

CURRICULUM VITAE

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Educational Training:

1964 – 68, University of Poona, B.Sc. (Chemistry-Major)

1968 – 72, University of Bombay, M.Sc. (Applied Biology)

1973 – 76, University of London, Ph.D. (Biochemistry)

Positions:

2009-Present Research Professor, Departments of Medicine and Cell Biology

1996-2008 Associate Professor (Research), Departments of Medicine and Cell Biology,

SUNY–Downstate Medical Center, Brooklyn, NY 11203.

1984-1995 Assistant Professor (Research), Department of Medicine SUNY–Downstate Medical Center, Brooklyn, NY 11203

Positions Held:

1990 – 95, Research Biologist and Principal Investigator, Division of Research, V.A. Medical Center, Brooklyn, NY 11209

1984 – 90, Research Associate and Co-investigator on NIH project, Division of Hematology, V.A. Medical Center, Brooklyn, NY 11209

1979 – 83, Research Associate, Biochemistry Department, Scripps Clinic and Research Foundation, La Jolla, CA

1976 – 79, Research Associate, supported by the Wellcome Trust, Department of Experimental Chemical Pathology, Westminster Hospital, London, SW1 (UK).

1973 – 76, Research Fellow, Commonwealth Tropical Medicine Research Award, Department of Experimental Chemical Pathology, Westminster Hospital, London SW1 (UK).

1970 – 73, Research Assistant, project on Nutritional Disorders of the Nervous System for National Institutes of Health (U.S.A.), at Neuropathology Unit, J.J. Hospital and Grant Medical College, Bombay-8, India.

1968 – 69, Research Assistant, Glaxo project on Toxic Amblyopia at Neuropathology Unit, J.J. Hospital and Grant Medical College, Bombay-8, India.

Academic activities:

1. Served as Case based Learning (CBL) facilitator for GI and intermediary metabolism and for Cells to genes.
2. Lectured to graduate students on past and ongoing research in my laboratory and have been invited to speak at seminars organized by the Department of Anatomy and Cell biology, Department of Microbiology and Immunology and the Division of Hematology/Oncology. Currently there are two graduate students working in my laboratory towards a Ph.D. degree. In addition, a post doctoral fellow supported by the Swiss National Science Foundation spent one year on a joint project with Kent State University and my laboratory and a graduate student from the University of Reus, Spain, has spent 4 months in my laboratory to complete part of a collaborative research project.
3. Served as examiner for Ph.D proposals in the Departments of Biochemistry and Anatomy - Cell biology.
4. Trained graduate students on laboratory rotation in various aspects of biochemical, cellular and molecular research techniques.
5. Accepted residents from the Department of Medicine and fellows from the Division of Hematology/Oncology and from Pediatric Hematology for training in basic science research.
6. In addition to the academic activities listed above, I have served as an external examiner of a Ph.D. thesis at the University of Nancy, France; University of Reus, Spain and have provided mentoring support to a post-doctoral fellow at the University of Utah, for collaborative work.

Current Teaching and Academic activities:

Medical School: Approximately > 100 hrs

1. First year Biochemistry lectures 3hours.
2. Case based learning:
 - a. Cells to genes, 18hrs
 - b. GI and intermediary metabolism: 18hrs
3. Histology Laboratory: 65 hrs
Facilitators' discussions and preparations 2-4hrs
4. Interviewing applicants for medical school:

I interview one candidate every other week, typically 8-12 candidates per year.
Time allocation: 1hr for application review and 1-2hr for interview; total time, 16-24hrs

Graduate School: Approximately 80+ hrs

1. Course lecture: 6hrs

2. Thesis committees:

Thesis review at proposal, pre defense and final defense: Approximately 20hrs per candidate, 3 candidates per year, total 60hrs.

Thesis presentations and meetings, Approximately 6hrs per candidate, 3 candidates per year, total 18hrs

2008- Member, Executive Committee

2009- 2010, Chairman, Research Resources Subcommittee

National and International Collaborations:

The research in my laboratory has involved collaboration with investigators at various institutions. These collaborations have included Axis-Shield, Norway; University of Nancy, France; University Aarhus, Denmark; Cleveland Clinic and Kent State University, Cleveland Ohio; University of Nebraska and Medarex Inc. In addition to continuing collaborations with these institutions I have established new collaborations with investigators at the University of Aachen, Germany; University of Reus, Spain; Trinity College, Ireland; The Human Genome Center, NIH; North Shore/Long Island Jewish Health System, NY and the Texas Genome Center, St Antonio.

National and International service:

As a laboratory recognized for its contribution to research in the vitamin B12 and folate fields, my laboratory serves as a worldwide reference center for biochemical and genetic disorders affecting pathways and genes involving these two nutrients. We receive samples for analysis from all over the world and are able to provide this service to patients affected by these rare disorders.

Commercialized Technology:

1. Holo transcobalamin assay: In an exclusive licensing agreement with Axis-Shield, a clinical diagnostics company based in the UK and Norway, I have been involved in the development of an assay for holo transcobalamin, a sensitive and accurate measure of vitamin B12 status. This assay is being marketed worldwide by Abbot Laboratories as part of the tests included in their new instrumentation platform. This test is expected to replace the current serum total B12 assay to diagnose B12 deficiency with a annual market of over 1 billion dollars. In addition to agreed royalty payments, the exclusive agreement includes the purchase and use of the monoclonal antibody to transcobalamin developed in my laboratory.

2. Folate receptor autoantibody assay: We have now signed an exclusive agreement with Iliad Neurosciences, a New York based company to develop and market an assay for the identification of autoantibodies to folate receptors in serum. This autoantibody has a pathologic effect in a number of conditions such as neural tube defect pregnancy, infertility, and miscarriages in women and cerebral folate deficiency in infancy. Intervention with pharmacological doses of folate can overcome many of the pathological effects of the autoantibody and therefore detection of this autoantibody and early intervention is critical to preventing permanent embryonic damage in pregnancy and neuro-developmental abnormalities in infants. The fairly high prevalence of this

autoantibody in the elderly population could pose a risk factor for developing folate deficiency. The market potential for this test is predicted to be fairly large considering that every woman of child-bearing age, every newborn and people over the age of 65 years may benefit from screening for the folate receptor autoantibody.

3. Targeting Transcobalamin-Receptor Pathway in cancer therapy: This ambitious multi pronged approach to targeting cancer cells uses a novel essential nutrient depletion strategy to slow or block cancer cells from proliferating. This strategy is likely to be less toxic and less likely to induce resistance to therapy. The monoclonal antibodies, the TC ligand and the receptor are also candidate carriers for delivering known chemotherapeutic drugs, toxins, imaging compounds and radionuclides to tumors. This project is being developed with the support of a Toronto based biotechnology company, KYTO Biopharma.

Research Interests:

My research interests include biochemical and molecular aspects of vitamin B12 / folate absorption, transport and metabolism; Genetic abnormalities of vitamin B12 / folate dependent pathways; Cellular and metabolic consequences of vitamin B12 and folate deficiencies; Vitamin B12, folate and homocysteine metabolism in the elderly population with cardio-vascular disease and cognitive disorders including Alzheimer's dementia; Neuropathology of vitamin B12 and folate deficiency; B12, folate status and DNA methylation in the brain. Another area of research actively being pursued in my laboratory is the association of folate receptor autoimmunity with neural tube defect pregnancy and cerebral folate deficiency.

Current research in my laboratory is focused on fetal and neonatal brain development and the role of folate and B12 in this process. We have established a strong link between an autoimmune disorder that produces autoantibodies against the folate receptor alpha, a membrane receptor involved in folate transport to the fetus and to the brain. The association of these autoantibodies in women during pregnancy can cause abnormal fetal brain development and in the newborn can affect brain function. A strong link has been established between the presence of folate receptor autoantibodies and autism spectrum disorders. Folinic acid treatment has helped alleviate many of the core behavioral deficits in autistic children with these autoantibodies. Research in my laboratory is aimed at understanding the cause and effects of this autoimmune disorder and how best to prevent and treat the pathologic consequences. While a test to identify folate receptor autoantibodies in serum has been developed, we are looking into developing novel markers to identify women at risk of having an autistic child and children at risk of developing autism. Another aspect of my research is focused on cancer therapeutics based on vitamin B12 and folate analogs that are anti-metabolites, drug-conjugates and pro-drugs; selective targeting of drugs via the B12 and folate transport proteins and their receptors; vitamin B12 and folate depletion strategies to inhibit cell replication in malignancies utilizing monoclonal antibodies to block cellular uptake of these vitamins and to deliver drugs. These approaches are designed to provide preferential targeting of rapidly dividing cancer cells because of the increased expression of receptors for uptake and increased need for these vitamins in cellular replication. In continuing our work on characterizing vitamin B12 binding proteins and the genes encoding these proteins, we are now studying the membrane receptor for the cellular uptake of vitamin B12. Having isolated the protein and gene encoding this receptor, we are now in a unique position to characterize this gene. It also provides us the tools for gene knockout studies that may finally yield valuable information on the role of vitamin B12 in embryogenesis, and the nervous system and perhaps identify the

biochemical mechanism underlying the neuro-pathological manifestations of B12 deficiency which to date remains unexplained.

Miscellaneous Duties:

2014- Consultant, Iliad Neurosciences, New York
2013-2014, Visiting Professor, INSERM Unit, University of Nancy, France
2012- Consultant, PAM Labs
2010 – Consultant, Par/Strativa Pharma
2009 – 2011, Consultant, Covidien Inc.
2007- 2012, Member, Executive Committee, SUNY Downstate Medical Center
2008- 2010, Chairman, Research Resources Subcommittee
2007 – 2008 Consultant, IMMCO Diagnostics, Buffalo, NY.
1999 - Present, Consultant, KYTO Biopharma, Toronto, Canada.

1993-1997, Consultant and Collaborator, Receptagen Corporation, Seattle, WA; Department of Radiochemistry, University of Washington, Seattle, WA, the Biomedical Research Centre, University of British Columbia, Vancouver, Canada and The National Research Council, Ottawa, Canada.

1993 - 96, Member, Research and Development Committee.
V.A Medical Center, Brooklyn, NY 11209

1989 – 91, Chairman, Animal Research Subcommittee,
V.A. Medical Center, Brooklyn, NY 11209

1986 – 88, Member, Research and Development Committee,
V.A. Medical Center, Brooklyn, NY 11209

1986 – 88, Member, Animal Research Subcommittee,
V.A. Medical Center, Brooklyn. NY 11209

Prior Research Funding:

1991-1995, Study of Transcobalamin II, a vitamin B12 transport protein in the blood. V.A. Merit Review. Veterans Affairs. (Principal Investigator: E.V. Quadros)
Amount: \$726,845.

1993-1996, Receptor -Transcobalamin as a target for apoptosis and for delivery of macro molecules.
Receptagen Inc. Seattle, Washington. (Principal Investigator: E.V. Quadros)
Amount: \$263,000.

1994-1999, Kinetics of B12, Intrinsic Factor and other proteins. NIH. (S.P. Rothenberg, Principal Investigator; E.V. Quadros, CoInvestigator)

Amount: \$934,984.

1999 – 2000. Receptor-Transcobalamin II as a target for inducing apoptosis and for delivery of therapeutic compounds. BTwelve Inc. Toronto, CA. (Principal Investigator: E.V. Quadros,)

Amount: \$124,000

2000-01, Amount \$128,000

1999 - Axis Shield PLC, Oslo, Norway.

Monoclonal antibody based assay development.

1999 - 2000, Amount \$15,050. (Principal Investigator: E.V. Quadros)

2004-2005 – NIH (KO7), NIA Alzheimer's Disease Pilot Project.

Amount: \$20,000 (Principal Investigator: E.V. Quadros)

April 2006 – March 2009. NIH R21 HD051880-01

Amount: \$ 166,000 (Principal Investigator: E.V. Quadros)

July 2011, SUNY Technology accelerator award: \$50,000 (Principal Investigator: E.V. Quadros)

Sep 2005 – June 2012. NIH RO1 DK064732-01A1

Amount: \$ 1,100,000 (Includes ARRA and bridge funding) (Principal Investigator: E.V. Quadros)

Nov. 2006 – multi year contract, KYTO Biopharma, Toronto, Canada.

Amount: \$ 134,000 for 2009 - 13. (Principal Investigator: E.V. Quadros)

Current Research Funding:

1. Autism Speaks June 2013 – May 2016

Basic and Clinical Research Grant

Amount: \$449,00 (Principal Investigator: E.V. Quadros)

Patents

1. The use of monoclonal antibodies to human transcobalamin II to deprive cells of cobalamin. EU Patent # 0783526, Issued March, 2006.
2. Method for detecting the affinity of folate receptor autoantibodies US#7846672B2, 2010
3. Transcobalamin receptor polypeptides, nucleic acids, and modulators thereof, and related methods of use in modulating cell growth and treating cancer and cobalamin deficiency. PUPA/US60/790330. 2014.

Symposia Publications:

1. **Quadros, E.V.**, Jackson, B., Hoffbrand, A.V. and Linnell, J.C. (1979). Interconversion of cobalamins in human lymphocytes in vitro and the effect of nitrous oxide on synthesis of cobalamin coenzymes. Third European Symposium on Vitamin B12 and Intrinsic Factor. (Zagalak, B. and Friedrich, W. eds), pp. 1045- 1054.
2. **Quadros, E.V.** and Rothenberg, S.P. (1990). The structure and biosynthesis of human Transcobalamin II. Cobalamin '88 - Proceedings of the First International Symposium on Biomedicine and Physiology of Vitamin B₁₂, p. 281-288, The Children's Medical Charity, London.
3. Rothenberg, S.P. and **Quadros, E.V.** (1990). Ligand binding and radioimmuno assay for cobalamin. Cobalamin '88 - Proceedings of the First International Symposium on Biomedicine and Physiology of Vitamin B₁₂, p. 401-414, The Children's Medical Charity, London.

Book Chapters

1. Rothenberg, S.P. and **Quadros, E.V.** (1995). Transcobalamin II and the membrane receptor for the transcobalamin II-cobalamin complex. In Bailliere's Clinical Haematology (Wickramasinghe, S.N. ed) 8: 449-514.
2. Rothenberg, S.P., and **Quadros, E.V.** (1997). Quantitative methods for measurement of transcobalamin II (C.A.Wagner, Ed) Methods in Enzymology. 281: 261-268.
3. Quian, L., **Quadros, E.V.**, and Rothenberg, S.P. (1997). Molecular methods for analysis and expression of transcobalamin II. (C.A. Wagner, Ed) Methods in Enzymology. 281: 269-281.
4. Rothenberg, S.P., **Quadros, E.V.** and Regec, A. (1999). Transcobalamin II. In Vitamin B12 (Bannerjii, R. Ed). John Wiley and Sons Publ.
5. **Quadros, E.V.** Quantitative assay of vitamin B₁₂ In Modern Analytical Methods on Fat Water-Soluble Vitamins. (W.O. Song and G.R. Beecher Ed.) John Wiley & Sons Publ. (2001). p 313-328.
6. Ramaekers, V.T. and **Quadros, E.V.** (2010). Folate receptor autoimmunity in cerebral folate deficiency. (R.C. Dale and A Vincent Ed.) Clinics in Developmental Medicine, 184 – 185, Mac Kieth Press, London, UK.

Thesis Publications:

1. **Quadros, E.V.** (1972). Nutritional disorders of the nervous system: Studies on vitamin B₁₂, thiocyanate and folates. M.Sc. Thesis, University of Bombay, India.
2. **Quadros, E.V.** (1976). Studies on the distribution of cobalamins in man and animals and on cellular synthesis of cobalamin coenzymes in-vitro. Ph.D. Thesis, University of London (UK).

Conferences and meetings: (Abstracts deleted)**PEER REVIEWED PUBLICATIONS:**

1. Dastur, D.K., **Quadros, E.V.**, Wadia, N.H., Desai, M.M. and Bharucha, E.P. (1972) Effect of vegetarianism and smoking on Vitamin B₁₂, thiocyanate and folate levels in the blood of normal subjects. *Br. Med. J.* 3:260-262.
2. Wadia, N.H., Desai, M.M., **Quadros, E.V.** and Dastur, D.K. (1972) Role of vegetarianism, smoking and hydroxocobalamin in optic neuritis. *Br. Med. J.* 3:264-267.
3. Dastur, D.K., Santha Devi, N., **Quadros, E.V.**, Gagrath, B.M., Wadia, N.H., Desai, M.M., Singhal, B.S. and Bharucha, E.P. (1975) Interrelationships between the B-vitamins in B₁₂ deficiency neuromyelopathy: A possible malabsorption-malnutrition syndrome. *Am. J. Clin. Nutr.* 28:255-270.
4. **Quadros, E.V.**, Matthews, D.M., Wise, L.J. and Linnell, J.C. (1975) Known and unknown cobalamins in the rat. *Clin. Sci. Mol. Med.* 48:4-5.
5. **Quadros, E.V.**, Matthews, D.M., Wise, L.J. and Linnell, J.C. (1976) Tissue distribution of endogenous cobalamins in the Rat, Cat and Guinea Pig. *Biochim. Biophys. Acta* 421:141-152.
6. Dastur, D.K., Santha Devi, N., **Quadros, E.V.**, Gagrath, B.M., Wadia, N.H., Desai, M.M. and Bharucha, E.P. (1976) B-vitamins in malnutrition alcoholism: interrelationships in blood and CSF. *Br. J. Nutr.* 36:143-159.
7. **Quadros, E.V.**, Matthews, D.M., Hoffbrand, A.V. and Linnell, J.C. (1976) Synthesis of cobalamin coenzymes by human lymphocytes in vitro and the effects of folates and metabolic inhibitors. *Blood* 48:609-619.
8. Linnell, J.C., **Quadros, E.V.**, Matthews, D.M., Morris, H.P. and Poirier, L.A. (1977) Altered cobalamin distribution in rat hepatomas and in the livers of rats treated with diethylnitrosamine. *Cancer Res.* 37:2975-2978.

9. Hansen, O.P., Drivsholm, A., Hippe, E., **Quadros, E.V.** and Linnell, J.C. (1978) Interrelationships between vitamin B₁₂ and folic acid in myelomatosis: cobalamin coenzyme and tetrahydrofolic acid function. *Scand. J. Haematol.* 20:360-370.
10. **Quadros, E.V.**, Hamilton, A., Matthews, D.M. and Linnell, J.C. (1978) Isolation of ⁵⁷Co-cobalamin coenzymes at high specific activity from *Streptomyces griseus*. *J. Chromatogr.* 160:101-108.
11. Myasishcheva, N.V., **Quadros, E.V.**, Matthews, D.M. and Linnell, J.C. (1979) Interference by methylcobalamin analogues with synthesis of cobalamin coenzymes in Human Lymphocytes in vitro. *Biochim. Biophys. Acta*, 588:81-88.
12. Linnell, J.C., **Quadros, E.V.**, Elliott, P.G. and Malleson, P. (1980) Defective adenosylcobalamin synthesis in a case of transcobalamin-II deficiency. *J. Inher. Metab. Dis.* 3:95-96.
13. Linnell, J.C., **Quadros, E.V.**, England, J.M., Down, M.C. and Reynolds, E.G. (1981) Abnormal Cobalamin metabolism in a case of juvenile pernicious anemia with neurological symptoms. *J. Inher. Metab. Dis.* 4:149-150.
14. Jacobsen, D.W., Green, R., **Quadros, E.V.** and Montejano, Y.D. (1982) Rapid analysis of cobalamin coenzymes and related corrinoid analogs by high-performance liquid chromatography. *Anal. Biochem.* 120:394-403.
15. **Quadros, E.V.**, Rothenberg, S.P., Pan, Y. Ch and Stein, S. (1986) Purification and molecular characterization of human transcobalamin II. *J. Biol. Chem.* 261:15455-15460.
16. **Quadros, E.V.**, Rothenberg, S.P. and Polu, S. (1988) A specific radioimmunoassay for the measurement of 5' deoxyadenosyl cobalamin in serum. *Brit. J. Haematol.* 69:551-557.
17. **Quadros, E.V.**, Rothenberg, S.P. and Jaffe, E. (1989) Human endothelial cells synthesize and secrete functional transcobalamin II. *Amer. J. Physiol.* 256:C296-C303.
18. Platica, O., Janeczko, O., Regec, A., **Quadros, E.V.** and Rothenberg, S.P. (1989) Isolation of the complementary DNA for human transcobalamin II. *Proc. Soc. Exptl. Biol. Med.* 192:95-97.
19. Platica, O., Janeczko, R., **Quadros, E.V.**, Regec, A., Romain, R. and Rothenberg, S.P. (1991) The cDNA sequence and the deduced amino acid sequence of human transcobalamin II share homology with rat intrinsic factor and human transcobalamin I. *J. Biol. Chem.* 266:7860-7863.
20. **Quadros, E.V.**, Sai, P. and Rothenberg, S.P. (1993) Functional human transcobalamin II Isoprotein are secreted by insect cells using the baculovirus expression system. *Blood.* 81:1239-1245.

21. **Quadros, E.V.**, Sai, P. and Rothenberg, S.P. (1994) Characterization of the human placental membrane receptor for transcobalamin II- Cobalamin. *Arch.Biochem.Biophys.*308:192-199.
22. Regec, A. **Quadros, E.V.**, Platica, O. and Rothenberg, S.P. (1995) The cloning and characterization of the human transcobalamin II gene. *Blood.* 85: 2711-2719.
23. **Quadros, E.V.** and Jacobsen, D.W. (1995) The dynamics of cobalamin utilization in L-1210 mouse leukemia cells; a model of cellular cobalamin metabolism. *Biochim. Biophys. Acta.*1244: 395-403.
24. **Quadros, E.V.**, Rothenberg, S.P. and McLoughlin, P. (1996) Characterization of monoclonal antibodies to functional epitopes of human transcobalamin II. *BBRC* 222:149-154.
25. Pathare, P.M., Wilbur, S.D., Heusser, S., **Quadros, E.V.**, McLoughlin, P., and Morgan, A.C. (1996) Synthesis of cobalamin-biotin conjugates that vary in the position of coupling. Evaluation of cobalamin derivative binding to transcobalamin II. *Bioconjugate Chemistry.* 7:217-232.
26. Wilbur, S.D., Hamlin, D.K., Pathare, P.M., Heusser, S., Vessella, R.L., Buhler, K.R., Stray, J.E., Daniel, J., **Quadros, E.V.**, McLoughlin, P. and Morgan, A.C. (1996) Synthesis and nca-radioiodination of arylstannyl-cobalamin conjugates. Evaluation of arylido-cobalamin conjugate binding to transcobalamin II and biodistribution in mice. *Bioconjugate Chemistry.* 7: 461-474.
27. McLean, G.R., **Quadros, E.V.**, Rothenberg, S.P., Morgan, A.C., Schrader, J.W. and Ziltener, H.J. (1997) Antibodies to transcobalamin II block in-vitro proliferation of leukemic cells. *Blood* 89: 235-242.
28. Pathare, P.M., Wilbur, D.S., Hamlin, D.K., Heusse, S., **Quadros, E.V.**, McLoughlin, P., and Morgan, A.C. (1997) Synthesis of cobalamin dimers using isophthalate cross-linking of corrin ring carboxylates and evaluation of their binding to transcobalamin II. *Bioconjugate Chem.* 8: 161-172.
29. Wilbur, S.D., Pathare, P.M., Hamlin, D.K., Rothenberg, S.P. and **Quadros, E.V.** (1999) Radioiodination of cyanocobalamin conjugates containing hydrophobic linkers: Preparation of a radionated cyanocobalamin monomer and two dimers and assesment of their binding with transcobalamin II. *Bioconjugate Chemistry.* 10: 912-920.
30. **Quadros, E.V.**, Regec, A., Khan, K.M.F., Quadros, E. and Rothenberg, S.P. (1999) Transcobalamin synthesized in the intestinal villi facilitates transfer of cobalamin to the portal blood. *Amer. J. Physiol.* 277: G161-G166.
31. Sobti, P., Rothenberg, S.P. and **Quadros, E.V.** (2000) Radio-enzymatic assay for reductive catalysis of N⁵,N¹⁰-methyltetrahydrofolate by methylenetetrahydrofolate reductase. *J. Biochem. Biophys. Methods* 46: 11 - 20.

32. Ullend M, Eilertsen, I., **Quadros, E.V.**, Rothenberg, S.P., Fedosov, S.N., Sundrehagen, E. and Orning, L. (2002) Direct assay for cobalamin bound to transcobalamin (holotranscobalamin) in serum. *Clin Chem* 48:526 – 532.
33. Qian, L., **Quadros, E.V.**, Rejec, A., Zitouan, J. and Rothenberg, S.P. (2002) Congenital Transcobalamin II deficiency due to errors in RNA editing. *Blood Cells Mol. Dis.* 28: 134-142.
34. Rejec, A., **Quadros, E.V.** and Rothenberg, S.P. (2002) Transcobalamin II expression is regulated by transcription factor(s) binding to a hexameric sequence (TGGTCC) in the promoter region of the gene. *Arch. BioChem. Biophys.* 407: 202-208.
35. Namour, F., Helfer, A-C., **Quadros, E.V.**, Alberto, J-M., Bibi, Haim., Orning, L., Rosenblatt, D and Gueant, J-L. (2003) Transcobalamin deficiency due to activation of an intra exonic cryptic splice site. *Brit. J. Haemat.* 123: 915-920.
36. Gordon, M.M., Brada, N., Ramacha, A., Badell, I., delRio, E., Baiget, M., Santer, R., **Quadros, E.V.**, Rothenberg, S.P. and Alpers, D.H. (2004) A genetic polymorphism in the coding region of the gastric intrinsic factor gene is associated with congenital intrinsic factor deficiency. *Hum. Mutat.* 23: 85-91.
- 37 Fawwaz, Y., Rothenberg, S.P., Rao, S., Gordon, M.M., Alpers, D.H. and **Quadros, E.V.** (2004) Inherited deficiency of intrinsic factor due to a four base deletion in the gene. *Blood.* 103: 1515-1517.
38. Rothenberg, S.P., daCosta, M.P., Sequeira, J.M., Cracco, J., Roberts, J.L., Weedon, J. and **Quadros, E.V.** (2004) Autoantibodies against folate receptors in women with a pregnancy complicated by a neural tube defect. *NEJM.* 350: 134-142.
39. **Quadros, E.V.**, Nakayama, Y., Sequeira, J.M. (2005) The binding properties of the human receptor for the cellular uptake of vitamin B12 *Biochemical and Biophysical Research Communications* 327 1006–1010
40. Ramaekers, V.Th., Rothenberg, S.P., Sequeira, J.M., Opladen, T., Blau, N., **Quadros, E.V.**, Selhub, J. (2005) Autoantibodies against folate receptors are associated with the infantile onset cerebral folate deficiency syndrome *NEJM.* 352, 1985–1991.
41. Fedosoy, S.N, Örning, L, Løvli, T., **Quadros, E.V.**, Thompson K, Berglund, L Petersen, T.E. (2005) Mapping the functional domains of human transcobalamin using monoclonal antibodies. *FEBS J.* 272, 3889 – 3898.
42. Orning, L., Rian, A., Campbell, A., Brady, J., Fedosov, S., Bramlage, B., Thompson, K and **Quadros, E.V.** (2006) Characterization of a monoclonal antibody with specificity for holo-transcobalamin. *Nutr. Metab. (Lond).* 3:3
43. Guéant, J-L., Chabi, N., Guéant-Rodriguez, R-M., Osvaldo, M., Debard, R., Payet, C., Lu, X., , Villaume, C., Bronowicki, J-P., **Quadros, E.V.**, Sanni, A., Amouzou, E., Bing, X.,

Chen, M., Anello, G., Bosco, P., Romano, A., Arrieta, H., Sanchez, B., Romano, A., Herbeth, B., Anwar, W., Namour, F. (2007) Environmental influence on the world-wide prevalence of a 776C>G variant in the transcobalamin gene (TCN2). *J. Med. Genet.* 44, 363 – 367.

44. Ramaekers, V.Th. and **Quadros, E.V.** Folate receptor autoimmunity in cerebral folate deficiency. In *Inflammatory and Autoimmune Disorders of the Nervous System in Children* Chapter 19, pp 302 – 316, Mac Keith Press, London, 2010

45. Ramaekers, V.Th., Sequeira J.M., Artuch R., Blau N., Temudo T., Ormazabal A., Pineda, M., Aracil A., Roelens F., Laccone F and **Quadros E.V.** (2007) Folate Receptor Autoantibodies and Cerebral Folate Deficiency In Rett Syndrome. *Neuropediatrics* 38: 179 – 183.

46. Garcia-Cazorla, A., **Quadros, EV.**, Nascimento, A., Garcia-Silva, MT., Paz Briones PhD, Montoya, J., Ormazábal, A., Artuch, R., Sequeira, JM., Blau, N., Arenas, J., Pineda, M. and Ramaekers, VTh. (2007) Mitochondrial diseases associated with cerebral folate deficiency. *Neurology* 15:1360-1362.

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