

CURRICULUM VITAE

CARINE MAENHAUT

EDUCATION AND TRAINING

1983 - 1987: University education

Free University of Brussels, Belgium

MS chemistry (Biological Chemistry) with Summa Cum Laude

Title of the dissertation: Protooncogene c-myc mRNA regulation in thyroid cells
(director: Pr. J.E. Dumont). Grade: 19/20

1987 - 1992: PhD thesis in Biochemistry

Free University of Brussels

Institute of Interdisciplinary Research (IRIBHN, Campus Erasme)

Title of the thesis: Identification, characterisation and mRNA regulation of G-protein-coupled receptors: thyrotropin, adenosine A2 and serotonin 5-HT1D receptors

Director : Pr. J.E. Dumont

Grade: Summa Cum Laude

FELLOWSHIPS AND POSITIONS

- Oct. 1987 - Sept. 1990 : Fellowship from the "Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture" (IRSIA)
- Oct. 1990 - Sept. 1992 : Fellow of the "Fonds National de la Recherche Scientifique" (FNRS)
- Oct. 1992 - Sept. 1994 : Researcher of the "Fonds National de la Recherche Scientifique"(FNRS)
- Oct. 1994 - : Assistant Professor, University of Brussels

SCIENTIFIC AWARDS

- 1986-1987 "B. Libotte" prize for the best MS dissertation in biological chemistry
- Laureate of the "Solvay Awards" 1993, for the best PhD thesis
- 1993 « Association Belge contre le Cancer » prize
- 1994 Galien prize in Pharmacology
- 2001-2003 "Dr. Maurice Godin-Savelkoul" prize

SCIENTIFIC PUBLICATIONS

1. Dumont J.E., Roger P., Contor L., Reuse S., Taton M., Maenhaut C., Rickaert F., Lecocq R., Lamy F. (1987) Contrôle de la prolifération cellulaire par le système de l'AMP cyclique: l'exemple de la cellule thyroïdienne. Bull. et Mém. de l'Académie Royale de Médecine de Belgique 142, 258-267.
2. Raspe E., Reuse S., Maenhaut C., Roger P., Corvilain B., Laurent E., Mockel J., Van Sande J., Dumont J.E. (1989) Importance and variability of transducing systems in the control of thyroid cell function, proliferation and differentiation. In: "Growth Regulation of Thyroid Gland and Thyroid Tumors" (Goretzki P.E., Röher H.D.). Front. Horm. Res. Basel, Karger, vol. 18, 1-13.
3. Libert F., Parmentier M., Lefort A., Dinsart C., Van Sande J., Maenhaut C., Simons M.J., Dumont J.E., Vassart G. (1989) Selective amplification and cloning of four new members of the G protein-coupled receptor family. Science 244, 569-572.
4. Parmentier M., Libert F., Maenhaut C., Lefort A., Gérard C., Perret J., Van Sande J., Dumont J.E., Vassart G. (1989) Molecular cloning of the thyrotropin receptor. Science 246, 1620-1622.
5. Parmentier M., Libert F., Maenhaut C., Lefort A., Gérard C., Perret J., Van Sande J., Dumont J.E., Vassart G. (1989) Nucleotide sequence of the dog thyrotropin receptor cDNA. Nucl. Ac. Res. 17, 10493.
6. Dumont J.E., Lefort A., Libert F., Parmentier M., Raspe E., Reuse S., Maenhaut C., Roger P., Corvilain B., Laurent E., Mockel J., Lamy F., Van Sande J., Vassart G. (1990) Transducing systems in the control of human thyroid cell function, proliferation and differentiation. Advances in Experimental Medicine and Biology 261, 357-372.
7. Libert F., Parmentier M., Maenhaut C., Lefort A., Gérard C., Perret J., Van Sande J., Dumont J.E., Vassart G. (1990) Molecular cloning of a dog thyrotropin (TSH) receptor variant. Mol. Cell. Endocr. 68, R15-R17.
8. Maenhaut C., Libert F. (1990) An efficient morphological test for characterization of cyclic AMP coupled hormone receptors. Exp. Cell Res. 187, 104-110.
9. Maenhaut C., Lefort A., Libert F., Parmentier M., Raspe E., Roger P., Corvilain B., Laurent E., Reuse S., Mockel J., Lamy F., Van Sande J., Dumont J.E. (1990) Function, proliferation and differentiation of the dog and human thyrocyte. In: "Physiological Regulation and Biological Function of Thyrotropin" (Pfeiffer E.F., Reaven G.M.). Horm. Met. Res. suppl. series 23, 51-61.
10. Reuse S., Maenhaut C., Dumont J.E. (1990) Regulation of protooncogenes c-fos and c-myc expressions by protein tyrosine kinase, protein kinase C, and cyclic AMP mitogenic pathways in dog

primary thyrocytes: a positive and negative control by cyclic AMP on c-myc expression. *Exp. Cell Res.* 189, 33-40.

11. Reuse S., Pirson I., Pohl V., Maenhaut C., Roger P., Dumont J.E. (1990) The cyclic AMP cascade as a trigger or stimulant of epithelial cell proliferation: the example of the thyroid. *Excerpta Medica International Congress Series 925: Growth Factors in Health and Disease - Basic and Clinical Aspects* (Westermarck B., Betsholtz C., Hökfelt B.) Elsevier, 199-214.

12. Van Sande J., Raspe E., Perret J., Lejeune C., Maenhaut C., Vassart G., Dumont J.E. (1990) Thyrotropin activates both the cyclic AMP and the PIP2 cascades in CHO cells expressing the human cDNA of TSH receptor. *Mol. Cell. Endocr.* 74, R1-R6

13. Reuse S., Maenhaut C., Lefort A., Libert F., Parmentier M., Raspe E., Roger P., Corvilain B., Laurent E., Mockel J., Lamy F., Van Sande J., Vassart G., Dumont J.E. (1990) The control of human thyroid cell function, proliferation and differentiation. In "Activation and Desensitization of Transducing Pathways" (Konijn T.M., Houslay M.D., Van Haastert P.J.M.) NATO ASI Series, 44, 285-306, Springer-Verlag Berlin Heidelberg.

14. Maenhaut C., Van Sande J., Libert F., Abramowicz M., Parmentier M., Vanderhaegen J.J., Dumont J.E., Vassart G., Schiffmann S. (1990) RDC8 codes for an adenosine receptor with physiological constitutive activity. *Bioch. Bioph. Res. Comm.* 173, 1169-1178.

15. Maenhaut C., Roger P.P., Reuse S., Dumont J.E. (1991) Activation of the cyclic AMP cascade as an oncogenic mechanism: the thyroid example. *Biochimie* 73, 29-36.

16. Brabant G., Maenhaut C., Köhrle J., Scheumann G., Dralle H., Hoang-Vu C., Hesch R.D., von zur Mühlen A., Vassart G., Dumont J.E. (1991) Human thyrotropin receptor gene: expression in thyroid tumors and correlation to markers of thyroid differentiation and dedifferentiation. *Mol. Cell. Endocrinol.* 82, R7-R12.

17. Maenhaut C., Van Sande J., Massart C., Dinsart C., Libert F., Monferini E., Giraldo E., Ladinsky H., Vassart G., Dumont J.E. (1991) The orphan receptor cDNA RDC4 encodes a 5-HT1D serotonin receptor. *Biochem. Bioph. Res. Comm.* 180, 1460-1468.

18. Dumont J.E., Maenhaut C., Pirson I., Baptist M., Roger P.P. (1991) Growth factors controlling the thyroid gland. *Bailliere's Clinical Endocrinol. Metab.* 5, 727-754.

19. Dumont J.E., Maenhaut C., Lamy F. (1992) Control of thyroid cell proliferation and goitrogenesis. *Trends in Endocrinol. and Metab.* 3, 12-17.

20. Maenhaut C., Brabant G., Vassart G., Dumont J.E. (1992) In vitro and in vivo regulation of thyrotropin receptor mRNA levels in dog and human thyroid cells. *J. Biol. Chem.* 267, 3000-3007.

21. Pohl V., Maenhaut C., Gérard C., Vassart G., Dumont J.E. (1992) Differential regulation of thyrotropin receptor and thyroglobulin mRNA accumulation at the cellular level: an in situ hybridization study. *Exp. Cell Res.* 199, 392-397.
22. Dumont J.E., Lamy F., Roger P.P., Maenhaut C. (1992) Physiological and pathological regulation of thyroid cell proliferation and differentiation by thyrotropin and others factors. *Physiol. Rev.* 72, 667-697.
23. Ledent C., Parmentier M., Maenhaut C., Taton M., Pirson I., Lamy F., Roger P., Dumont J.E. (1992) The TSH cyclic AMP cascade in the control of thyroid cell proliferation: the story of a concept. *Thyroidology* 3, 97-102.
24. Vassart G., Brabant G., Costagliola S., Danguy D., Gérard C., Libert F., Ludgate M., Maenhaut C., Parmentier M., Paschke R., Perret J., Van Sande J., Dumont J.E. (1992) Molecular genetics of the thyrotropin receptor. *Exp. Clin. Endocrinol.* 100, 9-11.
25. Hoang-Vu C., Dralle H., Scheumann G., Maenhaut C., Horn R., von zur Mühlen A., Brabant G. (1992) Gene expression of differentiation and dedifferentiation markers in normal and malignant human thyroid tissues. *Exp. Clin. Endocrinol.* 100, 51-56.
26. Van Sande J., Allgeier A., Massart C., Czernilofsky A., Vassart G., Dumont J.E., Maenhaut C. (1993) The human and dog 5-HT_{1D} receptors can both activate and inhibit adenylate cyclase in transfected cells. *Eur. J. Pharmacol.* 247, 177-184.
27. Elisei R., Pinchera A., Romei C., Gryczynska M., Pohl V., Maenhaut C., Fugazzola L., Pacini F. (1994) Expression of thyrotropin receptor (TSH-R), thyroglobulin, thyroperoxidase, and calcitonin messenger ribonucleic acids in thyroid carcinomas: evidence of TSH-R gene transcript in medullary histotype. *J. Clin. Endocr. and Metab.* 78, 867-871.
28. Miot F., Wilkin F., Dremier S., Uyttersprot N., Lamy F., Dumont J.E., Maenhaut C. (1994) Cloning of cDNA specifically involved in the thyroid cAMP mitogenic pathway. *Horm. Res.* 42, 27-30.
29. Maenhaut C., Pirson I., Baptist M., Lamy F., Miot F., Roger P., Dumont J.E. (1995) La cascade mitogénique de l'AMPc dans la thyroïde et dans d'autres tissus. *Médecine/Science* 11, 204-213.
30. Ledent C., Parma J., Pirson I., Taton M., Roger P., Maenhaut C., Van Sande J., Pohl V., Lamy F., Parmentier M., Vassart G., Dumont J.E. (1995) Positive control of proliferation by the cyclic AMP cascade: An oncogenic mechanism of hyperfunctional adenoma. *J. Endocrinol. Invest.* 18, 120-122.

31. Brabant G., Cetin Y., Behrends J., Hoang-Vu C., Dumont J.E., Maenhaut C. (1995) Regulation of the cell-cell adhesion protein, E-cadherin, in dog and human thyrocytes in vitro. *Endocrinology* 136, 3113-3119.
32. Dumont J.E., Ermans A.M., Maenhaut C., Coppee F., Stanbury J.B. (1995) Large goiter as a maladaptation to iodine deficiency. *Clinical Endocrinology* 43,1-10.
33. Roger P.P., Reuse S., Maenhaut C., Dumont J.E. (1995) Multiple facets of the modulation of growth by cAMP. *Vit. and Horm.* 51, 59-191.
34. Wilkin F., Savonet V., Radulescu A., Petermans J., Dumont J.E., Maenhaut C. (1996) Identification of novel genes modulated in the thyroid of dogs treated with methimazole and propylthiouracil. *J. Biol. Chem.* 271, 28451-28457.
35. Pichon B., Jimenez-Cervantes C., Pirson I., Maenhaut C., Christophe D. (1996) Induction of Nerve Growth Factor-Induced gene-B (NGFI-B) as an early event in the cyclic adenosine monophosphate response of dog thyrocytes in primary culture. *Endocrinology* 137, 4691-4698.
36. Uyttersprot N., Pelgrims N., Carrasco N., Gervy C., Maenhaut C., Dumont J.E., Miot F.(1997) Moderate doses of iodide in vivo inhibit cell proliferation and the expression of thyroperoxidase and Na⁺/I symporter mRNAs in dog thyroid. *Mol. and Cell. Endocrinology* 131, 195-203.
37. Savonet V., Maenhaut C., Miot F., Pirson I. (1997) Pitfalls in the use of several housekeeping genes as standards for quantitation of mRNA: the example of thyroid cells. *Analytical Biochemistry* 247, 165-167.
38. Wilkin F., Suarez-Huerta, N., Robaye B., Petermans J., Libert F., Dumont J.E., Maenhaut C. (1997) Characterization of a phosphoprotein whose mRNA is regulated by the mitogenic pathways in dog thyroid cells. *Eur. J. Biochem.* 248, 660-668.
39. Coulonval K., Maenhaut C., Dumont J.E., Lamy F. (1997) Phosphorylation of the three Rb protein family members is a common step of the cAMP-, the growth factor, and the phorbol ester-mitogenic cascades but is not necessary for the hypertrophy induced by insulin. *Exp. Cell Res.* 233, 395-398.
40. Dremier S., Pohl V., Poteet-Smith C., Roger P., Corbin J., Doskeland S., Dumont, J.E., Maenhaut C. (1997) Activation of cyclic AMP-dependent kinase is required but may not be sufficient to mimic cyclic AMP-dependent DNA synthesis and thyroglobulin expression in dog thyroid cells. *Mol. Cell. Biol.* 17, 6717-6726.
41. Uyttersprot N., Allgeier A., Baptist M., Christophe D., Coppee F., Coulonval K., Deleu S., Depoortere F., Dremier S., Lamy F., Ledent C., Maenhaut C., Miot F., Panneels V., Parma J., Parmentier

M., Pirson I., Pohl V., Roger P., Savonet V., Taton M., Tonacchera M., Van Sande J., Wilkin F., Vassart G., Dumont J.E. (1997) The cAMP in thyroid: from the TSH receptor to mitogenesis and tumorigenesis. In "Signal Transduction in Health and Disease, Advances in Second Messenger and Phosphoprotein Research" Vol.31, 125-140 , Lippincott-Raven Publishers, Philadelphia.

42. Jimenez-Cervantes C., Pichon B., Dumont J.E., Maenhaut C. (1998) Activation by thyroid stimulating hormone of nerve growth factor-induced gene-B expression in thyrocytes in culture: relation with proliferation and specific gene expression. *Biochimica and Biophysica Acta* 1403, 232-244.

43. Pirson I., Behrends J., Savonet V., Goffard J-C., Dumont J.E., Schurmans S., Maenhaut C. (1999) Identification and characterization of mRNAs differentially expressed in thyroid cells stimulated by a mitogenic treatment. *Biochimie* 81, 309-314.

44. Deleu S., Pirson I., Coulonval K., Drouin A., Taton M., Clermont F., Roger P., Nakamura T., Dumont J.E., Maenhaut C. (1999) IGF-1 or insulin, and the TSH cyclic AMP cascade separately control dog and human thyroid cell growth and DNA synthesis, and complement each other in inducing mitogenesis. *Mol. and Cell. Endocrinology* 149, 41-51.

45. Deleu S., Pirson I., Clermont F., Nakamura T., Dumont J.E., Maenhaut C. (1999) Immediate early gene expression in dog thyrocytes in response to growth, proliferation and differentiation stimuli. *J. Cell. Physiol.* 181, 342-354.

46. Dremier S., Vandeput F., Zwartkruis J., Bos J., Dumont J.E., Maenhaut C. (2000) Activation of the small G protein Rap1 in dog thyroid cells by both cAMP-dependent and -independent pathways. *Biochem. Bioph. Res. Comm.* 267, 7-11.

47. Deleu S., Allory Y., Radulescu A., Pirson I., Carrasco N., Corvilain B., Salmon I., Franc B., Dumont J.E., Van Sande J., Maenhaut C. (2000) Characterization of autonomous thyroid adenoma : metabolism, gene expression, and pathology. *Thyroid* 10, 131-140.

48. Pirson I., Fortemaison N., Jacobs C., Dremier S., Dumont J.E., Maenhaut C. (2000) The visual display of regulatory information and networks. *Trends in Cell Biology* 10, 404-408.

49. Dumont J.E., Pécasse F., Maenhaut C. (2001) Crosstalk and specificity in signalling. Are we crosstalking ourselves into general confusion ? *Cellular Signalling* 13, 457-463.

50. Venet, D., Pécasse F., Maenhaut C., Bersini H. (2001) Separation of samples into their constituents using gene expression data. *Bioinformatics* 17, S279-S287.

51. Pécasse, F., Venet D., Dumont J.E., Maenhaut C. (2001) Study of thyroid gene expression and regulation by DNA array technology : pitfalls and necessary controls in the use of commercial filters. *Arch. Physiol. Biochem.* 109, 337-349.

52. Venet D., Maenhaut C., Bersini H. (2001) Modeling and determination of the regulation of gene expression: the binary switch model. *Proceedings ICSB*, 239-247.

53. Dumont J.E., Dremier S., Pirson I., Maenhaut C. (2002) Cross signalling, cell specificity, and physiology. *Am. J. Physiol. – Cell Physiol.* 283, C2-C28.

54. Dremier S., Coulonval K., Perpete S., Vandeput F., Fortemaison N., Van Keymeulen A., Deleu S., Ledent C., Clément S., Schurmans S., Dumont J.E., Lamy F., Roger P.P., Maenhaut C. (2002) The role of cyclic AMP and its effect on protein kinase A in the mitogenic action of thyrotropin on the thyroid cell. *Ann. N.Y. Acad. Sci.* 968, 106-121.

55. Deleu S., Savonet V., Behrends J., Dumont J.E., Maenhaut C. (2002) Study of gene expression in thyrotropin-stimulated thyroid cells by cDNA expression array : ID3 transcription modulating factor as an early response protein and tumor marker in thyroid carcinomas. *Exp. Cell Res.* 279, 62-70.

56. Mircescu H., Steuve S., Savonet V., Degraef C., Mellor H., Dumont J.E., Maenhaut C., Pirson I. (2002) Identification and characterization of a novel activated RhoB binding protein containing a PDZ domain whose expression is specifically modulated in thyroid cells by cAMP. *Eur. J. Biochem.* 269, 6241-6249.

57. Dumont J.E., Maenhaut C., Lamy F., Pirson I., Clément S., Roger P.P. (2003) Growth and proliferation of the thyroid cell in normal physiology and in disease. *Ann. Endocrinol.* 64, 10-11.

58. Dremier S., Kopperud R., Doskeland S.O., Dumont J.E., Maenhaut C. (2003) Search for new cyclic AMP-binding proteins. *FEBS Letters* 546, 103-107.

59. Detours V., Dumont J.E., Bersini H., Maenhaut C. (2003) Integration and cross-validation of high-throughput gene expression data: comparing heterogeneous data sets. *FEBS Letters* 546, 98-102.

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61. Maenhaut C. (2004) Etude des cascades de signalisation impliquées dans la prolifération et la différenciation des cellules thyroïdiennes normales et tumorales. *Bull. et Mém. de l'Académie royale de Méd. de Belgique* 159, 389-395.

62. Behrends J., Clément S., Pajak B., Pohl V., Maenhaut C., Dumont J.E., Schurmans S. (2005) Normal thyroid structure and function in raphilin2-deficient mice. *Mol. Cell. Biol.*, 25, (in press).

63. Detours V., Wattel S., Venet D., Hutsebaut N., Bogdanova T., Tronko M., Dumont J.E., Franc B., Thomas G., Maenhaut C. (2005) Absence of a specific radiation signature in post-Chernobyl thyroid cancers. *Br. J. Cancer*, (in press).

64. Wattel S., Mircescu H., Venet, D., Burniat A., Franc, B., Andry, G., Van Sande J., Rocmans P., Detours V., Dumont J.E., Maenhaut C. Gene expression in thyroid autonomous adenoma provides insight on their pathology. (Submitted).

Articles en préparation:

65. Vandeput F., Zabeau M., Dumont J.E., Maenhaut C. Identification of differentially expressed genes in thyrotropin stimulated dog thyroid cells by the cDNA-AFLP technique.

66. Delys L., Detours V., Frank S., Weiss D., Bogdanova T., Tronko M., Dumont J.E., Franc B., Thomas G., Maenhaut C. Gene expression profiling in sporadic and post-Chernobyl papillary thyroid carcinomas.

67. Van Staveren W., Duprez L., Libert F., Weiss D., Detours V., Dumont J.E., Maenhaut C. Gene expression profiling in thyroid cancer cell lines: are they a good model to study the corresponding in vivo tumors?

68. Van Staveren W., Detours V., Libert F., Dumont J.E., Maenhaut C. Comparison of gene expression profiles of thyrotropin-treated human primary thyroid cell culture with hyperfunctioning autonomous adenomas.