

CURRICULUM VITAE

Name: Luis António Marques da Costa

Date of Birth: June 8, 1961.
S.Paulo. Brazil

Present Title and Affiliation:

Director of the Oncology Division at Hospital de Santa Maria
Professor of Medicine & Biology of Cancer – Faculdade de Medicina de Lisboa
Principal Investigator of Instituto de Medicina Molecular (IMM) – Research Leader of
The Clinical Translational Oncology Research Unit at IMM.

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Research Theme/ Focus

My interests in clinical research have been focus in the area of bone metastases since 1995. The clinical projects were designed and developed in Lisbon (Hospital de Santa Maria) in collaboration with the Penn State University (Dr. Allan Lipton research team). We tested the clinical value of type I bone collagen fragments to monitor treatment response in patients with bone metastases. The results achieved were published and have been used as biochemical parameters of response in clinical trials testing new drugs to treat bone metastases.

The interpretation of some of the results observed in our previous research lead us to disclose the role of matrix metalloproteinases (MMPs) in osteoclast independent mechanisms of bone degradation. Since then we pursue the hypothesis that MMPs, namely MMP1 have a central role in bone metastases progression and resistance to bisphosphonates. The purpose of this research is to identify biochemical pathway-based molecular targets and develop agents to intervene phenotypic cancer signaling in metastatic setting.

More recently, we became also interested in testing the role of collagen fragments derived from MMP1 activity over collagen type as growth/survival factors for cancer cells. In 2008 our Translational Research Unit was selected to receive the Therry Fox award. These basic research projects have been developed at IMM.

We are evaluating in a clinical trial the synergism interaction between bisphosphonates and taxanes in breast cancer and prostate cancer with bone metastases.

Over the years, we have been collaborating with Dr. Rakesh Kumar chairman of Department of Molecular & Cellular Oncology UT M. D. Anderson Cancer Center, Houston, Texas in research projects involving human breast tumor samples from our institution. As an example we identified a correlation between the presence of lymph node metastases and the expression of paxillin in tumor samples.

In the Oncology Division at Hospital de Santa Maria I have been collaborating as principal investigator of several international clinical trials (phase 2 and 3) testing the therapeutic effectiveness of new agents. Our division is active at the moment in 14 international clinical studies. In the last two years I have been acting as principal investigator in 12 clinical trials (breast cancer, colon cancer, bone metastases: breast cancer; prostate cancer; other solid tumors)

Education:

College in the city of Viseu-Portugal.	1978
Medical Education at the University of Lisbon	1979-1985
University degree in Medicine	1985

Professional Training – Hospital Appointments:

Internship, Hospital de Santa Maria. Lisbon	1986-1987
Residency and Fellowship in Internal Medicine, Hospital de Santa Maria, University of Lisbon.	1988-1993
Fellowship in Medical Oncology, Hospital de Santa Maria and Oncology Portuguese Institute,Lisbon	1990-1993
Visitor fellow at Hershey Medical Center (Grant from the Luso-American Foundation)	1992
Assistant Physician at the Oncology Unit, Hospital de Santa Maria, Lisbon	1993
Consultant in Oncology	1999
Chief in Oncology	2009
Director of the Oncology Division - Hospital de Santa Maria	Present situation
Member of the Oncology Committee at Hospital de Santa Maria	2005-

Academic Appointments:

Assistant Professor of Medicine, Faculdade de Medicina de Lisboa, University of Lisbon	1995-2002
PhD in Medical Oncology (Thesis on Bone Metastases) Professor of Medicine, Faculdade de Medicina de Lisboa, University of Lisbon	2002
Principal Investigator of the Molecular Medicine Institute (IMM) University of Lisbon	2002
Visiting Professor at the M.D. Anderson Cancer Center	2003, 2004
Head of the Clinical Translational Oncology Research Unit (CTORU) at IMM	2007-present
Member of Board Directors from the Master Course in Palliative Medicine at University of Lisbon	2004 – present
Member of Board Directors from the Master Course in Clinical Oncology	2006
Coordinator Professor of “Oncobiologia” – Teaching Unit at school of Medicine Faculdade de Medicina de Lisboa	2009-2010

Certification:

Certified Portuguese Board of Internal Medicine
Certified Portuguese Board of Medical Oncology
Certified member of ESMO (European Society of Medical Oncology)

Medical Societies:

Portuguese Board of Internal Medicine
Portuguese Board of Medical Oncology
American Society of Medical Oncology
European Society of Medical Oncology
European Association for Cancer Research
Member of the Direction Committee of the Portuguese Society of Oncology (2003-5)

Research support:

Principal Investigator, Prognostic Signatures in Colorectal Cancer (PSCC).
FCT: PIC/IC/82821/2007
FLAD: support to PhD in Oncology – 2002.
Principal Investigator, Analysis of RANK/RANKL and MMPs in clinical samples of solid tumors bone metastases – 2008-2010, Amgen, inc, USA –

Reviewer of Scientific Manuscripts

Annals of Oncology; Bone; British Journal of Cancer; Critical Reviews in Oncology/Hematology; Cancer Letters; European Journal of Cancer; Breast Cancer Research and Treatment; The Oncologist.
Member of the Editorial board of Harvard Medical School Portugal Program

Reviewer of Grants

European Research Council
Cancer Research UK

Main publications:

Biochemical markers of bone turnover in patients with metastatic bone disease.
Laurence M.Demers, **Luis Costa**, Vernon Chinchilli, Allan Lipton.
Clinical Chemistry, vol.41 n°10:1489-1494, 1995.

Effect of Fadrozole Hydrochloride (CGS 16949) on cholesterol, lipid, and hemostatic parameters in women with advanced breast cancer.
L.Costa, M.Kopreski, V.Chinchilli, R.Santen, H.Harvey, A.Lipton.
Cancer 85(1) 100-103, 1999.

Markers of Bone Resorption in Patients Treated with Pamidronate.
A.Lipton, L.Demers, E.Curley, V.Chinchilli, L.Gaydos, G.Hortobagyi, R.Theriault, D.Clemens, **L.Costa** et al.
European Journal of Cancer vol.33, n°13, 2021-2026, 1998.

Transcriptional Up-Regulation of Paxillin Expression by Heregulin in Human Breast Cancer Cells.
R. Vadlamudi, L.Adam, B.Tseng, **L.Costa**, R.Kumar.
Cancer Research 59 (12): 2843-2846, June 15, 1999.

Biochemical markers and Skeletal metastases.

Laurence Demers, **Luis Costa**, Allan Lipton.

Cancer suppl. Vol. 88: 2919-2926, June 15, 2000.

Bone markers in the management of metastatic bone disease.

A.Lipton, **L.Costa**, S.M.Ali and L.M.Demers.

Cancer Treatment Reviews, suppl. 1-5, 2001

Growth Factors regulate heterogeneous Nuclear Ribonucleoprotein K expression and Function.

Manitosh Mandal, Ratna Vadlamudi, Diep Nguyen, Rui-An Wang, **Luis Costa**, Rozita Bagheri-Yarmand, John Mendelson and Rakesh Kumar.

Journal of Biological Chemistry vol.276, n°13:9699-9704, 2001.

Safety and efficacy of bisphosphonates beyond 24 months in cancer patients.

S.M.Ali, F.J.Esteva, G.Hortobagyi, H.Harvey, J.Seaman, R.Knight, **L.Costa**, A.Lipton.

Journal of Clinical Oncology vol. 19, n°14: 3434-3437, 2001.

Use of markers of bone turnover for monitoring bone metastases and the response to therapy.

Allan Lipton, **Luis Costa**, Suhail Ali, Laurence Demers.

Seminars in Oncology vol.28, n°4, suppl 11: 54-59, 2001.

Prospective evaluation of the peptide-bound collagen type I cross-links N-telopeptide and C-telopeptide in predicting bone metastases status.

Luis Costa, Laurence M.Demers, A.Gouveia-Oliveira, J.Schaller, Eduardo B.Costa, Miguel C.Moura, Allan Lipton.

Journal of Clinical Oncology, vol. 20: 850-856, 2002.

Biochemical Markers and Skeletal Metastases

Laurence Demers, **Luis Costa**, Allan Lipton

Clinical Orthopaedics and Related Research, n° 415S, pp 1-10, 2003.

Baseline serum NTx Levels are Prognostic in Metastatic Breast Cancer Patients with Bone-only Metastasis

S.M.Ali, L.M.Demers, K.Leitzel, H.A.Harvey, D.Clemens, N.Mallinack, L.Engle, V.Chinchilli, **L.Costa**, C.Brady, J.Seaman & A.Lipton.

Annals of Oncology 15: 455- 459, 2004

“Role of Bisphosphonates for the Management of Skeletal Complications and Bone Pain from Skeletal Metastases”

Luis Costa; Allan Lipton and Robert Coleman

Supportive Cancer Therapy vol. 3, n° 3: 143-153, 2006

“Guidance on the use of bisphosphonates in solid tumours: recommendations of an international expert panel”

M. Aapro, P. A. Abrahamsson, J. J. Body, R. E. Coleman, R. Colomer, **L. Costa** , L. Crino`, L. Dirix, M. Gnant, J. Gralow, P. Hadji, G. N. Hortobagyi, W. Jonat, A. Lipton, A. Monnier, A. H. G. Paterson, R. Rizzoli, F. Saad & B. Thurlimann.

Annals of Oncology 19(3):420-432, 2008

“Bisphosphonates: Reducing the risk of skeletal complications from bone metastasis”

L.Costa

Breast Dec; 16 suppl 3: S16-20; 2007

“Low molecular weight protein tyrosine phosphatase genetic polymorphism and susceptibility for cancer development”

Irina Alho, Maria Clara Bicho, Raquel Carvalho, Alda Pereira da Silva, **Luis Costa**, Manuel Bicho.

Cancer Genetics and Cytogenetics 181 (2008): 20-24

“Clinical Characteristics and Therapeutic Options in Paget Disease of The Breast”

Isabel Fernandes, João Borges da Costa, Luis Soares de Almeida, Maria Pires de Miranda, Luis Costa, Marques Gomes.

Skin cancer. Vol 22, n°2 June 2007: 65-68

“Impact of Skeletal Complications on Patients' Quality of Life, Mobility, and Functional Independence”

Luis Costa, Xavier Badia; Edward Chow; Allan Lipton; Andrew Wardley

Supportive Care in Cancer (2008): 16: 879-889

“Effect of Bisphosphonates on Pain and Quality of Life in Patients With Bone Metastases”

Luis Costa and Pierre P Major.

Nature Clinical Practice Oncology (2009) vol. 6, n° 3: 163-174

“^{99m}Tc-Tricarbonyl Complexes Functionalized 1 with Anthracenyl Fragments: Synthesis, Characterization and Evaluation of Their Radiotoxic Effects in Murine Melanoma Cells

Rute F. Vitor, Teresa Esteves, Fernanda Marques, Paula Raposinho, Antonio Paulo, Sebastiao Rodrigues, Jose Rueff, Sandra Casimiro, **Luis Costa** and Isabel Santos.

***Cancer Biotherapy & Radiopharmaceuticals* (2009)**

“Phase I Trial of Zoledronic Acid + Imatinib Mesylate (Gleevec) in Patients With Bone Metastases”

Lipton A, Campbell Baird C, Harvey H, Kim C, Demers L, **Costa L.**

Am J Clin Oncol. (2010) Feb; 33(1):75-8.

“Prognostic Factors for Skeletal Complications From Metastatic Bone Disease in Breast Cancer”

Janet E. Brown, MD; Richard J Cook; Allan Lipton; **Luis Costa**; Robert E Coleman

Breast Cancer Res Treat (2010) 123:767–779

Zoledronic Acid: Its Use in the Treatment of Breast Cancer.

Luis I, Casimiro S, Ribeiro J and **Costa L**

Clinical Medicine Insights: Therapeutics (2010) **2**, 903-926.

“Optimizing Clinical Benefits of Bisphosphonates in Cancer Patients With Bone Metastases”

Matti Aapro, Fred Saad, **Luis Costa**

The Oncologist (2010): Volume 15, Issue #11, pages 1147-1158

“ A Randomized, Double-blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma”

David Henry, **Luis Costa**, Francois Goldwasser, Vera Hirsh, Vania Hungria, Jana Prausova, Giorgio Vittorio Scagliotti, Harm Sleeboom, Andrew Spencer, Saroj Vadhan-Raj, Roger von Moos, Wolfgang Willenbacher, Penella J Woll, Jianming Wang, Qi Jiang, Susie Jun, Roger Dansey, Howard Yeh.

J Clin Oncol (2011), in press

“Consensus on the Utility of Bone Markers in the Malignant Bone Disease Setting”.

R. Coleman; **L. Costa**;

Main Scientific Communications at International Meetings:

Number per meeting of accepted scientific communications (oral/poster) and published as abstract in peer review magazine.

Annual Meeting of the American Society of Clinical Oncology (ASCO)

1999-1; 2000-2; 2001-1; 2002-2; 2006-1; 2008-1; 2010-1

European Conference in Clinical Oncology (ECCO)

1993: 1; 1997-1; 2001-1; 2005-2; 2007-1; 2009-3

European Society of medical Oncology (ESMO)

1994-1; 1996-1; 2006- 1; 2008-1; 2010-2

Cancer Induced Bone Disease (CIBD)

1997-1; 1999-1; 2001-1; 2003-1; 2008-1.; 2009-3; 2010-1

North American Conference in Skeletal Complications of Malignancy

1999-1; 2003-1; 2004-1; 2007-1; 2009-2

San Antonio Breast Cancer Symposium (SABCS)

2000-1; 2006-1; 2008-1

European Breast Cancer Conference

1998-1; 2000-1; 2008-1; 2010-1

Invited Lectures (selection of last 7 years)

What do Bone Markers tell us about Clinical Status and Pathophysiology in Bone Metastases?

M.D. Anderson Cancer Center; December 2003

Endocrine Therapy in Breast Cancer: Clinical Aspects

XIV Porto Cancer Meeting –IPATIMUP; April 2004

Parathyroid Hormone-related Protein (PTHrP) in Breast Cancer Metastasis

M.D. Anderson Cancer Center; December 2004

The Role of Bisphosphonates in Breast Cancer

Second Central European Cooperative Oncology Group

Vienna; June 2005

Coosing the Optimum Treatment for Bone Complications

17th MASCC (Multinational Association of Supportive Care in Cancer);

Geneve, July 2005

The Role of RANK Ligand in Cancer-induced Bone Disease

Expanding Therapeutic Options in Oncology

Vienna; September 2006

Bone Metastasis: Preserving Patient Functional Independence

European Society of Medical Oncology

Istanbul; September 2006

“Maintaining patient autonomy: management of metastatic disease”

Luis Costa

Third Educational Breast Care Meeting

Conference designated for CME credit

Barcelona, May,2 - 2007

“Adjuvant Hormonal Treatment of Breast Cancer”

Luis Costa

20th European Congress of Obstetrics and Gynecology

Lisbon, March, 6 -2008

“Optimizing bisphosphonate therapy in breast and prostate cancers: How to better prevent bone complication?”

Invited speaker at oncology grand rounds

University of Alberta

Edmonton; September 17, 2008

Planned to 2011

“Clinical Impact of Bone-Targeted Therapies in Cancer”

Invited speaker at Gregorio Marañon Hospital, Madrid. January 17, 2011

“Established Benefits of Bisphosphonates in Early Breast Cancer”

Special lecture at the 8th Kyushu Regional Meeting of the Japanese Breast Cancer

Society, Japan February 19- 2011

“Metastases Prevention in Breast Cancer”

Skeletal Care Academy; Madrid; February 25, 2011.

International Advisory Boards in Bone Metastases:

Since 2001 is regularly invited to participate in International Advisory Boards as an expert in bone metastases field. During these meetings is called to provide is input in the development of scientific research programs (translational research and clinical studies) regarding new therapeutic targets.