

## Jose Baselga, M.D., Ph.D.



**Current Position:** Professor, Department of Medicine, Harvard Medical School  
Associate Director, MGH Cancer Center, Medicine,  
Massachusetts General Hospital  
Chief, Hematology/Oncology, Medicine, Massachusetts General  
Hospital

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### EDUCATION

9/76-6/82	MD	Medicine	Universitat Autònoma de Barcelona, Spain
11/92	Ph.D.		Universitat Autònoma de Barcelona, Spain
	Cum Laude and Extraordinary Award		

### FACULTY ACADEMIC APPOINTMENTS

7/94-6/96	Instructor, Medical, Memorial Sloan-Kettering Cancer Center, Cornell University Medical College, New York, NY.
1/96-7/10	Professor, Medicine, Universitat Autònoma de Barcelona, Spain
2010-	Professor, Medicine, Harvard Medical School, Boston, MA

### APPOINTMENTS AT HOSPITALS/AFFILIATED INSTITUTIONS

7/94-6/96	Clinical Assistant Physician, Breast/Gynecology Oncology Service, Department of Medicine
1/96-7/10	Chairman, Medical Oncology, Vall d'Hebron University Hospital, Barcelona, Spain
7/10 -	Physician, Medicine, Massachusetts General Hospital, Boston, MA.

### MAJOR ADMINISTRATIVE LEADERSHIP POSITIONS (2010—Present)

1996-2010	Chairman, Medical Oncology Service, Vall d'Hebron University Hospital, Barcelona, Spain
1996-2010	Director, Medical Oncology, Hematology and Radiation Oncology, Vall d'Hebron University Hospital, Barcelona, Spain
2007-2010	Director, Vall d'Hebron Institute of Oncology, Vall d'Hebron University Hospital, Barcelona, Spain
2010-	Associate Director, MGH Cancer Center, Massachusetts General Hospital
2010-	Division Chief, Division of Hematology/Oncology, Massachusetts General Hospital

### PROFESSIONAL SOCIETIES (Current)

1990	American Society of Clinical Oncology
2004-2006	Member, Board of Directors.
2008-2011	Member, Trials in Progress Track, Scientific Program Committee
1990	American Association for Cancer Research
2008-2011	Member, Board of Directors
1996	Spanish Cooperative Breast Cancer Group (SOLTI)
2009-	President
1996	European Society for Medical Oncology
2008-2009	President
2006-2012	Member, Board of Directors
2002	European Cancer Organization
2010-2011	Member, Board of Directors, Re-elected
2006	Ludwing Institute for Cancer Research
2006-	Member, Scientific Advisory Committee
2008	American-Italian Cancer Foundation
2008-	Member, Board of Directors
2008-2011	Member, Scientific Advisory Board
2010	Breast International Group
2010-	Member, Board of Directors

### EDITORIAL ACTIVITIES (Current)

1995-2011	Member, Editorial Advisory Board, Clinical Cancer Research
2009-2011	Senior Editor,
2001-	Member, Editorial Advisory Board, Investigational New Drugs
2002-	Member, Editorial Advisory Board, Annals of Oncology
2002-2011	Member, Editorial Advisory Board, Cancer Cell
2008-	Member, Editorial Advisory Board, Cancer Prevention Research
2009-	Advisor of the Highlights Section, Nature Reviews Cancer
2011-	Founding Editor in Chief, Cancer Discovery
1995-	Ad Hoc Reviewer: Journal of the National Cancer Institute Cancer Research, International Journal of Cancer European Journal of Cancer, Cancer, New England Journal of Medicine, Cell

## HONORS AND PRIZES

1989	Annual Research Competition for Residents, First Prize, Department of Medicine, State University of New York, Health Sciences Center
1990	Lederle Scholar in Clinical Oncology, Memorial Sloan-Kettering Cancer Center
1992	Travel Award, American Society of Clinical Oncology (ASCO)
1992-1993	Young Investigator Award, American Society of Clinical Oncology (ASCO)
1999	Young Investigator Award, American Association for Cancer Research (AACR)
2003	Honorary Membership Award, The European Society for Therapeutic Radiology and Oncology (ESTRO)
2004	Wun Ki Hong Visiting Professorship, UTM Anderson Cancer Center
2004	Distinguished Alumni Award, 29 <sup>th</sup> Annual Alumni Society Meeting, Memorial Sloan-Kettering Cancer Center
2005	Annual Award, European Society of Medical Oncology (ESMO), Career Recognition Award
2005	Professional Excellence Award in Biomedicine Research, Barcelona College of Physicians
2006	City Award "The Key to the City of Barcelona", Francisco Godia Foundation, Civic leadership in Barcelona
2006	Michael Clavel Lecture Award, 18 <sup>th</sup> EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, Contributions in early drug development
2006	San Salvatore Prize 2006, San Salvatore Foundation, Achievements in breast cancer research
2007	AICF Prize For Scientific Excellence in Medicine, American Italian Cancer Foundation
2008	Civil Order of Health – Commander with Plaque, Ministry of Health, Government of Spain; Contribution to the advanced of biomedical science in Spain
2008	Rosenthal Family Foundation Award, American Association for Cancer Research, Academic career in translational oncology
2008	Rey Jaime I Award in Medical Research, King Jaime I Foundation, Achievements in biomedical research in cancer
2010	Bruce A. Chabner Chair in Hematology Oncology, Massachusetts General Hospital Cancer Center, Academic career achievements in Hematology/Oncology
2010	Bob Pinedo Cancer Care Prize, The Society for Translational Oncology (STO), Exceptional contribution to improved care for cancer patients
2010	Gold Medal, Queen Sofia Spanish Institute, Achievements in biomedical research in cancer
2011	Honorary Doctoral Degree, Valencia University, Career excellence and innovation in biomedical research in cancer

## PUBLICATIONS

>250 publications in peer-reviewed journals.

## NARRATIVE REPORT ON CAREER AND RESEARCH INTERESTS

My career is focused towards the development of novel molecular targeted agents, with special emphasis in breast cancer. I have directed the pre-clinical and early clinical development of therapies against the Epidermal Growth Factor Receptor (EGFR) and the closely related HER2 receptor. My current work has expanded towards the early clinical development of mTOR and PI3Kinase inhibitors. In the process, I have been deeply involved in the creation of a new paradigm for translational and clinical research, generating hypotheses in the lab and moving them swiftly into clinical trials. On the administration front, I have led the transformation of the Vall d'Hebron Hospital Oncology from a small clinical service to a full cancer center with a large multidisciplinary research program and currently among the largest in Europe. I have recently moved to the Mass General Hospital Cancer Center.

I have devoted 20 years to the development of anti-EGFR agents in the laboratory and in the clinic. I lead the initial clinical studies that identified the optimal dose and schedule of a series of EGFR agents. I was also the first one to report clinical activity with anti-EGFR (and anti-HER2) agents and have led the full clinical development of this class of agents. Our latest work is focused in triple negative breast cancer.

I have also been closely involved in the development of anti-HER2 therapies, being the lead investigator in the first publication that demonstrated the clinical activity of the anti-HER2 monoclonal antibody trastuzumab (Herceptin) in patients with advanced HER2 over expressing breast cancer. I continue to lead state-of the art world-wide clinical trials with trastuzumab including in the neo-adjuvant and adjuvant setting. In the laboratory, I reported the synergy between paclitaxel and trastuzumab that lead to the registration clinical trial. We have also been able over the years to identify a number of mechanisms of resistance to anti-HER2 agents. Some of them including p95HER2 and hyper-activation of the PI3K-AKT-mTOR pathway are therapeutic targets themselves and we are exploring them. Our latest work includes the clinical development of novel anti-HER2 antibodies such as pertuzumab that have shown remarkable activity.

I have pioneered the development of pharmacodynamic markers of target inhibition with signal transduction inhibitors in preclinical models and translated into early clinical trials where we sequentially interrogate tumors. Among a long list of findings, we observed that inhibition of mTOR induced intra-tumoral activation of compensatory feedback loops that resulted in activation of multiple pathways. We have now identified that this activation is mediated via the IGF-1R and clinical trials with anti-mTOR and anti-IGF-1R agents given combined have shown remarkable results in patients with Luminal B hormone refractory breast cancer.

In addition to my research and administrative functions described above, I have also been deeply involved in teaching. I established the first elective in oncology at the medical school in Barcelona in 1996 and I have also been involved in teaching of residents and fellows. At the European level, I created a number of International Fellowships during my ESMO presidency from which a large number of oncologists have benefited.

Talk at IAAO2011

**Session: Therapeutic Inhibition of Oncogenic Signaling**

**Title: PI3K pathway: Therapeutic Targeting of Malignancy**

Publications selected for PI3K, mTOR and AKT, and those published in 2011

1. O'Reilly KE, Rojo F, She QB, Solit D, Mills GB, Smith D, Lane H, Hofmann F, Hicklin DJ, Ludwig DL, **Baselga J**, Rosen N. "mTOR inhibition induces upstream receptor tyrosine kinase signaling and activates AKT". *Cancer Res.* 2006 Feb 1;66(3):1500-8.
2. Carracedo A, Ma L, Teruya-Feldstein J, Rojo F, Salmena L, Alimonti A, Egia A, Sasaki AT, Thomas G, Kozma SC, Papa A, Nardella C, Cantley LC, **Baselga J**, Pandolfi PP. "Inhibition of mTORC1 leads to MAPK pathway activation through a PI3K-dependent feedback loop in human cancer". *J Clin Invest.* 2008 Sep;118(9):3065-74.
3. **Baselga J**. "Novel agents in the era of targeted therapy: what have we learned and how has our practice changed?" *Ann Oncol.* 2008 Sep;19 Suppl 7:vii281-8.
4. Serra V, Markman B, Scaltriti M, Eichhorn P, Valero V, Guzman M, Botero ML, Llonch E, Atzori F, Di Cosimo S, Maira M, Garcia-Echeverria C, Parra JL, Arribas J, and **Baselga J**. "NVP-BEZ235, a dual PI3K/mTOR inhibitor, prevents PI3K signaling and inhibits growth of cancer cells with activating PI3K mutations" *Cancer Res.* 2008 Oct 1;68(19):8022-30.
5. Eichhorn P, Gili M, Scaltriti M, Serra V, Guzman M, Nijkamp W, Beijersbergen R, Valero V, Seoane J, Bernards R and **Baselga J**. "Phosphatidylinositol 3-kinase hyperactivation results in lapatinib resistance that is reversed by the mTOR/phosphatidylinositol 3-kinase inhibitor NVP-BEZ235." *Cancer Res.* 2008 Nov 15;68(22):9221-30.
6. Di Cosimo S, **Baselga J**. "Targeted therapies in breast cancer: Where are we now ?" *Eur J Cancer.* 2008 Dec;44(18):2781-90.
7. Carracedo A, **Baselga J**, Pandolfi PP. "Deconstructing feedback-signaling networks to improve anticancer therapy with mTORC1 inhibitors." *Cell Cycle.* 2008 Dec 15;7(24):3805-9
8. **Baselga J**, Semiglazov V, Van Dam P, Manikhas A, Bellet M, Mayordomo J, Campone M, Kubista E, Greil R, Bianchi G, Steinseifer J, Molloy B, Tokaji E, Gardner H, Phillips P, Stumm M, Lane HA, Dixon JM, Jonat W and Rugo HS. "Phase II randomized neoadjuvant study of the mTOR inhibitor everolimus (RAD001) in combination with letrozole versus placebo and letrozole in patients with Her+ breast cancer." *J Clin Oncol.* 2009 Jun 1;27(16):2630-7.
9. **Baselga J**. Targeting the phosphoinositide-3 (PI3) kinase pathway in breast cancer. *Oncologist.* 2011;16 Suppl 1:12-9.
10. Chandarlapaty S, Sawai A, Scaltriti M, Rodrik-Outmezguine V, Grbovic-Huezo O, Serra V, Majumder PK, **Baselga J**, Rosen N. AKT inhibition relieves feedback suppression of receptor tyrosine kinase expression and activity. *Cancer Cell.* 2011 Jan 18;19(1):58-71.
11. Isakoff SJ, **Baselga J**. Trastuzumab-DM1: building a chemotherapy-free road in the treatment of human epidermal growth factor receptor 2-positive breast cancer. *J Clin Oncol.* 2011 Feb 1;29(4):351-4.
12. Scaltriti M, Eichhorn PJ, Cortés J, Prudkin L, Aura C, Jiménez J, Chandarlapaty S, Serra V, Prat A, Ibrahim YH, Guzmán M, Gili M, Rodríguez O, Rodríguez S, Pérez J, Green SR, Mai S, Rosen N, Hudis C, **Baselga J**. Cyclin E amplification/overexpression is a mechanism of trastuzumab resistance in HER2+ breast cancer patients. *Proc Natl Acad Sci U S A.* 2011 Mar 1;108(9):3761-6.
13. Gianni L, Dafni U, Gelber RD, Azambuja E, Muehlbauer S, Goldhirsch A, Untch M, Smith I, **Baselga J**, Jackisch C, Cameron D, Mano M, Pedrini JL, Veronesi A, Mendio la C, Pluzanska A, Semiglazov V, Vrdoljak E, Eckart MJ, Shen Z, Skiadopoulos G, Procter M, Pritchard KI, Piccart-Gebhart MJ, Bell R; Herceptin Adjuvant (HERA) Trial Study Team. Treatment with trastuzumab for 1 year after adjuvant chemotherapy in patients with HER2-positive early breast cancer: a 4-year follow-up of a randomised controlled trial. *Lancet Oncol.* 2011 Mar;12(3):236-44.
14. Wu Y, Amonkar MM, Sherrill BH, O'Shaughnessy J, Ellis C, Baselga J, Blackwell KL, Burstein HJ. Impact of lapatinib plus trastuzumab versus single-agent lapatinib on quality of life of patients with trastuzumab-refractory HER2+ metastatic breast cancer. *Ann Oncol.* 2011 Mar 15.
15. Scaltriti M, Serra V, Normant E, Guzman M, Rodriguez O, Lim AR, Slocum KL, West KA, Rodriguez V, Prudkin L, Jimenez J, Aura C, **Baselga J**. Antitumor Activity of the Hsp90 Inhibitor. IPI-504 in HER2-Positive Trastuzumab-Resistant Breast Cancer. *Mol Cancer Ther.* 2011 May;10(5):817-24.
16. Fuentes G, Scaltriti M, **Baselga J**, Verma CS. Synergy between trastuzumab and pertuzumab for human epidermal growth factor 2 (Her2) from colocalization: an in silico based mechanism. *Breast Cancer Res.* 2011 May 22;13(3):R54.
17. Serra V, Scaltriti M, Prudkin L, Eichhorn PJ, Ibrahim YH, Chandarlapaty S, Markman B, Rodriguez O, Guzman M, Rodriguez S, Gili M, Russillo M, Parra JL, Singh S, Arribas J, Rosen N, **Baselga J**. PI3K inhibition results in enhanced HER signaling and acquired ERK dependency in HER2-overexpressing breast cancer. *Oncogene.* 2011 Jun 2;30(22):2547-57.