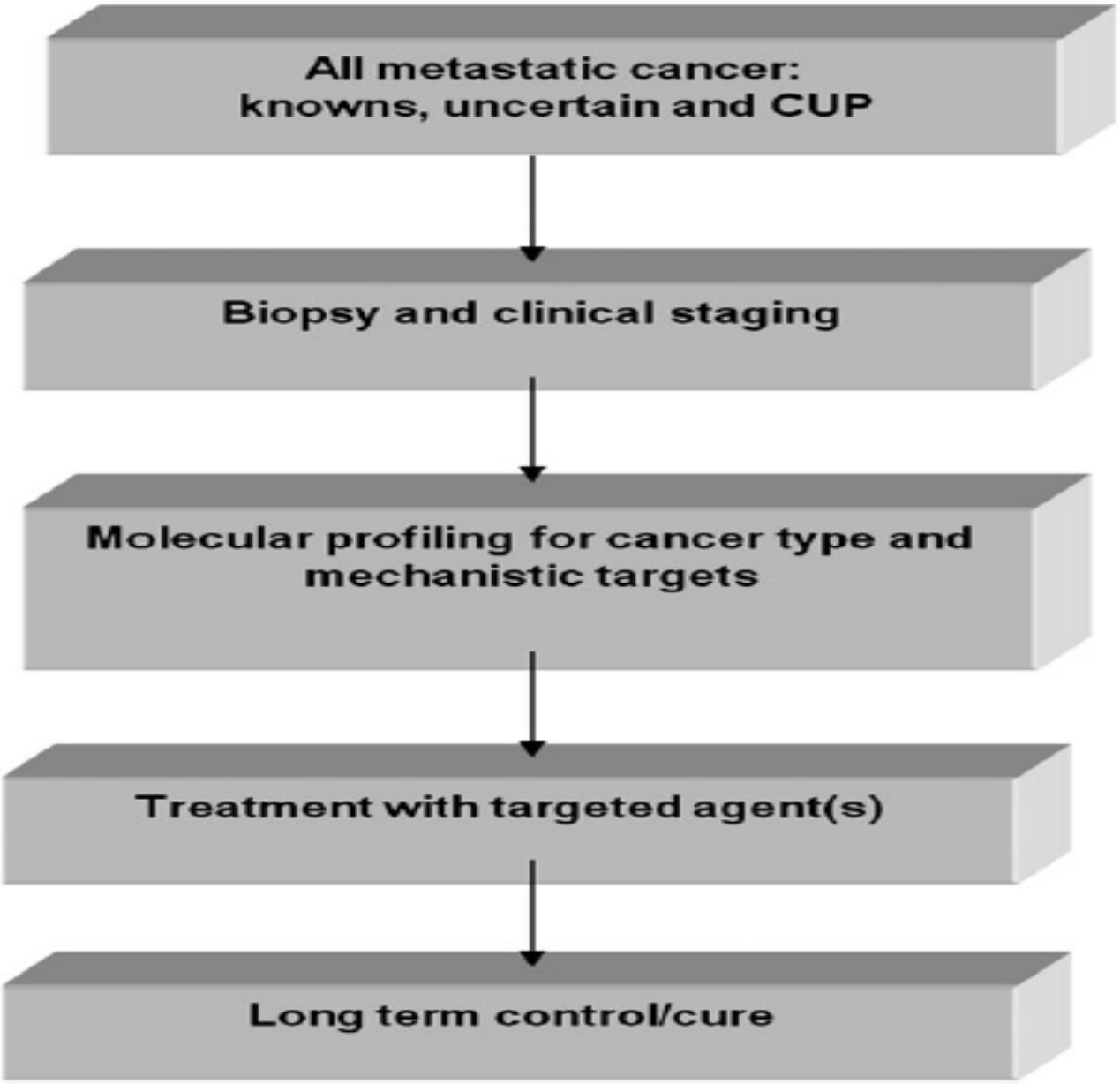


Figure 2. Ultimate model of metastatic cancers, diagnosis and treatment.

Oncogene (2006) 25, 6436–6446
 0950-9232/06 $30.00

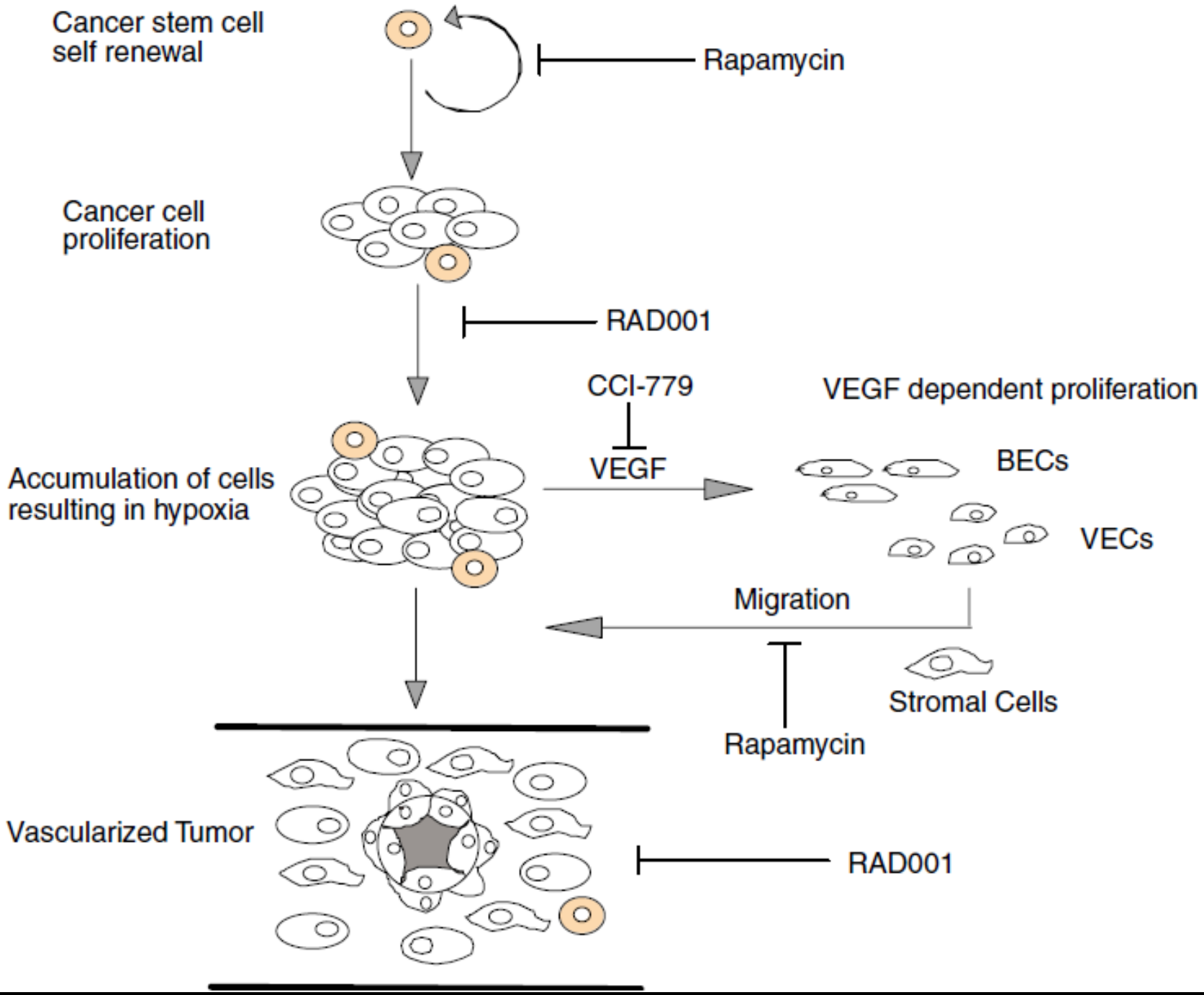
www.nature.com/onc

REVIEW

mTOR and cancer therapy

JB Easton and PJ Houghton

Department of Molecular Pharmacology, St Jude Children's Research Hospital, Memphis TN, USA


Cancer stem cell self renewal
Rapamycin
Cancer cell proliferation
RAD001
CCI-779
VEGF dependent proliferation
Accumulation of cells resulting in hypoxia
VEGF
BECs
VECs
Migration
Stromal Cells
Rapamycin
Vascularized Tumor
RAD001

ARTICLE IN PRESS

Cancer Treatment Reviews xxx (2013) xxx–xxx

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Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv

Anti-Tumour Treatment

mTOR inhibitors in advanced breast cancer: Ready for prime time?

Lesley-Ann Martin[a], Fabrice André[b,c,*], Mario Campone[d], Thomas Bachelot[e,g], Guy Jerusalem[f,h]

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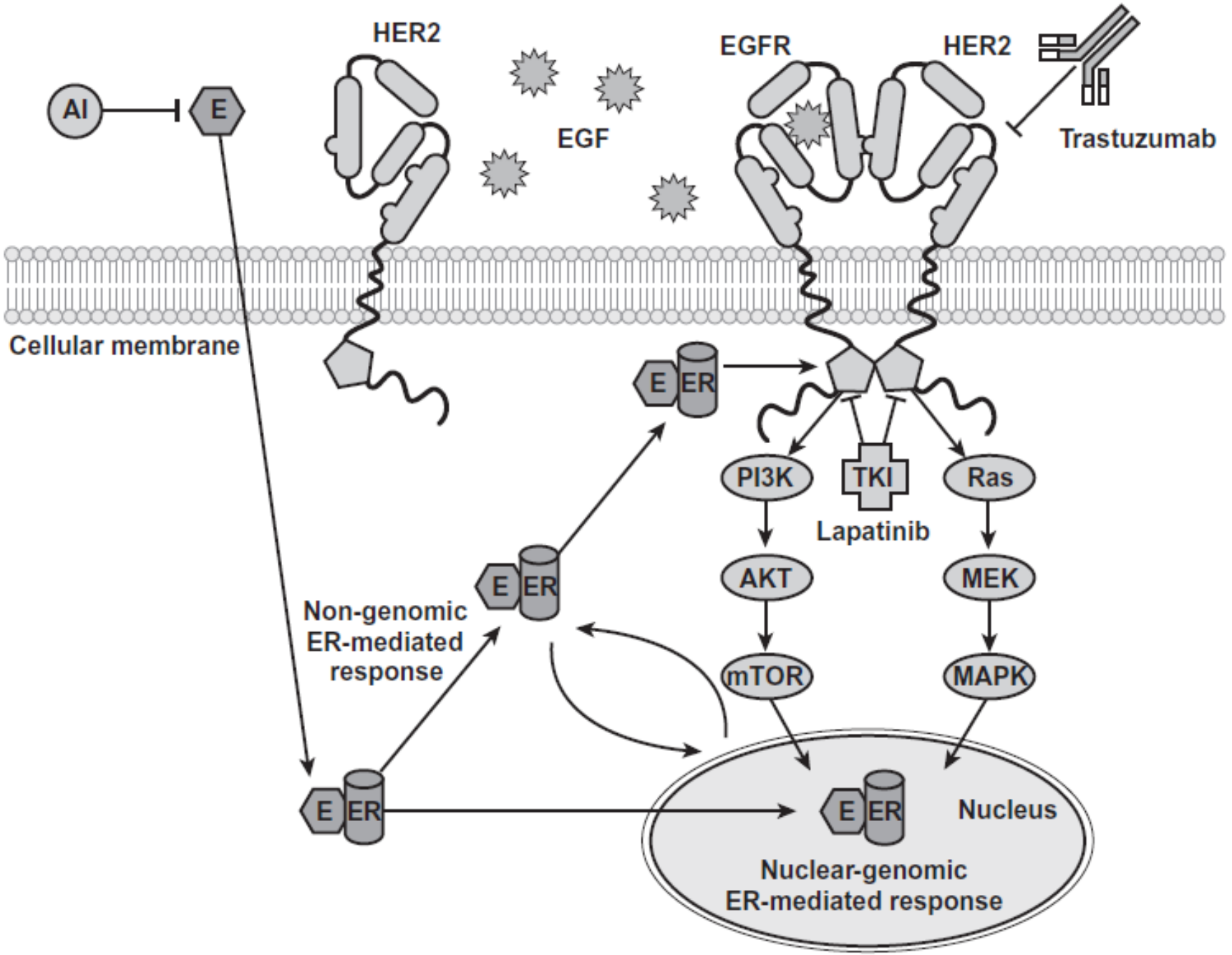
[b] Institut National des Sciences et de la Recherche Médicale (INSERM), U981, Université Paris Sud, Breast Cancer Unit, Institut Gustave Roussy, 39 Rue C. Desmoulins, 94805 Villejuif, France
[c] Department of Medical Oncology, Breast Cancer Unit, Institut Gustave Roussy, 39 Rue C. Desmoulins, 94805 Villejuif, France
[d] Institut de Cancérologie de l'Ouest/René Gauducheau, Nantes Saint Herblain, France
[e] Departement de Cancerologie Medicale, Université Lyon 1, Centre Léon Bérard, 28 Rue Laennec, 69373 Lyon, France
[f] Medical Oncology, CHU Sart Tilman Liege, University of Liege, 4000 Liege, Belgium

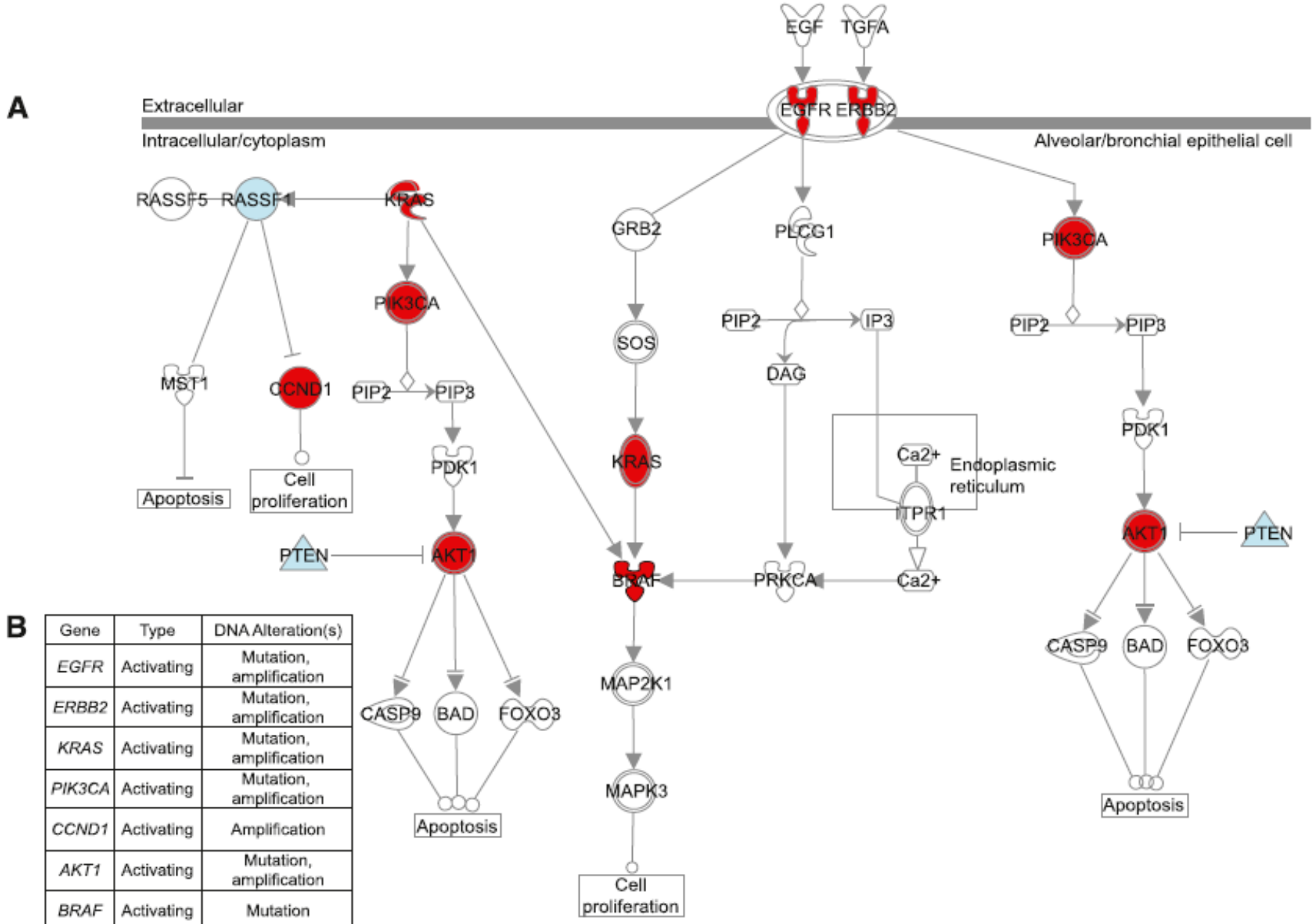

HER2
EGFR
HER2
AI
E
EGF
Trastuzumab
Cellular membrane
E ER
PI3K
TKI
Ras
Lapatinib
AKT
MEK
E ER
Non-genomic
ER-mediated
response
mTOR
MAPK
E ER
E ER
Nucleus
Nuclear-genomic
ER-mediated response

GENOME RESEARCH

Translating cancer 'omics' to improved outcomes

Emily A. Vucic, Kelsie L. Thu, Keith Robison, et al.

Genome Res. 2012 22: 188-195
Access the most recent version at doi:10.1101/gr.124354.111



B

Gene	Type	DNA Alteration(s)
EGFR	Activating	Mutation, amplification
ERBB2	Activating	Mutation, amplification
KRAS	Activating	Mutation, amplification
PIK3CA	Activating	Mutation, amplification
CCND1	Activating	Amplification
AKT1	Activating	Mutation, amplification
BRAF	Activating	Mutation
PTEN	Inactivating	Mutation, deletion, methylation
RASSF1	Inactivating	Mutation, deletion, methylation

Cytokines in the pathogenesis of cancer cachexia

Josep M. Argilés, Sílvia Busquets and Francisco J. López-Soriano

Curr Opin Clin Nutr Metab Care 6:401–406.

Figure 1. Different factors contributing to cancer cachexia

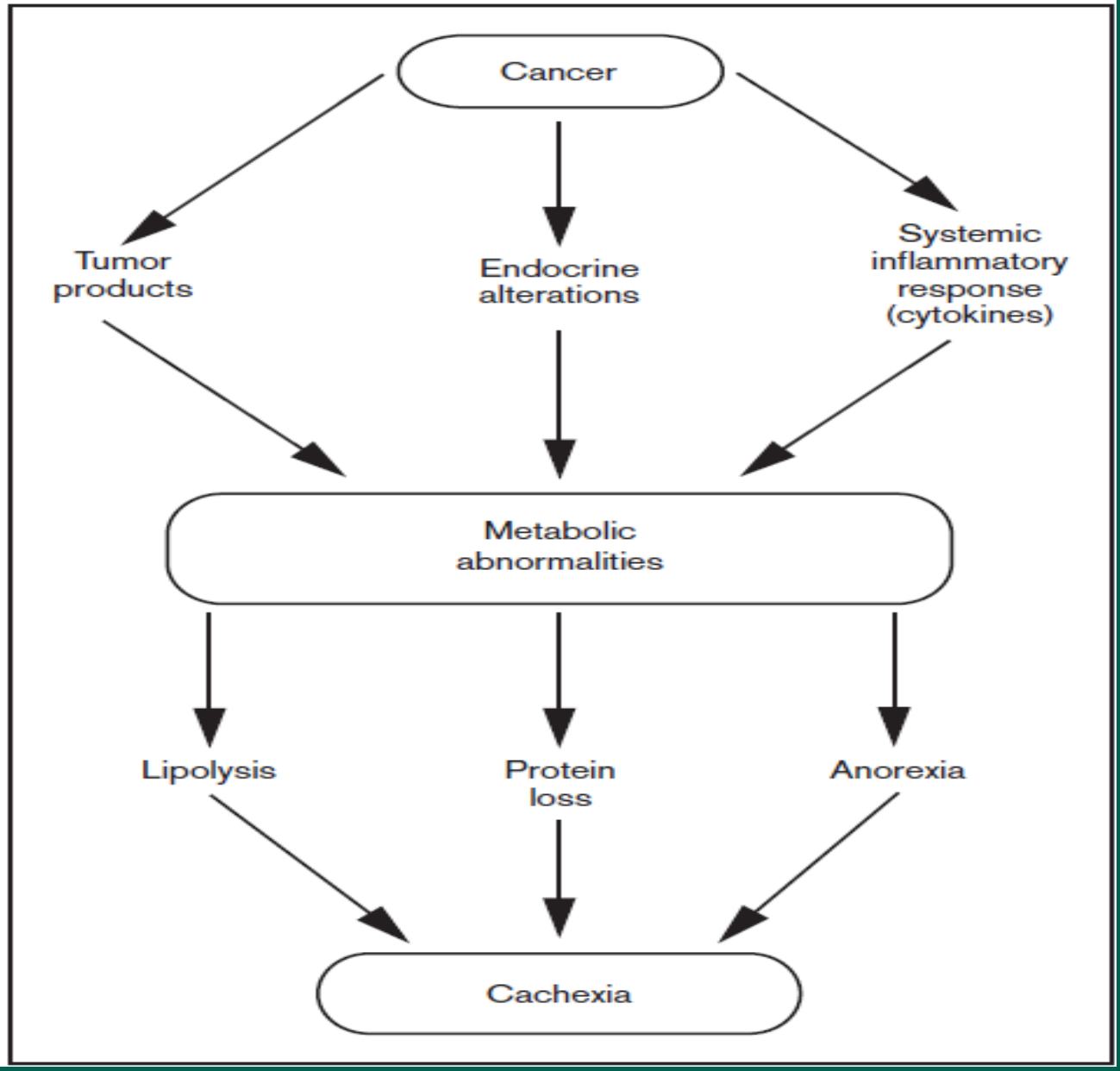
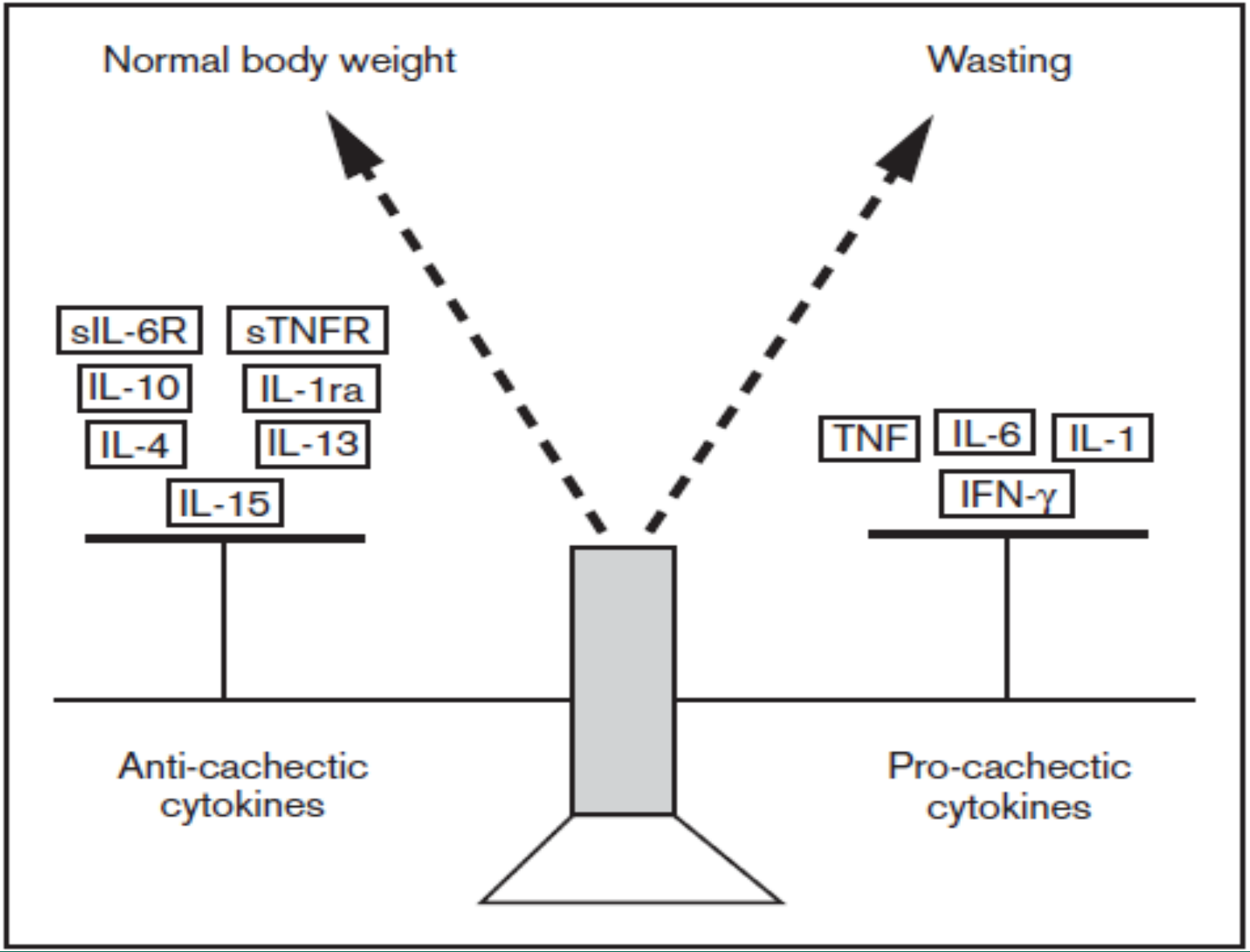


Figure 2. Cytokines and cachexia



CA CANCER J CLIN 2011;61:69-90

Global Cancer Statistics

Ahmedin Jemal, DVM, PhD[1]; Freddie Bray, PhD[2]; Melissa M. Center, MPH[3]; Jacques Ferlay, ME[4]; Elizabeth Ward, PhD[5]; David Forman, PhD[6]

- **GLOBOCAN 2008** estima em torno de 12,7 milhões de casos de câncer e 7,6 milhões de mortes em 2008;

- 56% dos casos e 64% das mortes ocorreram em países em desenvolvimento

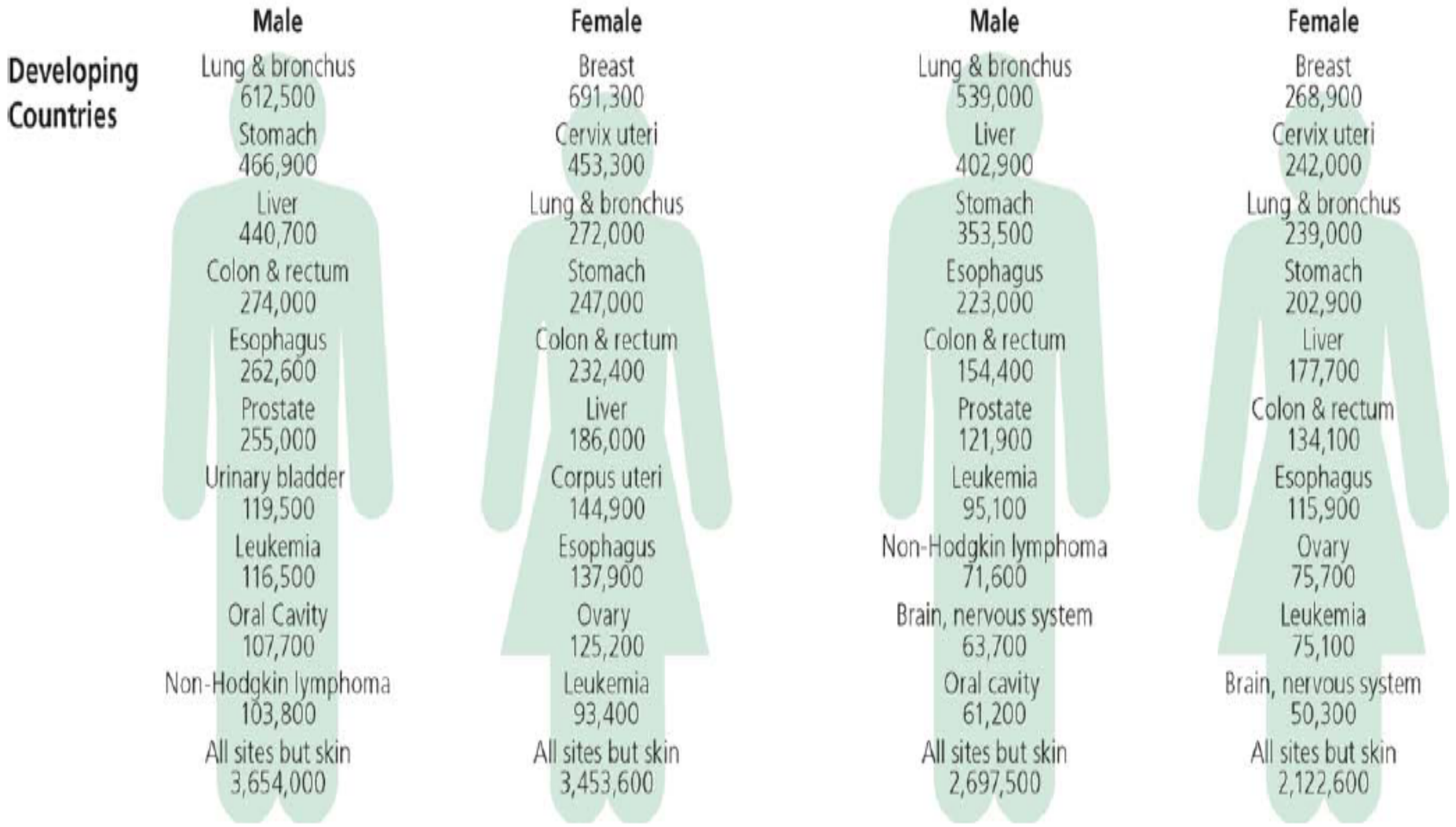


FIGURE 2. Estimated New Cancer Cases and Deaths Worldwide for Leading Cancer Sites by Level of Economic Development, 2008. Source: GLOBOCAN 2008.

CÂNCER:
EPIDEMIOLOGIA

Mais de 1 milhão de americanos a cada ano, mais comuns: próstata, colorretal, pulmão e mama;

Mais de 500 mil mortes ao ano nos EUA.

American Cancer Society, 2000

CÂNCER:
EPIDEMIOLOGIA

25% das causas de câncer são causados pelo sobrepeso, obesidade e sedentarismo;

Fatores ambientais entre 80-90% das causas;

Avanço da idade ⬆ probabilidade.

Vainio e Bianchini, 2002

CÂNCER:
EPIDEMIOLOGIA

Identificação precoce e os tratamentos aprimorados;

Atual taxa de sobrevida relativa: 5 anos (60% dos casos).

American Cancer Society, 2000

CÂNCER: TRATAMENTO

3 MODALIDADES:

- **Cirurgia;**
- **Radioterapia;**
- **Terapia sistêmica (medicamentos): quimioterapia, terapia endócrina e biológica.**

Vainio e Bianchini, 2002

Local da Irradiação	Efeitos Adversos Comuns
Pele	**Vermelhidão, dor, ressecamento, *peeling*, descamação, elasticidade reduzida**
Cérebro **Faringe** **Glândula salivar** **Tórax**	**Náuseas e vômitos, fadiga, perda da memória** **Ulceração da boca** **Xerostomia (boca seca)** **Um certo grau de fibrose pulmonar irreversível, o coração pode receber irradiação, acarretando a inflamação ou fibrose pericárdica; aterosclerose prematura, miocardiopatia**
Abdome **Pelve**	**Vômitos, diarréia** **Diarréia, dor pélvica, fibrose vesical, ocasionalmente incontinência e disfunção sexual**
Articulações	**Fibrose do tecido conjuntivo e das cápsulas articulares; possível redução na AM**

Current Treatment Options in Oncology
DOI 10.1007/s11864-010-0121-5

Alternative Therapies

Exercise Therapy in the Management of Solid Tumors

*Lee W. Jones, PhD**
Jeffrey Peppercorn, MD
Jessica M. Scott, PhD
Claudio Battaglini, PhD

Published online: 20 July 2010

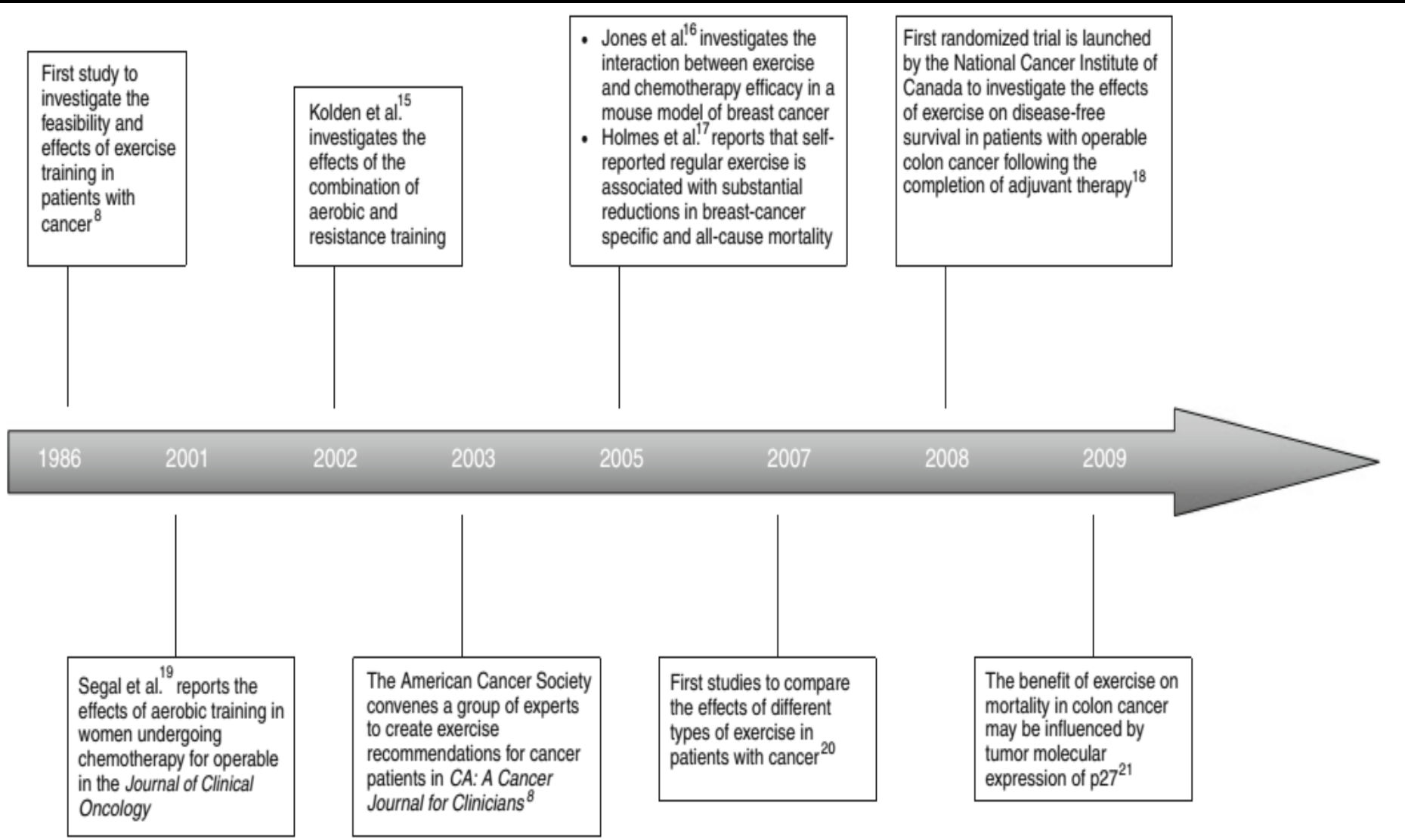


Figure 1. Exercise–oncology research timeline

ATIVIDADE FÍSICA

Tipo, duração, intensidade e freqüência

Dose

Thune e Furberg, 2001

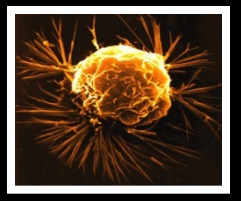
Balanço energético?

Hormônios?

Mecânica?

Imunidade?

Reparo DNA?



Célula normal

5-20 anos

Câncer

ATIVIDADE FÍSICA

50% câncer de cólon

3h caminhada/semana

17% câncer de cólon

Colditz et al., 1997

CÂNCER E EXERCÍCIO:

Direcionamentos da aula

O **exercício** melhora o estado patológico no paciente com câncer?

O **exercício** pode efetivamente prevenir o câncer?

Como e quais as modalidades de exercício a serem aplicadas em pacientes **c/ câncer?**

CÂNCER E EXERCÍCIO:

Direcionamentos da aula

O **exercício** é seguro para indivíduos com câncer durante o tratamento?

Qual a intensidade, volume, duração e freqüência do exercício para pacientes com câncer?

Quais as **adaptações** agudas e crônicas ao **exercício** em indivíduos com **câncer?**

SPECIAL COMMUNICATIONS

Roundtable Consensus Statement

American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors

EXPERT PANEL

Kathryn H. Schmitz, PhD, MPH, FACSM
Kerry S. Courneya, PhD
Charles Matthews, PhD, FACSM
Wendy Demark-Wahnefried, PhD
Daniel A. Galvão, PhD
Bernardine M. Pinto, PhD
Melinda L. Irwin, PhD, FACSM
Kathleen Y. Wolin, ScD, FACSM
Roanne J. Segal, MD, FRCP
Alejandro Lucia, MD, PhD
Carole M. Schneider, PhD, FACSM
Vivian E. von Gruenigen, MD
Anna L. Schwartz, PhD, FAAN

0195-9131/10/4207-1409/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0b013e3181e0c112

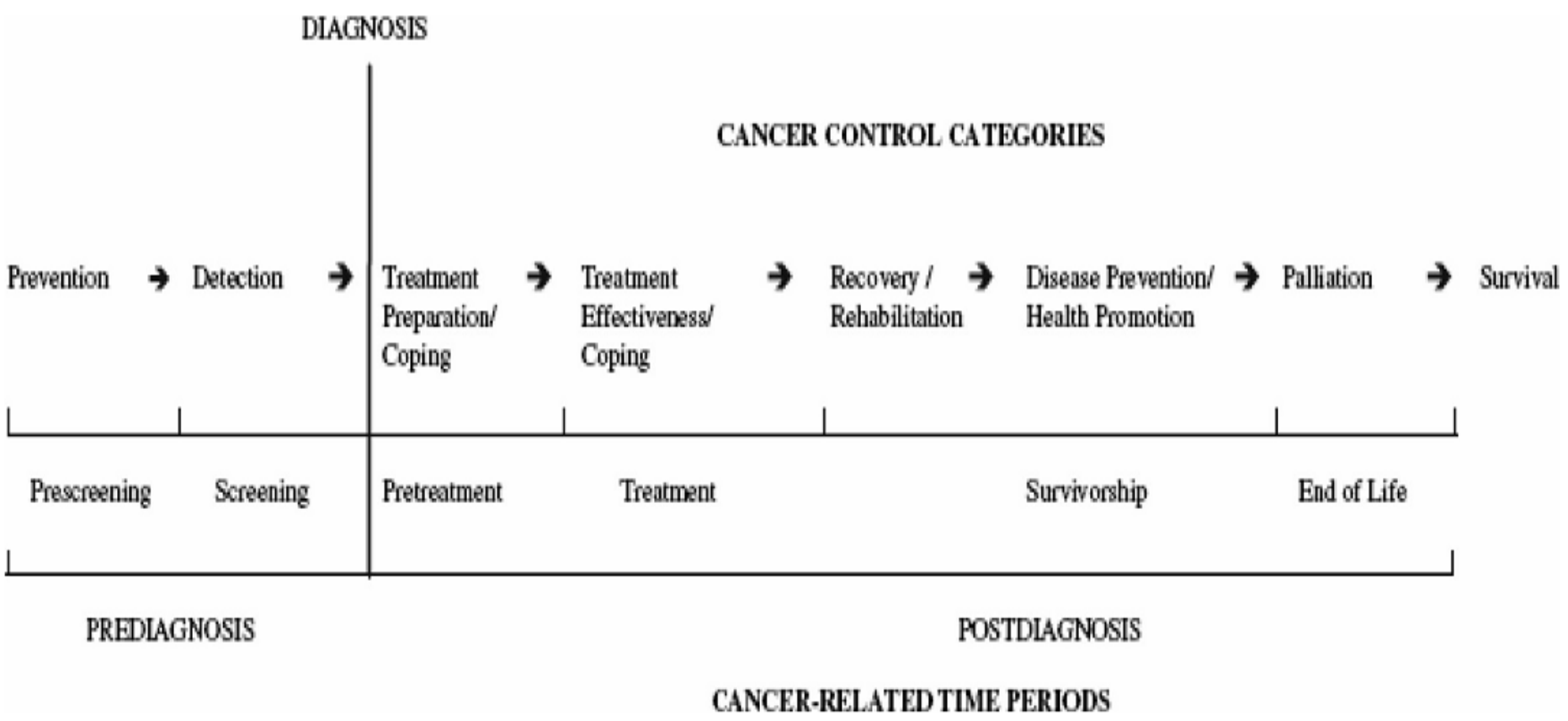


FIGURE 1—Physical activity and cancer control framework. (Reprinted from Courneya KS, Friedenreich CM. Physical activity and cancer control. *Semin Oncol Nurs.* 2007;23(4):242–52. Copyright © 2007 Elsevier. Used with permission.)

TABLE 1. Persistent changes resulting from the most commonly used curative therapies.

	Surgery	Chemotherapy	Radiation	Hormonal Therapy, Oophorectomy or Orchiectomy	Targeted Therapies
Second cancers		✔	✔		
Fatigue	✔	✔	✔	✔	✔
Pain	✔	✔	✔	✔	✔
Cardiovascular changes: damage or increased CVD risk		✔	✔	✔	✔
Pulmonary changes	✔	✔	✔		
Neurological changes:					
Peripheral neuropathy		✔			
Cognitive changes	✔	✔	✔	✔	✔
Endocrine changes					
Reproductive changes (e.g., infertility, early menopause, impaired sexual function)	✔	✔	✔	✔	✔
Body weight changes (increases or decreases)	✔	✔		✔	
Fat mass increases	✔	✔		✔	
Lean mass losses	✔	✔		✔	
Worsened bone health		✔	✔	✔	
Musculoskeletal soft tissues: changes or damage	✔		✔	✔	
Immune system					
Impaired immune function and/or anemia		✔	✔	✔	✔
Lymphedema	✔		✔		
Gastrointestinal system: changes or impaired function	✔	✔	✔	✔	✔
Organ function changes	✔				
Skin changes			✔	✔	✔

TABLE 5. Overview of evidence regarding the efficacy of exercise interventions for specific outcomes in cancer survivors.[a]

Outcome	Breast (during Chemotherapy and Radiotherapy)	Breast (after Chemotherapy and Radiotherapy)	Prostate	Colon	Adult Hematologic (No HSCT)	Adult HSCT	Gynecologic
No. studies reviewed[b]	21	32	12	4	4	11	1
Safety (no exercise-related adverse events reported)	13	15	6		1	6	
Physical function	2	4	4			1	
Physical fitness							
Aerobic fitness	10	10	5	1	3	5	
Muscular strength	5	6	4			2	
Flexibility		5	1				
Physical activity level	5	8	4	1		1	1
Body size (weight, BMI, body composition, muscle mass)	4	8	6		1	2	1
Bone health	2	1					
Safety about lymphedema-related outcomes	2	7					
QOL	4	12	6		1	3	
Energy level or vigor/vitality		3	1				
Fatigue	4	4	5		3	3	
Sleep	1				1		
Depression		3			1		
Anxiety	3	3					
Physiological outcomes (e.g., hemoglobin, blood lipids, IGF pathway hormones, oxidative stress, inflammation, or immune parameters; includes PSA for prostate cancer)	3	6	2	2			
Symptoms/adverse effects (including pain)	3	3	1		1		

IGF, insulin-like growth factor.

[a] Numbers in the table reflect the number of studies with a significant positive effect on the outcomes listed.

[b] For breast, only RCTs meeting criteria for high internal validity were reviewed. See text for description of criteria of internal validity criteria. For other sites, all intervention studies were included.


CÂNCER E
EXERCÍCIO:
ADAPTAÇÕES E BENEFÍCIOS

CÂNCER E EXERCÍCIO:

Durante e após o tratamento

Programas de TA de 2-16 semanas;

Melhora na capacidade funcional, composição corporal, atividade células NK, estados de humor e qualidade de vida

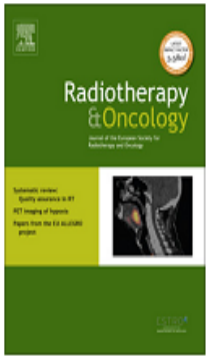
Courneya et al., 1999; Keats et al., 1999; McBride et al., 2000; Hardman, 2001; Galvão e Newton, 2005; De Caro et al., 2006; Haydon et al., 2006.

Radiotherapy and Oncology xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Review

The effect of progressive resistance training on lean body mass in post-treatment cancer patients – A systematic review

Simon Lønbro *

Dept. of Public Health, Section for Sports Science, Aarhus University; and Dept. of Experimental Clinical Oncology, Aarhus University Hospital, Denmark

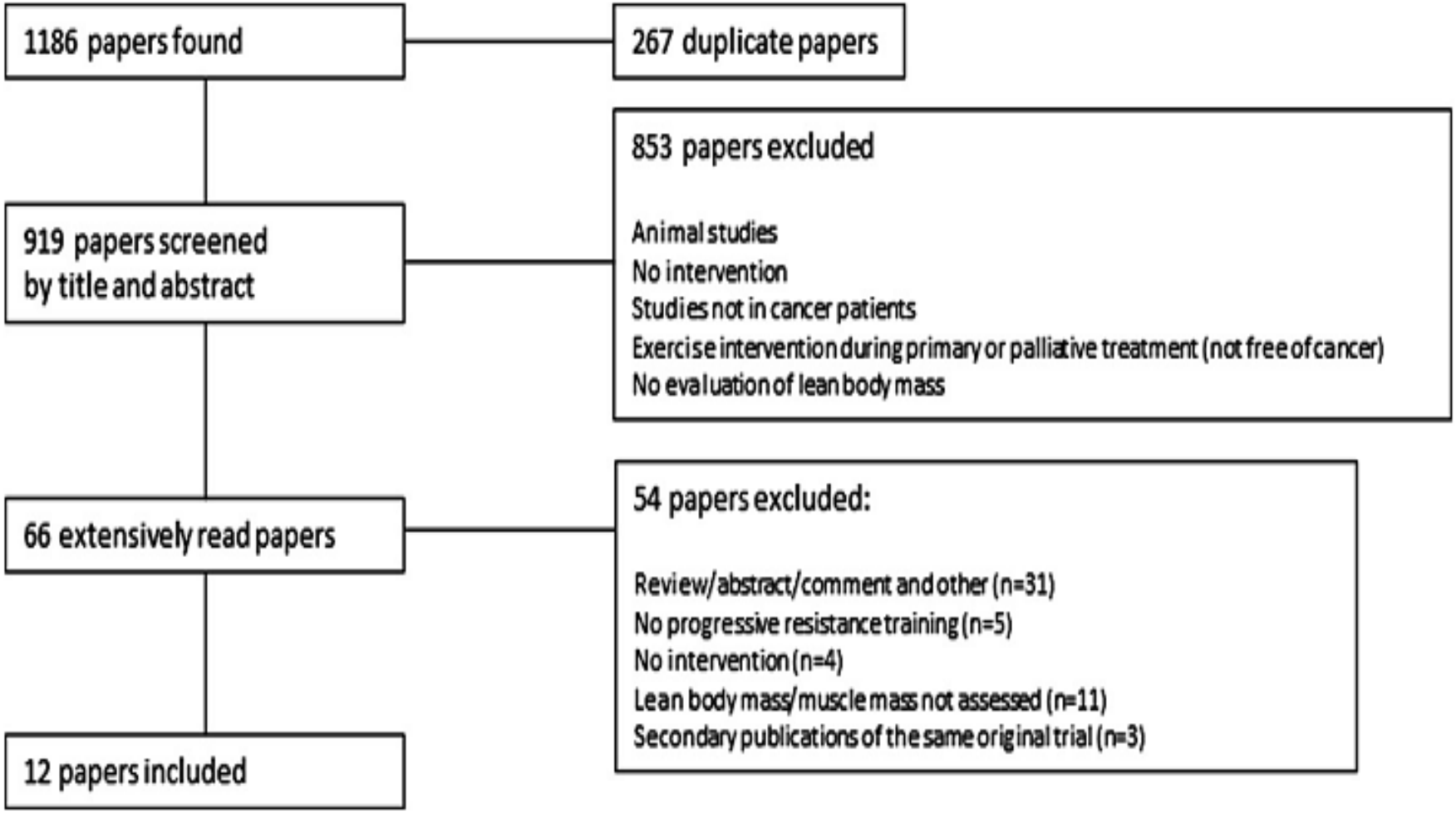


Fig. 1. Flow chart illustrating the systematic inclusion of the literature.

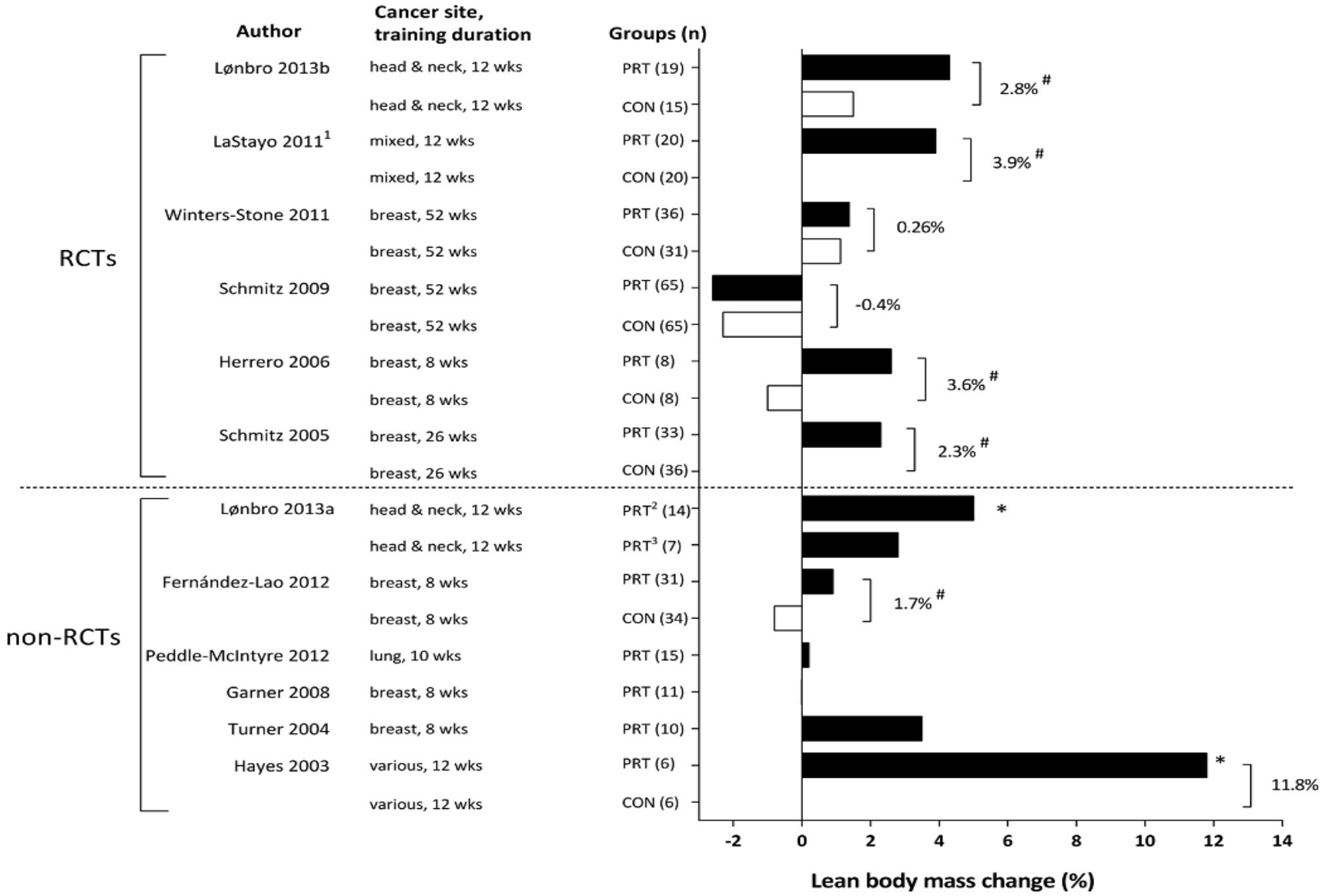


Fig. 2. Relative changes over time reported in the all groups of the include trials performing progressive resistance training (PRT) and the control groups (CON) of the RCTs and non-randomized controlled trials. The effect of progressive resistance training was calculated as the relative change following progressive resistance training minus the relative change in the control groups. Significant group difference in RCTs and controlled non-RCTs are denoted # ($p < 0.01$) and significant change over time within group in all other non-RCTs are denoted *($p < 0.01$). The number of patients in each group represents the number of patients included in the statistical analyses of the given study.1: Muscle mass evaluated as Quadriceps cross sectional area. 2: The group of the trial completing progressive resistance training with dietary protein and creatine supplementation. 3: The other group of the same trial completing progressive resistance training with placebo supplementation.

Precauções especiais ao realizar o teste de esforço nos sobreviventes do câncer

Adaptado de Courneya, Mackey e Jones, 2000

Complicação	Precaução
Hemograma completo Nível de hemoglobina < 8,0 g/dl Contagem absoluta de neutrófilos ≤ 0,5 x 10^9/l Contagem de plaquetas < 50 x 10^9/l	Evitar testes que exigem um transporte significativo de O_2 (testes aeróbios máximos). Garantir a esterilização apropriada do equipamento. Evitar testes que aumentam o risco de sangramento (exercícios de alto impacto).
Febre > 38^0C	Pode indicar infecção sistêmica e deve ser investigada (evitar teste).
Ataxia/vertigem/neuropatia sensorial periférica	Evitar os testes que exigem equilíbrio e coordenação significativos (esteira roalnte, pesos livres).
Caquexia intensa (perda de mais de 35% do peso pré-morbido)	A perda de massa muscular costuma limitar o exercício para uma intensidade leve, dependendo do grau de caquexia (evitar teste).

Precauções especiais ao realizar o teste de esforço nos sobreviventes do câncer

Adaptado de Courneya, Mackey e Jones, 2000

Complicação	Precaução
Feridas/ulcerações na boca	Evitar as peças bucais para testes aeróbios. Utilizar mascaras faciais.
Dispnéia	Evitar os testes máximos.
Dor óssea	Evitar os testes que elevam os riscos de fratura (testes de alto impacto/ estresse, como esteira rolante e 1RM).
Náuseas/vômitos intensos	Evitar os testes máximos.
Fadiga/fraqueza externa	Iniciar os testes com um rendimento de potência mais baixo, utilizar pequenos aumentos progressivos, evitar testes máximos
Feridas cirúrgicas/hipersensibilidade	Escolher um teste que evita a pressão/traumatismo no local cirúrgico.
Estado funcional precário	Evitar teste de esforço

QUESTIONÁRIO PARA HISTÓRIA DO CÂNCER

- Data do diagnóstico do câncer (dia/mês/ano):
- Tipo de câncer (ex: mama, cólon):
- Estágio do câncer ao ser feito o diagnóstico (I, II, III, IV):
- O tratamento inclui/irá cirurgia? S N (circundar)

  Caso afirmativo: Que tipo de cirurgia?

  Data da cirurgia (dia/mês/ano):

  Limitações impostas pela cirurgia:
- O tratamento inclui/irá radioterapia? S N (circundar)

  Caso afirmativo: Início e datas finais (dia/mês/ano):

  Esquema de tratamento:

  Locais do corpo irradiados:

  Efeitos colaterais agudos/crônicos:
- O tratamento inclui/irá quimioterapia? S N (circundar)

  Caso afirmativo: Início e datas finais (dia/mês/ano):

  Esquema de tratamento:

  Locais do corpo irradiados:

  Efeitos colaterais agudos/crônicos:
- Queira descrever tudo mais que seja relevante acerca do diagnóstico ou tratamento do seu câncer:

Adaptado de Courneya, Mackey e Quinney, 2000