

CURRICULUM VITAE

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CONTACT INFORMATION

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PERSONAL INFORMATION

Date of birth: 1 April, 1964
Place of Birth: Verona, Italy
Residence: Via Casella 49, 65012 Cepagatti (PE), Italy

ORCID ID: 0000-0002-7091-8621

DEGREES

December 2007: Masters degree in "Molecular Pathology and Oncological Biotechnologies", School of Medicine, University of Ferrara, Italy; top grade with Honours.

July 1996: Doctorate (PhD) in "Microbial Biotechnologies", VIII cycle, University of Ancona, Italy.

March 1991: Agricultural Sciences degree, University of Padova, Italy; top grade with Honours.

PROFESSIONAL EXPERIENCE

January 2004-present: Research Scientist, Cancer Pathology Unit, CeSI-MeT (now CAST), "G. d' Annunzio" University of Chieti-Pescara, Italy.

September 2013-present: Research Scientist, Oncoxx Biotech Srl., Chieti, Italy.

April 1999-December 2003: Postdoctoral Fellow, Laboratory of Experimental Oncology, Department of Cell Biology and Oncology, Consorzio Mario Negri Sud, S. M. Imbaro (Chieti), Italy.

May 1998-March 1999: Research Assistant, Department of Agricultural and Environmental Biotechnologies, University of Ancona, Italy (permanent position). Career development into cancer research (with resignation from position at University of Ancona).

May 1996-April 1998: Postdoctoral Fellow, Laboratory of Microbiology, Department of Agricultural and Environmental Biotechnologies, University of Ancona, Italy.

October 1992-October 1995: PhD, “Microbial Biotechnologies”, VIII cycle. Department of Agricultural and Environmental Biotechnologies, University of Ancona, Italy, and Department of Biochemistry and Molecular Biology (Prof Peter W. Piper), University College London, London, U.K.

November 1991-October 1992: Post-graduate. Department of Biochemistry and Molecular Biology (Prof Peter W. Piper), University College London, London, U.K.

March 1991-October 1991: Post-graduate. National Research Programme for Advanced Biotechnologies, Interdipartimental Research Centre for Innovative Biotechnologies (C.R.I.B.I), University of Padova, Italy.

October 1988-February 1991: Pre-graduate training in molecular biology. Department of Agricultural Biotechnology (Prof Marco P. Nuti), University of Padova, Italy.

June-September 1988: Pre-graduate training in molecular biology. Department of Dairy and Food Microbiology (Prof Fergal O' Gara), University College Cork, Cork, E.I.R.E.

PATENTS

Saverio Alberti, **Emanuela Guerra** and Marco Trerotola

USE OF CIRCULATING SERUM TROP-2 AS NEW TUMOR BIOMARKER.

- Italian application number: 102015000074105; Italian filing date 19.11.2015; **granted** 26.04.2018.
- PCT/EP2016/025148; filing date 17.11.2016; Pub. No.: WO/2017/084763; granted EPO Patent 3377903, 21.08.2019; under consideration USPTO.

Emanuela Guerra and Saverio Alberti

HUMANIZED ANTI-TROP-2 MONOCLONAL ANTIBODIES AND USES THEREOF

- Priority number: IT2014CH00032; priority date 04.12.2014.
- PCT/EP2015/078672; filing date 04.12.2015; Pub. No.: WO/2016/087651; intention to grant EPO 28.11.2019; granted USPTO Patent 10501555, 10.12.2019; under consideration Cina, Canada, India.

Saverio Alberti and **Emanuela Guerra**

USE OF TROP-2 AS PREDICTIVE MARKER OF RESPONSE TO ANTI-TUMOR THERAPY BASED ON INHIBITORS OF CD9, AKT AND MOLECULES OF THE TETRASPANIN SIGNALLING NETWORK

- Priority number: IT2012CH00008; priority date 16.05.2012.
- PCT/IT2013/000139; filing date 16.05.2013; Pub.No.: WO/2013/171777; granted EPO Patent 2850433, 15.08.2018.

Saverio Alberti and **Emanuela Guerra**

OLIGONUCLEOTIDIC SEQUENCES ABLE TO SILENCE THE EXPRESSION OF THE CYCLIN D1 -TROP2 CHIMERA AND USES THEREOF IN MEDICAL FIELD.

- Priority number: IT2008CH00021; priority date 25.09.2008.

- PCT/IT2009/000437; filing date: 25.09.2009; Pub.No.: WO/2010/03530; granted EPO Patent 761029, 20.04.2016; granted USPTO Patent 13121137, 13.08.2013; granted Canada Patent 2743354, 21.11.2017; granted Australia Patent 297961, 12.02.2015

PROFESSIONAL ACTIVITY and ACCOMPLISHMENTS

After my initial years of research activity in the field of industrial and food biotechnology, I moved into cancer research, joining the group of Prof Saverio Alberti. I had already gained a strong expertise in molecular biology through research projects successfully accomplished in Italy (University of Padova, University of Ancona) and abroad (University College London, London, U.K., University College Cork, Cork, E.I.R.E) in the course of which I had gained my PhD and had become an established member of the Food and Environmental Microbiology group at the University of Ancona.

In joining Prof Alberti group first at the Department of Cell Biology and Oncology, Consorzio Mario Negri Sud, and then at the Cancer Pathology Unit of CeSI, 'G. d' Annunzio' University Foundation, I gained a Masters degree in Molecular Pathology and Oncological Biotechnologies at the University of Ferrara School of Medicine (Italy), and engaged in understanding the role of the TROP family of transmembrane glycoproteins in cancer, stem cell biology and hereditary diseases, with the aim to develop novel therapeutic approaches. During this time we characterized a novel oncogenic mechanism determined by the overexpression of a post-transcriptionally-derived fusion mRNA between *CYCLIN D1* and *TROP2*, and demonstrated for the first time that fusion-specific siRNA treatment selectively abolishes the growth of expressing cancer cells (Guerra *et al.*, *Cancer Research*, 2008; Patent WO/2010/03530). This was then extended to a number of other mRNA fusions discovered in Prof Alberti lab (Plebani *et al*, *Neoplasia*, 2012), further proving the broad significance and feasibility of the approach. Further investigations over the Trop-2-dependent signaling network also lead us to the identification of Trop-2 as a marker of response to AKT-targeted anti-tumor therapies (Guerra *et al*, *Oncogene*, 2012; Guerra *et al*, *Clinical Cancer Research*, 2016; Patent WO/2013/171777).

In 2004 we set to generate engineered animal models devoid of Trop expression/function, which could faithfully recapitulate the human genetic diseases associated to inactivating mutations in the *TROP* genes. We showed that Trop-1 is a stem cell marker (Zanna *et al*, *Cancer*, 2007), and succeeded in obtaining the *TROP1* knock-out (KO) murine model that showed that *TROP1* inactivation is indeed causative for congenital tufting enteropathy (Guerra *et al*, *PLOS One*, 2012).

While deepening our understanding of Trop-2 as a driver of cancer growth and metastasis (Trerotola *et al*, *Oncogene* 2013; Guerra *et al*, *Oncogene*, 2013; Trerotola *et al*, 2021, accepted for publication), since 2007 we have been engaged in the development of novel anti-Trop-2 monoclonal antibodies for anticancer therapy .

EXPERTISE

Development of monoclonal antibodies for cancer diagnosis and therapy. In-vivo efficacy of antitumor drugs. Molecular and cell biology. Animal models of tumor progression. Transgenic mouse models. Intellectual property.

COLLABORATIONS

- Prof Hiromitsu Nakauchi, Director, Center for Stem Cell Biology and Regenerative Medicine, Institute of Medical Science, University of Tokyo (Japan) and Research Leader, California Institute for Regenerative Medicine, Stanford University, CA.
- Dr Loren Michel, Washington University School of Medicine, Saint Louis, MO.
- Dr J. Tso, JN Biosciences, Mountain View, CA.
- Prof Barbara Barboni, Full professor in Veterinary Physiology. University of Teramo, Italy.
- Dr Daniela Marzioni, Department of Experimental and Clinical Medicine, School of Medicine, Polytechnic University of Marche, Ancona, Italy
- Prof Rino Stuppia, Medical Genetics, “G. d’ Annunzio” University School of Medicine, Chieti (Italy).
- Prof Roberta Di Pietro, Histology, “G. d’ Annunzio” University School of Medicine, Chieti (Italy).
- Prof Gian Mario Tiboni, Centre for Medically Assisted Reproduction, "Gaetano Bernabeo" Hospital, Ortona (Chieti) and “G. d’ Annunzio” University School of Medicine, Chieti (Italy).
- Dr Lorenza Ronfani, Core Facility for Conditional Mutagenesis, San Raffele Hospital, Milano (Italy).

PROFESSIONAL DUTIES

Associate Editor for Clinical Case Reports

Reviewer for

- Human Molecular Genetics
- Human Genetics
- BMC Clinical Pathology (open reviewing)
- Frontiers in Genetics

Project reviewer for the French National Research Agency

UNIVERSITY LECTURING AND SUPERVISING

2011: “Animal Models in Biomedical Research”, lecturing for the Molecular Genetics course of the School of Pharmacy, University of Chieti.

2009-2010: “Knock-out mice in oncology”, lecturing for the Masters degree in “Molecular Pathology

and Oncological Biotechnologies” of the School of Medicine, University of Ferrara, Italy

2000: “RNA and c-DNA preparation and analysis”, lecturing and demonstrating for the Masters degree in "Molecular biology in oncology and clinical pathology" of the Research Centre in Oncology “Giovanni XXIII”, Rionero del Vulture (PZ), and the School of Medicine, Catholic University, Rome.

1999: Organization and supervision of the practical courses in Microbiology and Microbial Genetics, Department of Agricultural and Environmental Biotechnologies, University of Ancona, Italy.

1996: “Microbial Ecology”, lecturing for the Agriculture BSc course of the University of Ancona, Italy. Supervision of undergraduate and PhD students in the Laboratory of Dr Enrico Berardi, University of Ancona, Italy.

1992: Supervision of Masters students in the Laboratory of Prof. Peter W. Piper, Department of Biochemistry and Molecular Biology, University College London, London, U.K.

AWARDS

March 2013: “Medicina Abruzzo” (Abruzzo Medicine), 5th edition (awarded to the Cancer Pathology Unit, CeSI).

March 2009: “Medicina Abruzzo” (Abruzzo Medicine), 2nd edition (awarded to the Cancer Pathology Unit, CeSI).

March 2001: “Scholar-in-Training Award”, AACR-Pezcoller Foundation (personal award).

2002 – 2011: “Cassa di Risparmio della Provincia di Chieti” Foundation Scholarship.

1997-1998: University of Ancona Post-Doctorate Scholarship.

1992-1995: Universities of Sassari and Ancona Doctorate Scholarship.

1991-1992: University of Ancona and University College London International Higher Education and Training Scholarship.

1991: University of Padova, National Research Programme for Advanced Biotechnologies Scholarship.

1988: University of Padova and University College Cork “Erasmus” pre-graduate scholarship.

PEER-REVIEWED PUBLICATIONS

1. Trerotola M, **Guerra E**, Ali Z, Aoisi AL, Ceci M, Simeone P, Acciarito A, Zanna P, Vacca G, D' Amore A, Boujnah K, Garbo V, Moschella A, Lattanzio R, Alberti S.. Trop-2 cleavage by ADAM10 is an activator switch for cancer growth and metastasis. *Neoplasia*, Epub 2021 Apr 8.
2. Relli V, Trerotola M, **Guerra E**, Alberti S. Abandoning the Notion of Non-Small Cell Lung Cancer. *Trends Mol Med*. 25 (7) 585-594 (2019).
3. Relli V, Trerotola M, **Guerra E**, Alberti S. Distinct lung cancer subtypes associate to distinct drivers of tumor progression. *Oncotarget* 9 (85) 35528-35540 (2018).
4. Avellini C, Licini C, Lazzarini R, Gesuita R, **Guerra E**, Tossetta G, Castellucci C, Giannubilo SR, Procopio A, Alberti S, Mazzucchelli R, Olivieri F and Marzioni D. The trophoblast cell surface antigen 2 and miR-125b axis in urothelial bladder cancer. *Oncotarget* 8 (35) 58642-58653 (2017).
5. **Guerra E.**, Trerotola M., Tripaldi R., Aloisi A.L., Simeone P., Sacchetti A., Relli V., D' Amore A., La Sorda R., Lattanzio R., Piantelli M. and Alberti S. Trop-2 induces tumor growth through Akt and determines sensitivity to Akt inhibitors. *Clin. Cancer Res*. 22 (16) 4197-4205 (2016).
6. **Guerra E.**, Piantelli M. and Alberti S. Cancer chemoprevention: Evidence of a nonlinear dose response for the protective effects of resveratrol in humans and mice. *Science Transl. Med*. 8:350 350le2 (2016).
7. **Guerra E.**, Cimadamore A., Simeone P., Vacca G., Lattanzio R., Botti G., Gatta V., D' Aurora M., Simionati B., Piantelli M. and Alberti S. p53, cathepsin D, Bcl-2 are joint prognostic indicators of breast cancer metastatic spreading. *BMC Cancer* (2016) 16:649 (<https://bmccancer.biomedcentral.com/articles/10.1186/s12885-016-2713-3>).
8. Li Y., Melnikov A. A., Levenson V., **Guerra E.**, Simeone P., Alberti S. and Deng Y. A seven-gene CpG-island methylation panel predicts breast cancer progression. *BMC Cancer* 15 (417): 1-12 (2015)
9. **Guerra E.**, Lattanzio R., La Sorda R., Dini F., Tiboni G.M., Piantelli M. and Alberti S. *mTrop1/Epcam knockout mice develop congenital tufting enteropathy through dysregulation of intestinal E-cadherin/ β -catenin*. *PLoS One* 7(11): e49302 (2012). [corrigendum: *PLoS One* 8(5), (2013)]. **Corresponding author**.
10. **Guerra E.**, Trerotola M., Aloisi A.L., Tripaldi R., Vacca G., La Sorda R., Lattanzio R., Piantelli M. and Alberti S. The Trop-2 signalling network in cancer growth. *Oncogene* 32(12):1594-600 (2013).
11. Trerotola M., Cantanelli P., **Guerra E.**, Tripaldi R., Aloisi A.L., Bonasera V., Lattanzio R., de Lange R., Weidle U.H., Piantelli M. and Alberti S. Up-regulation of Trop-2 quantitatively stimulates human cancer growth. *Oncogene* 32(2):222-33 (2013).
12. Plebani R., Oliver G.R., Trerotola M., **Guerra E.**, Cantanelli P., Apicella L., Emerson A., Albiero A., Harkin P.D., Kennedy R.D. and Alberti S. Long-range transcriptome sequencing reveals cancer cell growth regulatory chimeric mRNA. *Neoplasia* 14(11):1087-96 (2012).
13. Trerotola M., **Guerra E.** and Alberti S. Letter to the editor: efficacy and safety of anti-Trop antibodies. *BBA Rev. Cancer* 1805: 119–120 (2010).

14. Weidle U.H., Evtimova V., Alberti S., **Guerra E.**, Fersis N. and Kaul S. Cell growth stimulation by CRASH, an asparaginase-like protein overexpressed in human tumors and metastatic breast cancers. *Anticancer Res.* 29(4): 951-964 (2009).
15. **Guerra E.**, Trerotola M., Dell' Arciprete R., Bonasera V., Palombo B., El-Sewedy T., Ciccimarra T., Crescenzi C., Lorenzini F., Rossi C., Vacca G., Lattanzio R., Piantelli M. and Alberti S. A bi-cistronic Cyclin D1-TROP2 mRNA chimera demonstrates a novel oncogenic mechanism in human tumors. *Cancer Res.* 68: (19): 8113-8121 (2008).
16. Zanna P., Trerotola M., Vacca G., Bonasera V., Palombo B., **Guerra E.**, Rossi C., Lattanzio R., Piantelli M. and Alberti S. Trop-1 are conserved growth stimulatory molecules that mark early stages of tumor progression. *Cancer* 110 (2): 452-464 (2007).
17. Carletti E., **Guerra E.** and Alberti S. The forgotten variables of DNA array hybridization. *Trends Biotech.* 24 (10): 443-448 (2006).
18. **Guerra E.**, Chye P.P., Berardi E. and Piper P.W. Hypoxia abolishes transience of the heat-shock response in the methylotrophic yeast *Hansenula polymorpha*. *Microbiol.* 151 (3): 805-11 (2005).
19. Romani A., **Guerra E.**, Trerotola M. and Alberti S. Detection and analysis of spliced chimeric mRNAs in sequence databanks. *Nucleic Acids Res.* 31 (4 e17): 1-8 (2003).
20. **Guerra E.**, Vacca G., Palombo B. and Alberti S. Prognostic value of mutations of *TP53* and *RAS* genes in breast cancer. *Int. J. Biol. Markers* 18(1): 49-53 (2003).
21. Nasr A. F., Nutini M., Palombo B., **Guerra E.** and Alberti S. Mutations of *TP53* induce loss of DNA methylation and amplification of the TROP1 gene. *Oncogene* 22(11): 1668-77 (2003).
22. Mannazzu I., Simonetti E., Marinangeli P., **Guerra E.**, Budroni M., Thangavelu M. and Clementi F. SED1 gene length and sequence polymorphisms in feral strains of *Saccharomyces cerevisiae*. *Appl. Environ. Microbiol.* 68(11), 5437-44 (2002).
23. **Guerra E.** and Alberti S. Molecular prognostic indicators for breast cancer. *Tumori* 87(6): S23-25 (2001).
24. Calabrese G., Crescenzi C., Morizio E., Palka G., **Guerra E.** and Alberti S. Assignment of TACSTD1 (alias TROP1, M4S1) to human chromosome 2p21 and refinement of mapping of the TACSTD2 (alias TROP2, M1S1) to human chromosome 1p32 by *in-situ* hybridization. *Cytogenet. Cell Genet.* 92(1-2):164-5 (2001).
25. Mannazzu I., **Guerra E.**, Ferretti R., Pediconi D. and Fatichenti F. Vanadate and copper induce overlapping oxidative stress responses in the vanadate-tolerant yeast *Hansenula polymorpha*. *Biochim. Biophys. Acta* 1475(2), 151-156 (2000).
26. **Guerra E.**, Sordi G., Mannazzu I., Clementi F. and Fatichenti F. Occurrence of wine yeasts on grapes subjected to different pesticide treatments. *Ital. J. Food Sci.* 11(3), 221-230 (1999).
27. **Guerra E.**, Mannazzu I., Sordi G., Tangherlini M., Clementi F. and Fatichenti F. Characterization of indigenous *Saccharomyces cerevisiae* from the Italian region of Marche: hunting for new strains for local wine quality improvement. *Annali di Microbiologia ed Enzimologia* 49(1), 79-88.

28. Mannazzu I., **Guerra E.**, Strabbioli R., Pediconi D. And Fatichenti F. The vanadate-tolerant yeast *Hansenula polymorpha* undergoes cellular reorganisation during growth in, and recovery from, the presence of vanadate. Microbiol. 144(9), 2589-2597 (1998).
29. Mannazzu I., **Guerra E.**, Strabbioli R., Pediconi D., Berrie C.P. and Fatichenti F. Recovery from vanadium involves the elimination of cellular structures in the yeast *Hansenula polymorpha*. Food Technol. Biotechnol 36(4), 299-303 (1998).
30. Mannazzu I., **Guerra E.**, Strabbioli R., Masia A., Maestrone G.B., Zoroddu M.A. and Fatichenti F. Vanadium affects vacuolation and phosphate metabolism in *Hansenula polymorpha*. FEMS Microbiol. Lett. 147(1), 23-28 (1997).