

Dr. Ronney Alphonso De Abreu

research Coordinator

INSTITUTE

University Medical Center, St. Radboud
Department of Pediatrics
Nijmegen, Netherlands

LABORATORY

Laboratory of Pediatrics & Neurology

MAIN FIELDS OF RESEARCH

- Pediatric Oncology
- Inborn Errors of Metabolism
- Tissue and Cell Culture

WORKING EXPERIENCE

Pre-academic: 1956 - 1972

- National Institute for Food Control, Paramaribo, Surinam 1956-1957
- National Pharmaceutical Institute , Paramaribo, Surinam 1956-1957
- Pharmaceutical Laboratory, Tilburg, Netherlands 1957-1959
- National Pharmaceutical Institute, Surinam 1959 - 1964
- Institute for Food Control, Nijmegen, Netherlands 1964 - 1967
- Catholic University of Nijmegen, Netherlands 1970-1973

Academic: 1972 - 2002

- Agricultural University of Wageningen 1973-1978
- University Medical Centre, St Radboud, Nijmegen, The Netherlands since 1978

INTERNATIONAL SCIENTIFIC ACTIVITIES

Invited working visits and Lectures:

1981 **Location** Universtät Wien

Title seminar: Studies on Purine and Pyrimidine Metabolism in Leukemic Cells.

Invited by: Austrian Clinical Society (Dr. M.M. Müller)

1984 **Location:** Universtät Wien

Title seminar: Pharmacokinetic Studies on 6-Mercaptopurine after Oral and Intravenous Administration.

Invited by: 2^e Medizinische Klinik, Universität Wien (Prof. Kaiser)

1986 **Location:** Universität Wien

Title seminar: Potential Synergism of Methotrexate and 6-Mercaptopurine in Leukemia.

Invited by: 2^e Medizinische Klinik, Universität Wien (Dr. M. Müller)

1987 **Location:** 1st European Symposium for the Study of Purine and Pyrimidine Metabolism in Man., Chateau-d'Oex, Switzerland

Title Invited Lecture: Purine Metabolism in Leukemia.

Organiser: Prof. Dr. F. Roch-Ramel. (Start Of the European Purine Society)

Co-organisers: Dr. A. Simmonds (London), Prof N. Zöllner (München) and Dr. R.A. De Abreu (Nijmegen)

1988 **Location:** Institute für Physiologische Chemie, Universität Mainz, Germany

Title Invited Lecture: Effects of Purine Antimetabolites on Human Malignant Lymphoblasts *In Vitro*.

Invited by: Prof. Dr. Breter

1988 **Location:** Medizinische Poliklinik der Universität München

Title Invited Lecture: Synergism of 6-Mercaptopurine and Methotrexate and its Consequences for Maintenance Therapy in Acute Lymphoblastic Leukemia.

Invited by: Prof. Dr. N. Zöllner

1989 **Location:** 2nd European Symposium for the Study of Purine and Pyrimidine Metabolism in Man., Gut-Ising, Duitsland

Title Invited Lecture: Screening of Purine and Pyrimidine Disorders by Way of CSF Examination.

Organiser: Prof. Dr. N. Zöllner

Co-organisers: Dr. A. Simmonds, Dr. R.A. De Abreu

1989 **Location:** Kansas University Medical School, Kansas City, USA

Title Seminar: "Synergism of Methotrexate and 6-Mercaptopurine in Human Malignant Lymphoblasts."

Invited by: Prof. Dr. T. Vats and Prof. Dr. R.C. Trueworthy

Sponsors Seminar: Department of Pediatrics Hematology Oncology,
Department of Pharmacy Practice
Department of Pharmaceutical Chemistry.

- 1990 **Location:** 1st Advent Symposium München
Title Invited Lecture: Acute Renal Insufficiency: Which Mechanisms are involved?
Organisers: Dr. U. Gresser and Prof. Dr. N. Zöllner
- 1991 **Location:** 2nd Advent Symposium München
Title Invited Lecture: Dihydropyrimidine Dehydrogenase Deficiency.
Organisers: Dr. U. Gresser and Prof. Dr. N. Zöllner
- 1992 **Location:** University of Rome
Title Invited Lecture lezing: Inborn Errors of Pyrimidine Metabolism
Invited by: Prof. Dr. A. Giacomello and Prof. Dr. C. Salerno
- 1992 **Location:** Symposium on Inborn Errors of Metabolism in Italy Guardiagelle, Abruzzo, Italie
Title Invited Lecture: Pyrimidine Disorders
Organiser: Prof. Dr. A. Giacomello
- 1993 **Location:** 1st Asian-European Workshop on Inborn Errors of Metabolism, Seoul, South Korea
Title Invited Lecture: APRT Deficiency in the Netherlands.
Organisers: Prof. Dr. Moon, Dr. Y. Shin
- 1994 **Location:** VII International Symposium Purine and Pyrimidine Metabolism in Man, Bloomington, Indiana, USA
Title Invited lecture: Nucleotide Metabolism. The Role of Thiopurines in Leukemia.
Organisers: Prof. Dr. Milton Taylor and Prof. Dr. George Weber
- 1994 **Location:** Thiopurine Meeting: Thiopurines. Biology and Pharmacology., University of Tromsø, Norway
Title invited Lecture: Effects of Methylated Thiopurines in Leukemic Cells.
Organiser: Prof. Dr. Jarle Aarbakke
- 1994 **Location:** 35th International Symposium on Regulation of Enzyme Activity and Synthesis in Normal and Neoplastic Tissue. Indianapolis, Indiana, USA
Title Invited Lecture: Thiopurine-Induced Disturbance of DNA Methylation in Human Malignancies.
Organiser: Prof. Dr. George Weber

- 1995 **Location:** Symposium of the European Society for the Study of Purine and Pyrimidine
Metabolism in Man, Vasto, Italië
Title Invited Lecture: The Use of Purine Antimetabolites and Purine Inhibitors in Leukemia
Organiser: Prof. Dr. A. Giacomello, Dr. A. Simmonds, Dr. R.A. De Abreu
- 1996 **Location:** 2nd Thiopurine Meeting: Thiopurines. Clinical application, Pharmacology and
Molecular Metabolism. Hamburg, Germany,
Title invited lecture: Intravenous Administration of 6-Mercaptopurine in Childhood Leukemia according to the SNWLK ALL-8 protocol. A Biochemical and Pharmacological Study.
Organisers: Prof. Dr. Janka en Prof. Dr. Jarle Aarbakke
- 1997 **Location:** Joint IXth International and 6th European Symposium for the Study of Purine and Pyrimidine Metabolism in Man, Gmunden, Austria
Title invited lecture: Thiopurine Treatment in Childhood Leukemia: Metabolic Aspects and Sensitivity.
Organiser: Prof. Dr. M. M. Müller
- 1998 **Location:** Kansas University Medical School, Kansas City, KS, U.S.A.
Title seminar: Synergism of Tiazofurin and 6-Thioguanine on the Apoptosis of Human Malignant Lymphoblasts.
Invited by: Prof. Dr. Robert C. Trueworthy
- Location:** University of Oklahoma, Oklahoma City, Ok, U.S.A.
Title lecture: Synergism of Methotrexate and 6-Mercaptopurine in Human Malignant Lymphoblasts.
Invited by: Prof. Dr. Linda Thompson
- Location:** St. Jude Childrens University Hospital, Memphis, TS, U.S.A.
Title seminar: 6-Mercaptopurine: I.V. Administration Against Oral Administration in Childhood Leukemia.
Invited by: Prof. Dr. William Evans
- Location:** Kaiser Josef Institut, Wenen
Title seminar: The Role of Phosphoribosyl Pyrophosphate in Purine Metabolism
Invited by: Prof. Dr. Mathias M. Müller and Dr. Anrea Griesmacher
- Location:** Anticancer Research Congress, Kalkidiki, Greece

Title Invited Lecture: Combination Therapy in Childhood Leukemia. In Vitro Studies of Thiopurines and Inhibitors of Purine Metabolisms on Apoptosis.
Organiser: Dr. John Delinassios

1999 **Location:** Cemeco Symposium: Inborn Errors of Metabolism, Cordoba, Argentinië.
Chairman Roundtable discussion: How to screen for purine and pyrimidine defects.
Organiser: Prof. Dodelson De Kremer

2000 **Location:** Guy's Hospital, Kings College, London
Title seminar: Role of Thiopurines in Childhood Leukemia and Rheumatoid Arthritis. Biochemical and Molecular mechanisms in Relation to Therapy.
Invited by: Dr. Anne Simmonds and Dr. John Duley

Location: 10th International Symposium on Purines and Pyrimidines in Man: Basic and Clinical Aspects, 14-19 mei 2000, Tel Aviv, Israël.
Title Invited Lecture: 6-Mercaptopurine: Efficacy and Bone Marrow Toxicity in Childhood Acute Lymphoblastic Leukemia. Association with Low (Thio)purine enzyme activity.
Organisers: Prof. O. Sperling en Prof. E. Shani

2001 **Location:** Cemeco Symposium: Inborn Errors of Metabolism, Cordoba, Argentina.
Title seminar: Can the SAM-SAH cycle be used as a model for new cytostatic agents?
Organiser: Prof. Dodelson De Kremer

2002 **Location:** Cemeco, Cordoba, Argentina.
Title seminar: Pharmacogenetic aspects of anti-purine and anti-pyrimidine drugs.
Organiser: Prof. Dodelson De Kremer

PUBLICATIONS

1. Berns AW, De Abreu RA, Kraaikamp M van, Benedetti EL, Bloemendal H. Synthesis of lens protein in vitro. V. Isolation of messenger-like RNA from lens by high resolution zonal centrifugation. *FEBS letters* 1971; 18: 159-163.
2. Lommen EJP, De Abreu RA, Trijbels JMF and Schretlen EDAM. The IMP dehydrogenase catalysed reaction in erythrocytes of normal individuals and patients with hypoxanthine guanine phosphoribosyltransferase deficiency. *Acta Paediatr* 1974; 64: 140-142.
3. Bresters TW, De Abreu RA, Kok A de, Visser J, Veeger C. The pyruvate-dehydrogenase complex from *Azotobacter Vinelandii*. 1. Purification and properties. *Eur J Biochem* 1975; 59: 335-345.
4. Grande HJ, Bresters TW, De Abreu RA, Kok A de, Visser J, Veeger C. The pyruvate-dehydrogenase complex from *Azotobacter Vinelandii*. 3. Stoichiometry and function of the individual components. *Eur J Biochem* 1975; 59: 355-363.
5. Veeger C, Visser AJWG, Krul J, Grande HJ, De Abreu RA, Kok A de. Fluorescence studies on lipoamide dehydrogenase, pyruvate dehydrogenase complexes and transhydrogenase. In: *Flavins and Flavoproteins*. Proc 4th Int Conf. Singer TP ed, Elsevier Publ Co, Amsterdam, 1976; 500-505.
6. De Abreu RA, Kok A de, Graaf-Hess AC de, Veeger C. Transformation of the 4-component pyruvate dehydrogenase complex from *Azotobacter Vinelandii* into a 3-component complex. *FEBS letters* 1977; 82: 89-92.
7. De Abreu RA, Kok A de, Graaf-Hess AC de, Veeger C. Determination of the chain stoichiometries from the number of reactive sulfhydryl groups in the pyruvate dehydrogenase complexes of *Azotobacter Vinelandii* and *Escherichia Coli*. *Eur J Biochem* 1977; 81: 357-364.
8. De Abreu RA, Vries J de, Kok A de, Veeger C. Crosslinking studies with the pyruvate dehydrogenase complexes from *Azotobacter vinelandii* and *Escherichia coli*. *Eur J Biochem* 1979; 79 379-387.
9. Veeger C, Visser AJWG, Eweg J-K, Grande HJ, De Abreu RA, Graaf-Hess AC de, Müller F. Fluorescence of oxidized and reduced flavins and flavoproteins. In: *Flavins and Flavoproteins*. Proc Int 6th Conf. Yagi K and Yamano T eds, Jap Scient Soc Press, 1980.

10. De Abreu RA, Baal JM van , Bakkeren JAJM, Bruyn CHMM de, Schretlen EDAM. A high-performance liquid chromatographic assay for identification and quantification of nucleotides in lymphocytes and malignant lymphoblasts. *J Chromatogr* 1982; 227: 45-52.
11. De Abreu RA, Baal JM van, Schouten TJ, Schretlen EDAM, Bruyn CHMM de. High-performance liquid chromatographic determination of plasma 6-mercaptopurine in clinically relevant concentrations. *J Chromatogr Biomed Appl* 1982; 227: 526-533.
12. De Abreu RA, Baal JM van, Bruyn CHMM de, Bakkeren JAJM, Schretlen EDAM. High-performance liquid chromatographic determination of purine and pyrimidine bases, ribonucleosides, deoxyribonucleosides and cyclic ribonucleotides in biological fluids. *J Chromatogr* 1982; 229: 67-75.
13. Smits MG, Gabreëls FJM, Froeling PGA, De Abreu RA, Thyssen HOM. Calcium-phosphate metabolism in autosomal recessive idiopathic strio-pallido-dentate calcinosis and Cockayne's syndrome. *Clin Neurol Neurosurg* 1983; 85: 145-153.
14. Smits MG, De Abreu RA, Froeling PGA, Gabreëls FJM. Presence of cerebral parathyroid hormone-responsive adenylcyclase in humans. *Ann Neurol* 1983; 14: 348-349.
15. Peters GJ, De Abreu RA, Oosterhof A, Veerkamp JH. Concentration of nucleotides and deoxynucleotides in peripheral and phytohemagglutinin-stimulated mammalian lymphocytes. *Biochim Biophys Acta* 1983; 759: 7-15.
16. De Abreu RA, Peters GJ, Veerkamp JH. Concentration of Nucleotides in peripheral blood lymphocytes of various mammalian species. In: *Purine and pyrimidine metabolism in man IVB: Biochemical, Immunological, and Cancer Research*, Bruyn de CHMM, Simmonds HA and Müller MM eds, Plenum Press, New York/London, 1984; 125-128.
17. Schouten TJ, De Abreu RA, Bruyn CHMM de, Kleyn E van der, Oosterbaan MJM, Schretlen EDAM, Vaan GAM de. 6-Mercaptopurine: Pharmacokinetics in animals and preliminary results in children. In: *Purine and pyrimidine metabolism in man IVB: Biochemical, Immunological, and Cancer Research*, Bruyn CHMM de, Simmonds HA and Müller MM eds, Plenum Press, New York/London, 1984: 367-370.
18. Bakkeren JAJM, De Abreu RA, Sengers RCA, Gabreëls FJM, Maas JM, Renier WO. Elevated urine, blood and cerebrospinal fluid levels of uracil and thymine in a child with dihydrothymine dehydrogenase deficiency. *Clin Chim Acta* 1984; 140: 247-256.
19. Bökkerink JPM, Schouten TJ, De Abreu Ra, Lippens RJJ, Vaan GAM de, Bruyn CHMM de, Laarhoven JPRM van. 6-Mercaptopurine en methotrexaat, zicht op een rationeel gebruik na 35 jaar? *Tijdschr Kindergeneesk* 1984; 52: 118-123.

20. Baal JM van, Leeuwen MB van, Schouten TJ, De Abreu RA. Sensitive high-performance liquid chromatographic determination of 6-mercaptopurine, 6-thioguanine, 6-mercaptopurineriboside and 6-thioguanosine in biological fluids. *J Chromatogr* 1984; 336: 422-428.
21. De Abreu RA, Peters GJ, Bakkeren JAJM, Veerkamp JH. Discrepancies in ribonucleotide concentrations in human lymphocytes isolated from heparinized and defibrinized blood. *Clin Chim Acta* 1985; 145: 349-355.
22. Janssen JThP, Baal JM van, Vierwinden G, De Abreu RA. Determination of nucleotide content in splenic lymphocytes from patients with Hodgkin's disease and controls. In Thesis: J.Th.P. Janssen, Characteristics of Lymphocytes in Hodgkin's Disease. 1985; chapter 9: 105-111.
23. Schouten TJ, De Abreu RA, Schretlen EDAM, Leeuwen MB, Baal JM van, Vaan GAM de. 6-Thioguanine: High-dose 2-H infusions in Goats. *J Cancer Res Clin Oncol* 1985; 110: 115-118.
24. Kraan PM van der, De Abreu RA, Laarhoven JPRM van, Bruyn CHMM de. Mogelijkheden van enzymgerichte chemotherapie bij leukemie. *Kanker* 1985; 3: 30-31.
25. Schouten TJ, De Abreu RA, Schretlen EDAM, Bruyn CHMM de, Kleyn E van der, Oosterbaan MJM, Vaan GAM de. 6-Mercaptopurine: Oral administration and i.v. bolus injections in dogs. *Eur J Paediatr Haematol Oncol* 1985; 2: 93-98.
26. Schouten TJ, De Abreu RA, Schretlen EDAM, Baal JM van, Leeuwen MB van, Vaan GAM de. 6-Mercaptopurine: High dose 24-hours infusion in goats. *J Cancer Res Clin Oncol* 1986; 112: 61-66.
27. Schouten TJ, De Abreu RA, Schretlen EDAM, Vaan GAM de, Kleyn E van der. 6-Mercaptopurine: Total body autoradiograms and plasma concentration-time curves of 6MP and metabolites from Marmoset monkeys. *Pediatr Hematol Oncol* 1986; 3: 159-165.
28. De Abreu RA, Bakkeren JAJM, Braakhekke J, Gabreëls FJM, Maas JM, Sengers RCA. Dihydrothymine dehydrogenase deficiency in a family, leading to elevated levels of uracil of uracil and thymine. In: Purine and pyrimidine metabolism in man VA: Clinical Aspects including Molecular Genetics, Nyhan WL and Seegmiller JE eds, Plenum Press, New York/London, 1986; 77-80.
29. De Abreu RA, Bökkerink JPM, Bakker MAH, Hulscher TW, Baal JM van, Bruyn CHMM de, Schretlen EDAM. Influence of methotrexate on purine and pyrimidine pools and on cell phase distribution of cultured human lymphoblasts. In: Purine and pyrimidine metabolism

in man VB: Basic Science Aspects, Nyhan WL and Seegmiller JE eds, Plenum Press, New York/London, 1986; 105-111.

30. De Abreu RA, Bökkerink JPM, Bakker MAH, Hulscher TW, Vaan GAM de, Bruyn CHMM de, Schretlen EDAM. Synergy of methotrexate and 6-mercaptopurine on cell-growth and clonogenicity of cultured human T-lymphoblasts. In: Purine and pyrimidine metabolism in man VB: Basic Science Aspects, Nyhan WL and Seegmiller JE eds, Plenum Press, New York/London, 1986; 129-134.
31. Bökkerink JPM, De Abreu RA, Laarhoven JPRM van, Bakker MAH, Hulscher TW, Schretlen EDAM, Bruyn CHMM de. Increased availability of phosphoribosylpyrophosphate as the basis for enhanced 6-mercaptopurine incorporation by methotrexate, in cultured human lymphoblasts. In: Purine and pyrimidine metabolism in man VB: Basic Science Aspects, Nyhan WL and Seegmiller JE eds, Plenum Press, New York/London, 1986; 135-139.
32. Kraan PM van der, Zandvoort PM van, De Abreu RA, Bakkeren JAJM, Laarhoven JPRM van, Bruyn CHMM de. Inhibition of ^3H thymidine incorporation by guanosine and deoxyguanosine in human peripheral lymphocytes and malignant lymphoid cell lines. In: Purine and pyrimidine metabolism in man VA: Clinical Aspects including Molecular Genetics, Nyhan WL, Thompson LF and Watts RWE eds, Plenum Press, New York/London, 1986; 547-551.
33. Kraan PM van der, Zandvoort PM van, De Abreu RA, Bakkeren JAJM, Laarhoven JPRM van, Bruyn CHMM de. Biphasic effects of adenosine on cell growth and cell cycle of human lymphoid cell lines. In: Purine and pyrimidine metabolism in Man VA: Clinical Aspects including Molecular Genetics, Nyhan WL, Thompson LF and Watts RWE eds, Plenum Press, New York/London, 1986; 553-559.
34. Kraan PM van der, Zandvoort PM van, De Abreu RA, Bakkeren JAJM, Laarhoven JPRM van, Bruyn CHMM de. Inhibition of ^3H thymidine incorporation by adenosine and deoxyadenosine in human peripheral lymphocytes and malignant lymphoid cell lines. In: Purine and pyrimidine metabolism in man VB: Basic Science Aspects, Nyhan WL and Seegmiller JE eds, Plenum Press, New York/London, 1986; 213-219.
35. Bökkerink JPM, Bakker MAH, Hulscher TW, De Abreu RA, Schretlen EDAM, Laarhoven JPRM van, Bruyn CHMM de. Sequence-, time- and dose-dependent synergism of methotrexate and 6-mercaptopurine in human malignant lymphoblasts. *Biochem Pharmacol* 1986; 35: 3549-3555.
36. Bökkerink JPM, De Abreu RA, Bakker MAH, Hulscher TW, Baal JM van, Vaan GAM de. Dose related effects of methotrexate on purine and pyrimidine nucleotides and on cell kinetic parameters in Molt-4 malignant T-lymphoblasts. *Biochem Pharmacol* 1986; 35: 3557-3564.

37. Peters WHM, Jansen PLM, Cuypers HTM, De Abreu RA, Nauta H. Deconjugation of glucuronides catalysed by UDP-glucuronyl transferase. *Biochim Biophys Acta* 1986; 873: 252-259.
38. Kraan PM van der, Zandvoort PM van, De Abreu RA, Baal JM van, Bakkeren JAJM. Inhibition of lymphoid cell growth by adenine ribonucleotide accumulation. The role of PRPP-depletion induced pyrimidine starvation. *Biochim Biophys Acta* 1987; 927: 213-221.
39. Bökkerink JPM, De Abreu RA, Bakker MAH, Hulscher TW. Potentiation of 6-mercaptopurine after time and dose dependent pretreatment with methotrexate in malignant human T- and B-lymphoblasts. In: *The Role of pharmacology in pediatric oncology*. Poplack PG, Massimo L and Cornaglia-Ferraris P eds, Dordrecht: Martinus Nijhoff Publishers, 1987: 185-191.
40. De Abreu RA, Bökkerink JPM, Bakker MAH, Hulscher TW, Baal JM van. The effect of methotrexate on purine and pyrimidine deoxyribo-nucleoside triphosphate pools and on cell viability and cell phase distribution in malignant human T- and B- lymphoblasts. In: *The Role of pharmacology in pediatric oncology*. Poplack PG, Massimo L, Cornaglia-Ferraris P eds, Dordrecht: Martinus Nijhoff Publishers, 1987: 191-195.
41. De Abreu RA, Bökkerink JPM, Vaan GAM de. Synergisme van methotrexaat an 6-mercaptopurine: In vitro studies aan humane maligne lymphoblastaire cellijnen. *Tijdschr NKC* 1987; 12: 54-57.
42. Braakhekke JP, Renier WO, Gabreëls FJM, De Abreu RA, Bakkeren JPM, Sengers RCA. Dihydrothymine dehydrogenase deficiency: a cause of cerebral dysfunction ? In: *Verhandlungen der Deutschen Gesellschaft für Neurologie 4*. Poeck K, Hacke W and Schneider R eds, Berlin: Springer Verlag, 1987: 306-307.
43. Braakhekke JP, Renier WO, Gabreëls FJM, De Abreu RA, Bakkeren JAJM, Sengers RCA. Dihydrothymine dehydrogenase deficiency. Neurological aspects. *J Neurol Sci* 1987; 78: 71-77.
44. Salemans J, Hoitsma AJ, De Abreu RA, Vos D de, Koene RAP. Pharmacokinetics of azathioprine and 6-mercaptopurine after oral administration of azathioprine. *Clin Transplant* 1987; 1: 217-221.
45. Smits P, Boekema P, De Abreu R, Thien T, Laar A van 't. Evidence for antagonism between caffeine and adenosine in the cardiovascular system in man. *J Cardiovasc Pharmacol* 1987; 10: 136-143.

46. Widdershoven J, Munster P van, De Abreu R, Bosman H, Lith Th van, Putten-van Meyel M van der, Motohara K, Matsuda I. Four methods compared for measuring descarboxy-prothrombin (PIVKA-II). *Clin Chem* 1987; 33: 2074-2078.
47. Bökkerink JPM, Bakker MAH, Hulscher TW, De Abreu RA, Schretlen EDAM. Purine de novo synthesis as the basis of synergism of methotrexate and 6-mercaptopurine in human malignant lymphoblasts of different lineages. *Biochem Pharmacol* 1988; 37: 2321-2327.
48. Bökkerink JPM, De Abreu RA, Bakker MAH, Hulscher TW, Baal JM van, Schretlen EDAM. Effects of methotrexate on purine and pyrimidine metabolism and cell kinetic parameters in human malignant lymphoblasts of different lineages. *Biochem Pharmacol* 1988; 37: 2329-2338.
49. Bökkerink JPM, De Abreu RA, Lippens RJJ, Schouten TJ, Vaan GAM de. Biochemische en klinisch-farmacologische aspecten van antimetabolieten bij de behandeling van leukemie. *Tijdschr Kindergeneesk* 1988; 56: 56-60.
50. Kraan PM van der, Zandvoort PM van, De Abreu RA, Bakkeren JAJM. Effects of 8-aminoguanosine on the toxicity of guanosine and deoxyguanosine for malignant and normal lymphoid cells. *J Leuk Biol* 1988; 44: 46-50.
51. Gerrits GPJM, Haagen AAM, De Abreu RA, Monnens LAH, Gabreëls FJM, Trijbels FJM, Theeuwes ALM and Baal van JM. Reference values of nucleosides and nucleobases in cerebrospinal fluid of children. *Clin Chem* 1988; 34: 1439-1442
52. Gerrits GP, Trijbels FJ, Monnens LA, Gabreëls FJ, De Abreu RA, Teeuwes AG, Raaij-Selten van B. Reference values for amino acids in cerebrospinal fluid of children determined using ion-exchange chromatography with fluorimetric detection. *Clin Chem Acta* 1989; 182: 75-94.
53. Bökkerink JPM, Damen FJM, Hulscher TW, Bakker MAH, De Abreu RA. Biochemical evidence for synergistic combination treatment with methotrexate and 6-mercaptopurine in acute lymphoblastic leukemia. In: *Haematology and Blood Transfusion vol 33, Acute Leukemias II, Prognostic Factors and Treatment Strategies*. Büchner T, Schellong G, Hiddemann W and Ritter J eds, Springer Verlag, Heidelberg, 1990: 110-117.
54. Raemakers-Franken PC, De Abreu RA, Willems JG, Drift C van der, Vogels GD. In vitro inhibition of cell growth of Molt-4 malignant human T-lymphoblasts by coenzyme F₄₂₀. *Biochem Pharmacol* 1991; 41: 561-566.

55. De Abreu RA. In: Urate Deposition in Man and its Clinical Consequences. Acute renal insufficiency: Which mechanisms are involved? Gresser U and Zöllner N, eds. Springer-Verlag, Berlin, 1991: 78-79.
56. Gerrits GPJM, Monnens LAH, De Abreu RA, Schröder CH, Trijbels JMF, Gabreëls FJM. Disturbances of cerebral purine and pyrimidine metabolism in young children with chronic renal failure. *Nephron* 1991; 58: 310-314.
57. Cornelissen M, Smeets D, Merckx G, De Abreu R, Kolée L, Monnens L. Analysis of chromosome aberrations and sister chromatid exchanges in peripheral blood lymphocytes of newborns after vitamin K prophylaxis at birth. *Pediatr Res* 1991; 30: 550-553.
58. Trueworthy RC, De Abreu RA, Lambooy LHJ, Bökkerink JPM, Stet EH. Action and sequence dependent interaction of acivicin and 6-thioguanine in human derived malignant T-ALL and CALLA⁺ cell lines. In: Purine and pyrimidine metabolism in man VIIA: Chemotherapy, ATP depletion, and Gout. Harkness RA, Elion GB and Zöllner N eds, Plenum Press, New York/London, 1991: 25-28.
59. Stet EH, De Abreu RA, Janssen YPG, Bökkerink JPM, Trijbels JMF. 6-Mercaptopurine metabolism in two leukemic cell lines. In: Purine and pyrimidine metabolism in man VIIA: Chemotherapy, ATP depletion, and Gout. Harkness RA, Elion GB and Zöllner N eds, Plenum Press, New York/London, 1991: 83-86.
60. De Abreu RA, Strien F van, Lambooy LHJ, Bökkerink JPM. Synergistic interaction of methotrexate and 6-mercaptopurine in human derived malignant T-ALL and CALLA⁺ cell lines. In: Purine and pyrimidine metabolism in man VIIA: Chemotherapy, ATP depletion, and Gout. Harkness RA, Elion GB and Zöllner N eds, Plenum Press, New York/London; 1991: 87-91.
61. Blom HJ, Engelen DPE, Boers GHJ, Stadhouders AM, Sengers RCA, De Abreu RA, Te Poele-Pothoff, Trijbels JMF. Lipid peroxidation in homocysteinaemia. *J. Inher. Metab. Dis.* 1992; 15: 419-422.
62. Bökkerink JPM, De Abreu RA, Stet EH, Damen FJM. Cell-kinetics and biochemical pharmacology of methotrexate and 6-mercaptopurine in human malignant T-lymphoblasts. *Klin. Pädiatr* 1992; 204: 293-298.
63. Kuypers KC, Dongen van JJM, Burg van der P, Roos MTh, Vonk J, De Abreu R, Korte de D, Noesel van CJM, Weening RS, Lier RAW. A combined immunodeficiency with oligoclonal CD8⁺, V β 3-Expressing, cytotoxic T lymphocytes in the peripheral blood. *J. Immunol.* 1992; 149: 3403-3410.

64. Stet EH, De Abreu RA, Janssen YPG, Bökkerink JPM, Trijbels JMF. A biochemical basis for synergism of 6-mercaptopurine and mycophenolic acid in MOLT F4, a human lymphoblastic T-cell line. *Biochim. Biophys. Acta* 1993; 1180: 277-282
65. Bökkerink JPM, De Abreu RA, Stet EH, Damen FJM, Hulscher TW, Bakker MAH, van Baal JM. 6-Mercaptopurine, cytotoxicity and biochemical pharmacology in human malignant T-lymphoblasts. *Biochem. Pharmacol.* 1993; 45: 1455-1463
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