

PATENTS

1. Thompson, J F; Potter, D. M.; Knight, D. R.; Gualberto, A.; Landschulz, K.T.; Chandrasiri Herath, M. A.; Rohlf, C. A3 Receptor-Mediated Cardioprotective Proteins and Therapeutic and Diagnostic Methods of Use. US 2005 0113302. WO/2004/084800
2. Gualberto, A; Cohen, B; Melvin CL; Roberts, ML. Combination Treatment For Non-Hematologic Malignancies Using An Anti-IGF-IR Antibody. US 2006 0018910. WO/2006/008639
3. Gualberto, A; Roberts, ML; Melvin, CL; Repollet, MI; Chianese, DA; Connely, MC; Terstappen, LW. Circulating Tumor Cell Assay. US 2006 810811. WO/2007/141626
4. Gualberto, A; Green, S. Biomarkers for Anti-IGF-IR Cancer Therapy. PC33981A

PUBLICATIONS

Doctoral Thesis

Papel regulador de la fructosa-2,6-difosfato en la glucolisis de diferentes tejidos. University of Seville School of Medicine

Book Chapters

1. Hixon, M. L., C. Muro-Cacho, C. Obejero-Paz and A. Gualberto (2000) Altered Mitotic Checkpoint in Vascular Smooth Muscle Cells of Individuals Predisposed to Hypertension. In "Vascular Protection: Molecular Mechanisms, Novel Therapeutic Principles and Clinical Applications" Editors: G.M. Rubanyi, V. J. Dzau & J. P. Cooke. Harwood, London, UK.
2. A. Gualberto (2011). Therapeutic approaches with antibodies to cell surface receptors in "Molecular Oncology: Causes of Cancer and Targets for Treatment" Editors: Edward Gelmann, Charles Sawyers, and Frank Rauscher III. Cambridge University Press (in press)

Peer-reviewed Manuscripts

1. F. Sobrino and A. Gualberto (1985). Hormonal regulation of fructose 2,6 bisphosphate levels in epididymal adipose tissue of rat. *FEBS lett.* **182**: 327-330.
2. F. Sobrino, A. Gualberto, and J. Gonzalez (1986). Regulation of fructose 2,6 bisphosphate levels and glycogen synthesis by dichloroacetate and phenazine methosulphate in rat adipose tissue. *Biochem. inter.* **12**: 767-774
3. F.Sobrino, J. Gonzalez, A. Gualberto, and G. Ruiz (1986) Short term stimulation by adenosine on basal and insulin induced glycogen synthesis in rat adipose tissue. *Biochim. Biophys. Acta* **885**: 43-48.
4. A. Gualberto, P. Molinero, and F. Sobrino (1987) The effect of experimental hypothyroidism on phosphofructokinase activity and fructose 2,6 bisphosphate levels in rat heart. *Biochem. J.* **244**: 137-142.
5. F. Sobrino, H. Rider, A. Gualberto and L. Hue (1987) Fructose 2,6 bisphosphate in rat erythrocytes. *Biochem. J.* **244**: 234-238.
6. F. Sobrino, A. Gualberto and E. Pintado (1988) Regulation of fructose 2,6 levels in cold acclimated brown adipose tissue of rat. *FEBS lett.* **229**:91-94.
7. C. de Miguel, A. Gualberto and F. Sobrino (1988) ACTH stimulates fructose 2,6 bisphosphate synthesis and glycolysis in Y-1 adrenal tumor cells. *Biochem. Inter.* **17**: 69-76.
8. A. Gualberto and E. D. Saggerson (1989) Differentiation of acute and slower acting effects of insulin on mitochondrial processes in brown adipose tissue of rat. *Biochem. J.* **258**: 308-311.
9. F. Martin, A. Gualberto, F. Sobrino and E. Pintado (1991) Thimerosal induces calcium mobilization, fructose 2, 6 bisphosphate synthesis and cytoplasmic alkalinization in rat thymus lymphocytes. *Biochem. Biophys. Acta* **1091**: 110-114.
10. A. Gualberto, C. Conde and F. Sobrino (1994) Cyclosporin A reverses alpha-adrenergic effects on glucose metabolism in rat thymic cells. *Biochim. Biophys. Acta* **1221**:199-205.
11. K. Walsh and A. Gualberto (1992) MyoD binds to the guanine tetrad nucleid acid structure with high affinity. *J. Biol. Chem.* **267**:13714-13718.

12. A. Gualberto, R.M. Patrick and K. Walsh (1992) DNA-binding protein with specificity for sites capable of guanine-guanine base pairing: High affinity to telomeres and gene regulatory elements. *Genes & Dev.* **6**:815-824.
13. A. Gualberto, D. Lepage, G. Pons, S.L. Mader, K. Park, M.L. Atchinson, and K. Walsh (1992) Functional antagonism between YY1 and the serum response factor. *Mol. Cell. Biol.* **12**:4209-4214.
14. C. Vincent, A. Gualberto, C. Patel and K. Walsh (1993) Different regulatory sequences control creatine kinase-M gene expression in directly injected skeletal and cardiac muscle. *Mol. Cell. Biol.* **13**:1264-1272.
15. P. Ruiz-Lozano, L. Lecea, C. Baesa, P. Perez, A. Gualberto, K. Walsh and P. Pons. (1994) Isolation, sequence and functional characterization of the rat muscle specific phosphoglycerate mutase gene. *Gene* **147**:243-248.
16. A. Gualberto, J. Lowry, I.M. Santoro and K. Walsh (1995). Parameters that influence the extent of site occupancy by a candidate telomere end-binding protein. *J. Biol. Chem.* **270**:4509-4517.
17. R. I. Scheinman, A. Gualberto, C. M. Jewell, J. A. Cidlowski and A. S. Baldwin Jr. (1995) Characterization of mechanisms involved in transrepression of NF-kappa B by activated glucocorticoid receptors. *Mol. Cell. Biol.* **15**:943-953.
18. A. Gualberto, M. L. Hixon, T. S. Finco, N. D. Perkins, G. J. Nabel and A. S. Baldwin Jr (1995). A proliferative p53 responsive element mediates TNF-alpha induction of the HIV-1 Long Terminal Repeat. *Mol. Cell Biol.* **15**:3450-3459.
19. A. Gualberto and A. S. Baldwin Jr. (1995). Sp1 synergizes p53 transactivation of the HIV-1 Long Terminal Repeat. *J. Biol. Chem.* **270**:19680-19683.
20. T. D. Tlsty, A. Briot, A. Gualberto, I. Hall, S. Hess, M. L. Hixon, D. Kuppuswamy, S. Romanov, M. Sage, and A. White (1995). Genomic instability and cancer. *Mutation Res.* **337**:1-7.
21. K. A. Martin, A. Gualberto, M. Kolman, E. S. Deneris, and K. Walsh (1997). Competitive regulation by YY1 and SRF at a muscle-specific CARG element does not appear to involve Phox1/Mhox. *DNA and Cell Biology* **16**:653-661.
22. A. Gualberto, G. Marquez, M. Carballo, G. L. Youngblood, S. W. Hunt III, A. S. Baldwin, and F. Sobrino (1998). p53 transactivation of the HIV-1 Long

Terminal Repeat is Blocked by PD 144795, a calcineurin inhibitor with anti-HIV properties. *J. Biol. Chem.* **273**:7088-7093

23. A. Gualberto, K. Kozakiewicz, K. Aldape and T. D. Tlsty (1998) An oncogenic form of p53 confers a dominant, gain-of-function phenotype that disrupts spindle checkpoint control. *Proc. Natl . Acad. Sci. USA* **95**:5166-5171

24. M. L. Hixon, A. I. Flores , M. W. Wagner and A. Gualberto (1998) Ectopic Expression of Cdc2/cdc28 Kinase Subunit Homo sapiens 1 Uncouples Cyclin B Metabolism from the Mitotic Spindle Cell Cycle Checkpoint. *Mol. Cell. Biol.* **18**:6224-6237.

25. M. A. Sussman, H. W. Lim, N. Gude, T. Taigen, e. N. Olson, J. Robbins, M. C. Colbert, A. Gualberto, D. F. Wiczorek, J. D. Molkenin (1998) Prevention of cardiac hypertrophy by calcineurin inhibition. *Science* **281**:1690-1693.

26. Z. Luo, K.-G. Shyu, A. Gualberto, and K. Walsh (1998) Calcineurin and pressure overload-induced cardiac hypertrophy. *Nature Medicine* **4**:1092-1093.

27. Ruiz-Lozano, P., M.L. Hixon, M.W. Wagner, A. Flores, K. Chien, A.S. Baldwin, and A. Gualberto (1999). p53 is a transcriptional activator of the muscle-specific phosphoglycerate mutase gene and contributes in vivo to the control of its cardiac expression. *Cell Growth & Diff.* **10**:295-306.

28. Walsh, K., I. Shiojima and A. Gualberto (1999) DNA replication and smooth muscle cell hypertrophy. *J. Clin. Invest.* **104**:673-674.

29. Hixon, M. L. and A. Gualberto (1999) Functions of Cks1 at mitosis. *Gene Ther Mol. Biol.* **4**:387-395.

30. Hixon, M. L. and A. Gualberto (2000). A p53 Mutant Gain-of-Function at the Mitotic Checkpoint. *Histol. Histopathol.* **15**: 551-556

31. Hixon, M. L. and A. Gualberto (2000) The control of mitosis. *Frontiers Biosc.* **5**:d50-57

32. Y. Eto, K. Yonekura, M. Sonoda, N. Arai, M. Sata, I. Yokoyama, A. Matsumoto, S. Sugiura, A. Gualberto, M. L. Hixon, M. W. Wagner and T. Aoyagi (2000). Calcineurin is activated in rat hearts with physiological left ventricular hypertrophy induced by voluntary exercise training. *Circulation* **101**:2134-2137

33. M. L. Hixon, C. Muro-Cacho, M. W. Wagner, C. Obejero-Paz, E. Millie, Y. Fujio, T. Hassold, K. Walsh and A. Gualberto (2000). PKB/Akt1 Mediates Signals that Control Vascular Smooth Muscle Cell Ploidy. *J. Clin. Invest.* **106**:1011-1020
34. M. L. Hixon, C. Obejero-Paz, C. Muro-Cacho, M. Wagner, E. Millie, J. Nagy, T. Hassold and A. Gualberto. CKs1 mediates vascular smooth muscle cell polyploidization in primary and secondary forms of hypertension (2000). *J. Biol. Chem.* **275**:40434-40442
35. M. Carballo, M. Conde, J. Tejedó, A. Gualberto, J. Jimenez, J. Monteseirin, C. Santa Maria, F. Bedoya, S. Hunt 3rd, E. Pintado, A. Baldwin Jr, F. Sobrino (2002). Macrophage inducible nitric oxide synthase gene expression is blocked by a benzothiophene derivative. *Mol Genet Metab.* **75**:360-368.
36. Y. Wang, G. Keulenaer, E. Weinberg, A. Gualberto, K. Landschulz, T. Turi, J. Thompson, R. Lee (2002) Biomechanical Regulation of the Endogenous Calcineurin Inhibitor Down Syndrome Candidate Region 1 (DSCR1) In Cardiac Myocytes. *Am J Physiol Heart Circ Physiol.* **283**:H533-H539.
37. M. L. Hixon and A. Gualberto. Vascular smooth muscle polyploidization: from mitotic checkpoints to hypertension. (2003). *Cell Cycle* **2**:105-111.
38. D. M. Gascoyne, M. L. Hixon , A. Gualberto, M. dM Vivanco (2003). Loss of Mitotic Spindle Checkpoint Activity Predisposes to Chromosomal Instability at Early Stages of Fibrosarcoma Development. *Cell Cycle* **2**:238-245.
39. B.D. Cohen, D.A. Baker, C. Soderstrom, G. Tkalcevic G, A.M. Rossi, P.E. Miller, M.W. Tengowski, F. Wang, A. Gualberto, J.S. Beebe and J.D. Moyer (2005). Combination therapy enhances the inhibition of tumor growth with the fully human anti-type 1 insulin-like growth factor receptor monoclonal antibody CP-751,871. *Clin Cancer Res.* **11**:2063-2073.
40. B. Comin-Anduix, A. Gualberto, J. A. Glaspy, R. Renterias, D. Reardon, E. Seja, B. Englahner, M. Ontiveros, J. S. Economou, B. Littman, J. Gomez-Navarro, A. Ribas (2006). Definition of an immunologic response using the major histocompatibility complex tetramer and enzyme-linked immunospot assays. *Clin Cancer Res.* **12**:107-116.
41. W.J. Chung, A. Gualberto and R. Fonseca (2006) IGF-IR is over-expressed in poor-prognostic sub-types of Multiple Myeloma. *Leukemia* **20**:174–176.

42. J.S. de Bono JS, G. Attard, A.A. Adjei, M.N. Pollak, P.C. Fong, P. Haluska, L. Roberts, C. Melvin, M. Repollet, D. Chianese, M. Connely, L.W. Terstappen, A. Gualberto (2007). Potential applications for circulating tumor cells expressing the insulin-like growth factor-I receptor. *Clin.Cancer Res.* **13**:3611-3616.
43. Haluska P, Shaw HM, Batzel GN, Yin D, Molina JR, Molife LR, Yap TA, Roberts ML, Sharma A, Gualberto A, Adjei AA, de Bono JS (2007). Phase I dose escalation study of the anti insulin-like growth factor-I receptor monoclonal antibody CP-751,871 in patients with refractory solid tumors. *Clin Cancer Res.* **13**:5834-5840.
44. Comin-Anduix B, Lee Y, Jalil J, Algazi A, Rocha P, Camacho LH, Bozon VA, Bulanhagui CA, Seja E, Villanueva A, Straatsma BR, Gualberto A, Economou JS, Glaspy JA, Gomez-Navarro J, Ribas A (2008). Detailed analysis of immunologic effects of the cytotoxic T-lymphocyte-associated antigen 4-blocking monoclonal antibody tremelimumab in peripheral blood of patients with melanoma. *J Transl Med.* **6**:22-30.
45. Lacy MQ, Alsina M, Fonseca R, Paccagnella ML, Melvin CL, Yin D, Sharma A, Enriquez Sarano M, Pollak MN, Jagannath S, Richardson P, Gualberto A (2008). Phase 1, Pharmacokinetic and Pharmacodynamic Study of the Anti-insulin Like Growth Factor Type 1 Receptor Monoclonal Antibody CP-751,871 in Patients with Multiple Myeloma. *J Clin Oncol.* **26**:3196-203.
46. D.D. Karp, L. G. Paz-Ares, L. J. Blakely, H. Kreisman, P. D. Eisenberg, R. B. Cohen, L. Garland, C. J. Langer, C. L. Melvin, A. Gualberto (2008). Efficacy of the anti-insulin like growth factor I receptor (IGF-IR) antibody CP-751871 in combination with paclitaxel and carboplatin as first-line treatment for advanced non-small cell lung cancer. *J Clin Oncol.* **27**:2516-2522
47. A. Gualberto and D.D. Karp (2008). Development of a monoclonal antibody against the insulin-like growth factor receptor for the treatment of non-small cell lung cancer. *Clin Lung Cancer* **10**:273-280
48. P Haluska, Worden F, Olmos D, Yin D, Schteingart D, Batzel G, Paccagnella ML, de Bono JS, Gualberto A and Hammer GD (2009). Safety, tolerability, and pharmacokinetics of the anti-IGF-1R monoclonal antibody CP-751,871 in patients with refractory adrenocortical carcinoma. *Cancer Chemother Pharmacol.* **65**:765-73
49. A. Gualberto and M Pollak (2009). Targeting the insulin-like growth factor receptor in oncology: early clinical trial results. *Oncogene* **28**:3009-3021

50. D.D. Karp, Pollak MN, Cohen RB, Langer CJ, Eisenberg PD, Haluska P, Yin D, Demers L, Hixon ML, Lipton A, Leitzel K, Terstappen LW, Garland L, Paz-Ares LG, Cardenal F, Gualberto A (2009). Phase 1 Pharmacokinetic and Pharmacodynamic Study of the anti-IGF-IR antibody CP-751,871 in combination with paclitaxel and carboplatin. *J Thorac Oncol.* **4**:1397-403.
51. A. Gualberto A, Pollak M. Clinical Development of Inhibitors of the Insulin-like Growth Factor Receptor in Oncology (2009). *Curr Drug Targets.* **10**:923-36.
52. D. Olmos, Postel-Vinay S, Molife LR, Okuno SH, Schuetze SM, Paccagnella ML, Batzel GN, Yin D, Pritchard-Jones K, Judson I, Worden FP, Gualberto A, Scurr M, de Bono JS, Haluska P (2009). Safety, pharmacokinetics, and preliminary activity of the anti-IGF-1R antibody figitumumab (CP-751,871) in patients with sarcoma and Ewing's sarcoma: a phase 1 expansion cohort study. *Lancet Oncol.* **11**:129-35.
53. A Gualberto (2010) Figitumumab (CP-751,871). *Expert Opin Biol Ther.* **10**:575-85
54. L R Molife, Fong PC, Olmos D, Arkenau T, Paccagnella L, Karavasilis V, Yap T, Shaw H, Reid R, Vidal L, Postel-Vinay S, Spicer J, Yin D, Gualberto A, Lipton A, Leitzel K, de Bono J (2010). The Insulin-like-Growth Factor-1 Receptor Inhibitor, CP-751,871, in Combination with Docetaxel in Patients with Advanced Solid Tumors: Results of a Phase 1b Dose Escalation, Open-Label Study. *Br J Cancer* **103**:332-339.
55. A Gualberto, Dolled-Filhart M, Gustavson M, Christiansen J, Wang YF, Hixon ML, Reynolds J, McDonald S, Ang A, Rimm DL, Langer CL, Blakely J, Garland L, Paz-Ares LG, Karp DD, Lee AV. (2010) Molecular Analysis of Non-Small Cell Lung Cancer (NSCLC) Identifies Tumor Subsets with Differential Sensitivity to IGF-IR Inhibition by Figitumumab. *Clin Cancer Res.* **16**:4654-4665
56. M Hixon, Paccagnella L, Perez-Olle R, Millham R, Gualberto A (2010). Development of Inhibitors of the IGF-IR/PI3K/Akt/mTOR pathway. *Rev Recent Clin Trials* **5**:189-208.
57. C Langer Besse B, Gualberto A, Brambilla E, Soria J-C (2010) The evolving role of histology in the management of advanced non-small cell lung cancer (NSCLC). *J Clin Oncol.* **28**:5311-5320
58. A Gualberto, Hixon ML, Karp DD, Li D, Green S, Dolled-Filhart M, Paz-Ares LG, Novello S, Blakely J, Langer CJ, Pollak MN. (2011). Circulating levels of free Insulin Growth Factor I identify Non Small Cell Lung Cancer

(NSCLC) patients who derive clinical benefit from Figitumumab. *Br J Cancer*. **104**:68-74.

59. CJ Langer, Besse B, Gualberto A, Brambilla E, Soria J-C (2011). Reply to A Fischer, et al. *J Clin Oncol*. **29**:3332-3333

60. H Juergens, Daw N, Geoerger B, Ferrari S, Villarroel M, Aerts I, Whelan J, Dirksen U, Hixon M, Yin D, Wang T, Green S, Paccagnella L, Gualberto A (2011). Preliminary Efficacy of the Anti-Insulin Like Growth Factor type 1 Receptor Antibody Figitumumab in Patients with Refractory Ewing Sarcoma. *J Clin Oncol*. *In press*

61. A Gualberto, Hixon ML, Pollak M (2011). Reply: 'Pre-treatment levels of circulating free IGF-1 identify NSCLC patients who derive clinical benefit from figitumumab'. *Br J Cancer* in press

62. A Gualberto. Brentuximab Vedotin, an Antibody–Drug Conjugate for the Treatment of CD30-Positive Malignancies. *Expert Opinion on Invest Drugs*. *Submitted*

63. JM. Reynolds, Lloyd DB, Bentivegna SC, Seymour AB, Borzillo GV, Hixon ML, Gualberto A (2011). Mutant Forms of the Insulin-Like Growth Factor 1 Receptor Identified in Lung and Colorectal Tumors are Sensitive to Inhibition by Figitumumab. *Submitted*

64. J Corral, Sanchez-Torres JM, O'Byrne K, Iglesias L, Canon JL, O'Flaherty J; Cortijo A, Garcia-Carbonero R, Yin D, Li D, Carpentieri M, Gualberto A, Paz-Ares L (2011). Phase I study of the IGF-IR inhibitor, figitumumab (CP-751,871), in combination with cisplatin and gemcitabine or cisplatin and pemetrexed in chemotherapy-naïve patients with advanced non-small cell lung cancer (NSCLC). *Submitted*