CURRICULUM VITAE

JOHANNES J.P. KASTELEIN

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University of Amsterdam
The Netherlands

Amsterdam, July 15

Biography of John J.P. Kastelein

John J.P. Kastelein (1954) is Professor of Medicine at the Department of Vascular Medicine at the Academic Medical Center (AMC) of the University of Amsterdam, where he holds the Strategic Chair of Genetics of Cardiovascular Disease. Professor Kastelein has published over 740 research papers in peer reviewed journals, including Nature Genetics, Lancet, New England Journal of Medicine, JAMA and Circulation and has a Hirsch index of 82 in April 2014. Among the 3000 Highly Cited Researchers 2014, Dr. Kastelein is on the 10th position for the Netherlands and on the 2nd position for the Unviversity of Amsterdam.

He received his medical degree in Amsterdam in 1980 where he subsequently received specialty training in internal medicine. Then, between 1986 and 1988, he was trained in medical genetics, lipidology and molecular biology at the University of British Columbia, Vancouver under the guidance of Prof. Dr. M.R. Hayden. In 1997 and 1998 he served a visiting Professorship at the Center for Molecular Medicine and Therapeutics at the University of British Columbia, Vancouver, Canada. Upon his return to the Netherlands, he was awarded a doctorate (Cum Laude) and in 1989 he founded the Lipid Research Clinic at the Academic Medical Center, AMC) in Amsterdam, which is currently serving as a tertiary referral centre and has become part of the department of Vascular Medicine.

The most important concept in Dr. Kastelein's research career, developed initially at the University of British Columbia, by his mentor Dr. Hayden, and subsequently transformed into practice at the AMC in Amsterdam, the Netherlands, is the "extreme genetics" approach. This approach teaches that the study of rare human disorders that are associated with premature coronary disease have broader relevance for the understanding of the etiology of heart disease in general and will yield therapeutic targets that are valid for all patients.

This approach has been very successful, in so far that Familial Hypercholesterolemia is now internationally recognized as the paradigm for the relationship between LDL-C and heart disease, a relationship substantiated by at least 50 peer reviewed manuscripts and 10 postdoctoral theses in Dr. Kastelein's curriculum vitae.

The same “extreme genetics” concept was applied to disorders of HDL-C and elevated triglycerides and lead to the discovery of the cholesterol efflux protein ABCA1 and later to gene therapy for lipoprotein lipase deficiency. These two innovative contributions to science have lead to important breakthroughs in the field of drug development for the prevention of cardiovascular disease (development of ABCA1 agonists) and in the area of gene therapy for hereditary disorders such as haemophilia, LCAT deficiency and others.

In 1995, Dr. Kastelein initiated a foundation for the active identification of patients with classical familial hypercholesterolaemia (FH) in the Netherlands (StoeH), for which he currently holds a position in the board of directors. This program has now been fully institutionalized and is operational under supervision of the RijksInstituut voor Volksgezondheid en Milieu (RIVM) and financially supported by the Ministry of Health with a total grant of approximately 30 million Euros. Since its inception, the StoeH has found over 18.000 individuals for whom a molecular diagnosis of FH could be made. The subsequent improvement of the treatment of these FH patients has saved many lives, as published in Lancet in 2001 and in the British Medical Journal in 2008.

Dr. Kastelein was president of the Dutch Atherosclerosis Society (DAS) and chairs the National Scientific Committee on Familial Hypercholesterolemia (EHC). He also is a member of the Royal Dutch Society for Medicine & Physics, the Council for Basic Science of the American Heart Association and the European Atherosclerosis Society and a Fellow of the European Society of Cardiology. He also is a boardmember of the International Task Force for CHD Prevention and was recently appointed to the Executive Board of the International Atherosclerosis Society (IAS) and is a recognized world leader in the significance of lipoprotein metabolism for the development of atherosclerotic vascular disease.

Dr. Kastelein is a principal investigator of the Bloodomics and CardioGenics consortia, two large European Union supported endavours under the Framework Programme 7, that aim to elucidate the molecular basis of atherosclerosis and premature coronary disease. Besides the scientific programmes aimed at the etiology of atherogenesis, Dr. Kastelein also serves on a number of executive and steering committees of large cardiovascular intervention studies,

including the IDEAL, TNT, CAPTIVATE, ENHANCE, ILLUMINATE, JUPITER, RADIANCE and numerous others of which TNT (2005), RADIANCE 1 (2007), ENHANCE (2008) and JUPITER (2008) are published in the New England Journal of Medicine, IDEAL (2006) in JAMA and RADIANCE 2 (2007) in Lancet.

Dr. Kastelein has directed 50 postdoctoral theses and currently, he works in a team of 7 internists, 6 postdoctoral fellows, 26 MD PhD students, and a large number of laboratory technicians and clinical trial / study coordinators

Dr. Kastelein is invited regularly to important meetings on vascular disease for invited or keynote lectures, at least 5 meetings per year (American Heart Association, American College of Cardiology, European Society of Cardiology, International Atherosclerosis Society, European Atherosclerosis Society, European Lipoprotein Conference, etc.). Overall, his invited lectures can be numbered in hundreds.

Dr. Kastelein was in 1997 a co-founder of Xenon Genetics Inc., a drug discovery company that has now changed its name into Xenon Pharmaceuticals Inc. and is based in Vancouver, Canada. One of Dr. Kastelein's concepts of using "extreme genetics" to clone human validated disease genes that can than be turned into useful therapeutic targets, was an important basis for the rise of Xenon and also lead to the cloning of the ATP-binding cassette A1 (ABCA1) gene, as published in Nature Genetics 1999.

Professor Kastelein was also one of the founders of Amsterdam Molecular Therapeutics Inc. (AMT), a gene therapy company based on the concept of gene replacement in hereditary lipoprotein disorders. AMT has enjoyed a successful Initial Public Offering (IPO) at EuroNext in Amsterdam in the summer of 2007. The results of the first successful human gene therapy trial were widely publicized in the media and are published in ATVB in 2008. Furthermore, this gene therapy (Glybera) has now been approved by the European commission and constitutes the first approved gene therapy worldwide. Amsterdam Molecular Therapeutics has now changed its name into UniQure, and Prof. Kastelein is the major consultant for Glybera. The review article on the history of Glybera as published in Human Gene Therapy in 2013 belonged to the 10 most referenced manuscripts in this journal.

Recently, Prof. Kastelein also founded Dezima Inc, a pharmaceutical company that develops assets for the treatment of dyslipidemia and is currently developing a cholesteryl ester transfer protein (CETP) inhibitor DEZ-001 (formerly TA-8995), inlicensed from Mitsubishi Tanabe Pharma Corporation (MTPC).

Last, Dr. Kastelein received the first Lifetime Achievement Award of the Dutch Heart Foundation in 2010 as well as the ZonMW Parel price and will receive the Anitschkov Price from the European Atherosclerosis Society for the best atherosclerosis research in Europe in June 2014. In 2014, Dr. Kastelein was also awarded the No.1 position among the Top Worldwide Expers in Hyperlipidemia Research and Treatment by Expertscape. He also was a recipient of the Huibregtsenprice 2014 for the best academic researcher in the Netherlands. He is listed on the worldwide list of the 400 most influential biomedical researchers, Eur J. Clin Invest 2013; 43: 1339-1365. Last, Thomson Reuters has ranked Dr. Kastelein among the top 1% of researchers for the most cited documents in his field and top 100 of the most influential clinical researchers globally in 2014.

BIOGRAPHY

Name:	Kastelein, Johannes Jacob Pieter
Place of birth:	Haarlemmermeer, the Netherlands
Date of birth:	13 January, 1954
Nationality:	Dutch

EDUCATION

1980	University of Amsterdam Medical Degree
1980-1982	Resident Internal Medicine Military Hospital Dr. A. Matthijsen, Utrecht
1982	Chief Resident, Haemodialysis Unit, Military Hospital Dr. A. Matthijsen, Utrecht
1982-1985	Resident, Internal Medicine, Slotervaart Training Hospital, Amsterdam
1983-1985	Postgraduate Courses and Exams: Haemostasis and Thrombosis Clinical Pharmacology Epidemiology and Biostatistics Immunology Respiration and Circulation
1985	Boerhaave Courses: Renovascular Hypertension Left Ventricular Hypertrophy Electrocardiography
1985	Medical Council of Physicians and Surgeons, Canada Evaluation Examination for Canadian Medical Degree, Paris, France
1985-1986	Resident, Internal Medicine, Academic Medical Center, University of Amsterdam, Amsterdam
1986-1987	Research Fellow, Department of Laboratory Medicine, University of British Columbia, Vancouver

1987	Clinical Fellow, Department of Medical Genetics, University of British Columbia, Vancouver
1987-1988	Junior Scientist, Lipidologist, Lipid Research Clinic, University of British Columbia, Vancouver
1988	Registration as a Medical Specialist
1989	Young Scientist Award. International Society for Thrombosis and Haemostasis, XIIth Congress, Tokyo, Japan,
1991	Academic Thesis The Molecular Basis of Inherited Disorders of Lipoprotein Metabolism (with honours)
1997 - 1998	Visiting Professor, University of British Columbia, Dept. Of Medical Genetics, Vancouver, Canada.
1999	Co-Chairman Department of Vascular Medicine, Academic Medical Center, University of Amsterdam
2000	Established Investigator Netherlands Heart Foundation
2002	Professor of Medicine; Strategic Chair of Cardiovascular Genetics, University of Amsterdam
2003	Chairman Department of Vascular Medicine, Academic Medical Center, University of Amsterdam
2010	Life Time Achievement Award, Netherlands Heart Foundation

FUNCTIONS

- Professor of Medicine, Academic Medical Center, University of Amsterdam.
- Board, Dutch National Foundation for the Identification of Familial Hypercholesterolemia (StOEH).
- Board, International Task Force for Prevention of Coronary Heart Disease
- Executive Board, International Atherosclerosis Society
- Chairman, European Consensus Conference on HDL-C
- Chairman, National Scientific Committee on Familial Hypercholesterolemia.
- Co-founder, Xenon Pharmaceuticals Inc.
- Co-founder, UniQure (formerly Amsterdam Molecular Therapeutics Inc.)
- Co-founder, CardiAlpha Clinical Network Europe
- Founder and Director, Network of Imaging Centers Europe (NICE)
- Board, Dutch Atherosclerosis Society
- Scientific Affairs, Vascular Research Network
- Committee for Clinical Scientific Research of NWO (Dutch Organization for pure Scientific Research
- International Associate Editor, European Heart Journal
- Board of Directors and co-founder, Dezima Pharma Inc.

MEMBERSHIPS

- Dutch Atherosclerosis Society
- Dutch Lipoprotein Club
- Royal Society for Medicine and Physics, Amsterdam
- Council for Basic Science of the American Heart Association
- Scientific Advisory Board, Dutch Heart Foundation
- International Atherosclerosis Society
- European Atherosclerosis Society
- European Society of Cardiology
- Steering Committee TNT trial
- Steering Committee IDEAL trial
- Steering Committee METEOR trial
- Steering Committee DISCOVERY trial
- Steering Committee ENHANCE trial
- Steering Committee RADIANCE I and II trial
- Steering Committee ILLUMINATE trial
- Steering Committee JUPITER trial
- Steering Committee ACHIEVE trial
- Steering Committee AQUARIUS trial
- Steering Committee CHARON trial
- Steering Committee SAVOR trial
- Steering Committee MARINE trial
- Steering Committee AKKA trial
- Steering Committee CANTOS trial
- Steering Committee ACCELERATE trial
- Steering Committee Sanofi PCSK9 phase III programme (ODYSSEY programme)
- Steering Committee REALIZE study
- Steering Committee GLAGOV study
- Steering Committee EUCLID study

- Steering Committee phase II programme Eli Lilly PCSK9 monoclonal
- Steering Committee Novartis DGAT inhibitor programme
- Steering Committee PASCAL studies
- Steering Committee STRENGTH trial
- Steering Committee AEGIS-1 trial
- Steering Committee EVOLVE-II trial
- Steering Committee SPIRE trial programme
- Steering Committee ApoCIII, Lp(a), ApoB programme Isis
- Steering Committee DRIVE trial
- Steering Committee SPIRE trials

CONSULTANCIES

- Catabasis Pharmaceuticals Inc.
- Pronova Biopharma Norge A.S.
- Omthera Pharmaceuticals Inc.
- The Medicines Company
- Amgen Inc.
- Alnylam Pharmaceuticals
- CSL Behring LLC
- AstraZeneca Inc.
- Resverlogix Corp.
- Aegerion Pharmaceuticals Inc.
- Genzyme
- Amarin Pharma Inc.
- Vascular BioGenics Ltd.
- Isis Pharmaceuticals Inc.
- LSP Advisory Inc.
- Boehringer Ingelheim Pharma GmbH
- INC Research LLC

- Hoffman – La Roche Ltd.
- Forbion Capital Partners Inc.
- Pfizer Inc.
- Kinemed Inc.
- Bristol Myers Squibb company
- Eli Lilly and Company
- Sticares Cardiovascular Research Foundation
- Sanofi Aventis
- Merck Sharp and Dohme Corp.
- Xenon Pharmaceuticals Inc.
- AtheroNova Inc.
- UniQure Inc.
- Cerenis Therapeutics S.A.
- Medpace Inc.
- Regeneron Pharmaceuticals Inc.
- Synexus Ltd.
- Genentech
- Novartis Pharmaceuticals Corporation
- Esperion Pharmaceuticals
- Cymabay

PhD PROJECTS PRESENT

Drs. J. Besseling	FH
Drs. J.A.M. Braamskamp	FH in children
Drs. J.C. van Cappelleveen	Premature Atherosclerosis
Drs. D.M. Kusters	FH in children
Drs. B. Sjouke	FH

PhD PROJECTS PAST

Dr.Ir. J.C. Defesche	The molecular basis and treatment of familial hypercholesterolemia 29 January 1993
Dr. P.J. Lansberg	The molecular basis and treatment of familial hypercholesterolemia 29 January 1993
Dr. T. Bruin	Human Lipoprotein lipase; molecular genetics & structure function analysis. 9 March 1994 (with honours)
Dr. H.C. Knipscheer	The pharmacological treatment of primary hyperlipidemia. 21 December 1994
Dr. S.M. Bijvoet	The molecular biology of familial chylomicronemia. 21 December 1994
Dr. Y.Y. van der Hoek	Lipoprotein(a): structure/function analysis and metabolism. 7 September 1995
Dr. J.A. Kuivenhoven	Genetic factors contributing to HDL cholesterol levels. 3 December 1996
Dr. B.E. Groenemeijer	Genetic factors contributing to dyslipidemia and coronary artery disease. 3 June 1997
Dr. M.E. Wittekoek	Familial Hypercholesterolemia. Molecular genetics and clinical expression. 4 December 1998
Dr. S.N. Pimstone	Genetic and environmental determinants of dyslipidemia and coronary artery disease. 17 December 1998
Mr. Dr. M.J. Van Dam	Dyslipidemia, diagnosis and treatment. 26 October 2001
Dr. M.A.W. Umans-Eckenhausen	Genetic insights, clinical efficacy and practical implications of genetic screening for Familial Hypercholesterolemia. 28 November 2002

Dr. P.R.W. de Sauvage Nolting	Genetics and therapy of familial hypercholesterolemia. 11 December 2002
Dr. S de Jongh	Familial Hypercholesterolemia in childhood. 13 December 2002
Dr. M.D. Trip	The spectrum of premature atherosclerosis: from single gene to complex genetic disorder. 19 December 2002
Dr. S. van Wissen	Aggressive lipid lowering in patients with familial hypercholesterolaemia. 6 March 2003
Dr. A. Wiegman	Pediatric implications of heterozygous Familial Hypercholesterolaemia. 1 July 2003
Dr. R. Singaraja	The role of abca1 in atherosclerosis: lessons from in vitro and in vivo models 17 September 2003
Dr. G.J. de Grooth	Cholesteryl Ester Transfer Protein. Its role in cardiovascular disease and drug development. 2 December 2003
Dr. A. Jansen	Familial hypercholesterolemia. The determination of phenotype 9 December 2003
Dr. J.I. Rotmans	Therapeutic Strategies to Prevent Stenosis in Arteriovenous Grafts for Hemodialysis 27 January 2005
Dr. E.S. van Aalst-Cohen	Diagnostic criteria and risk factors for cardiovascular disease in familial hypercholesterolemia. 15 March 2005
Dr. S.M. Boekholdt	Genetic and biochemical risk factors in coronary artery disease. 15 March 2005 (with honours)
Dr. G.K. Hovingh	Molecular defects in the metabolism of the HDL particle and the consequences for atherosclerosis progression. 15 April 2005
Dr. S.W. Fouchier	Genetic determinants of cholesterol homeostasis. 15 April 2005

Dr. J. Rodenburg	Familial Hypercholesterolemia in Childhood: Diagnostics, Therapeuticall Options and Risk Stratification. 13 September 2005
Dr. J.S. Rana	The Cardiovascular Metabolic Syndrome 19 October 2005
Dr. J. Rip	Lipoprotein Lipase, Hypertriclyceridemie and Atherosclerosis 15 September 2006
Dr. R.J. Bisoendial	High-density lipoprotein and C-reactive protein, friend and foe in cardiovascular disease 12 December 2006
Dr. M.C. Nierman	Lipoprotein Lipase S447X; from beneficial gene variant to gene therapy 13 December 2006
Dr. R.C. Özsoy	The dyslipidemia of chronic renal failure and the effects of statin therapy 15 May 2007
Dr. M. Nieuwdorp	Metabolic and vascular dysfunction during hyperglycemia induced inflammation. The role of the endothelial Glycocalyx on vascular homeostatis in vivo 7 September 2007
Dr. K.C.M.C. Koeijvoets	Complex genetics of monogenic familial hypercholesterolemia 12 September 2007
Dr. R.S. Birjmohun	HDL on the crossroads of inflammation, coagulation and atherosclerosis 28 Mei 2008
Dr. M.C. Meuwese	Targetting the vessel wall in cardiovascular prevention. 10 September 2008
Dr. R.R. Sankatsing	Atherosclerosis in the HIV and non-HIV setting: detecting and modifying cardiovascular risk 19 November 2008
Dr. W.A. van der Steeg	Improving Cardiovascular Disease Prevention: From Risk Assessment to Novel Therapy 6 February 2009
Dr. S.I. van Leuven	Inflammation and its Echo in Atherosclerosis 23 June 2009

Dr. S.F.C. Vaessen	Apolipoproteins A-I and A-V as gene therapeutic targets to intervene in lipid metabolism 17 September 2009
Dr. A. El Harchaoui	The Puzzle of High-Density Lipoprotein in Cardiovascular Prevention 3 December 2009
Dr. F. Akdim	LDL-Cholesterol lowering beyond statins 29 April 2010
Dr. R. Franssen	Abnormalities in lipoprotein metabolism: from dysfunctional HDL to abnormal processing of triglyceride-rich lipoproteins 26 October 2010
Dr. A. van der Graaf	Familial Hypercholesterolemia: Cardiovascular Disease Prevention from Childhood into Adolescents 28 October 2010
Dr. A.M.H. Vergeer	HDL Genes and HDL Drugs 10 June 2011 (with honours)
Dr. A.G. Holleboom	Genetic Disorders of HDL Metabolism: from model to mechanism 17 June 2011
Dr. A.Q. Reuwer	Prolactin and Vascular Disease; a first cautious assessment 20 september 2011
Dr. L.N. Broekhuizen	Glycocalyx, Cardiometabolic disease and Inflammation 23 september 2011
Dr. S. Sivapalaratnam	The molecular basis of early onset cardiovascular disease. 14 september 2012
Dr. B.M. Sondermeijer	Cardiovascular Metabolism 19 oktober 2012
Dr. R. Huijgen	Familial Hypercholesterolemia: The Dutch Approach 20 december 2012
Dr. R. Duivenvoorden	Innovative Imaging Techniques for improved characterization of atherosclerosis and the assessment of novel therapies. 5 september 2013 (with honours)
Dr. H.J. Avis	Childhood initiated statin therapy in familial hypercholesterolemia. 10 september 2013

Dr. Steffi Maiwald Rare genetic variants associated with early onset CVD
3 maart 2015

PUBLICATIONS

1983

1. Het koerierssyndroom. J. Geerling, **J.J.P. Kastelein**, D. Agenant. *Ned. Tijdschr. Geneeskd.* 1983; 127: 874-64.

1985

2. Urinary creatine: Biochemical indicator for evaluation of sickle cell crises. C. Beyer, L.W. Statius van Eps, **J.J.P. Kastelein**, D.P.M. Brandjes, W.M. Mairuhu, A. van den Ende. *Clin. Chem.* 1985; 31; 1232-1234.

1986

3. First trimester prenatal diagnosis for Huntington disease using DNA probes. M.R. Hayden, **J.J.P. Kastelein**, J. Hewitt, S. Langlois, R.D. Wilson, S. Fox, C.M. Hilbert, M. Bloch. *Lancet* 1987; I: 1284-85.

4. Insufficient evidence to invoke defects in or around the AI gene as the cause for familial hypoalphalipoproteinemia. M.R. Hayden, **J.J.P. Kastelein**, S. Langlois. *Atherosclerosis* 1987; 67: 271-72.

1988

5. A polymorphic DNA marker which represents a conserved expressed sequence in the region of the Huntington Disease gene. M.R. Hayden, J. Hewitt, J.J. Wasmutn, **J.J.P. Kastelein**, J. Haines, B. Smith, M. Conneally, C.M. Hilbert, S. Allard. *Am. J. Hum. Genet.* 1988; 42: 125-31.

6. Characterization of six partial deletions in the low-density lipoprotein (LDL) receptor gene causing familial hypercholesterolemia (FH). S. Langlois, **J.J.P. Kastelein**, M.R. Hayden. *Am. J. Hum. Genet.* 1988; 43: 60-68.

1989

7. A major insertion accounts for a significant proportion of mutations underlying human lipoprotein lipase deficiency. S. Langlois, S. Deeb, **J.J.P. Kastelein**, J.D. Brunzell, M.R. Hayden. *Proc. Natl. Acad. Sci.* USA 1989;86:948-952.

8. Niertubulusfunctiestoornissen door azijnzuur. G.H.C. Schardijn, **J.J.P. Kastelein**, L.W. Statius van Eps. *Ned. Tijdschr. Geneeskd.* 1989;133:556-558.

1990

9. The gene causing familial hypoalphalipoprotenemia is not caused by a defect in the Apo AI-CIII-AIV gene cluster in a Spanish family. **J.J.P. Kastelein**, J.L. Haines, M.R. Hayden. *Human. Genet.* 1990; 84: 396-400.

10. A missense mutation at codon 188 of the human lipoprotein lipase gene causes lipoprotein lipase deficiency in persons of different ancestries. M.V. Monsalve, H. Henderson, G. Roederer, P. Julien, S. Deeb, **J.J.P. Kastelein**, L. Peritz, R. Devlin, T. Bruin, M.R.V. Murthy, C. Gagne. J.D. Brunzell, M.R. Hayden. *J. Clin. Invest.* 1990;86:728-734

1991

11. The prediction of the therapeutic response to cholesterol lowering drugs in an 11-year old boy with homozygous familial hypercholesterolemia. H.D. Bakker, P.P.M. Schilte, T. Bruin, M.C.L. Schaap, P.J. Lansberg and **J.J.P. Kastelein**. *J. Inher. Metab. Dis.* 1991:14;3.

12. De Low-Density Lipoprotein (LDL)-receptor. Caput Selectum. **J.J.P. Kastelein**, J.W. ten Cate. *Ned. Tijdschr. Geneeskd.* 1991;135:646-651.

13. High-Density Lipoproteine. **J.J.P. Kastelein**. *Ned. Tijdschr. Klin. Chem.* 1991;16:106-109.

14. Een patient met de homozygote vorm van Familiaire Hypercholesterolemie. J.W. Gorter, **J.J.P. Kastelein**, P.J. Lansberg, P.P.M. Schilte, H.D. Bakker. *Ned. Tijdschr. Kindergeneesk.* 1991;59:88-91.

15. The molecular defect causing fish eye disease: An amino acid exchange in lecithin: cholesterol acyltransferase (LCAT) leads to the selective loss of alpha-LCAT activity. H. Funke, A. von Eckardstein, P.H. Pritchard, **J.J.P. Kastelein**, J.J. Albers, C.C. Droste, G. Assmann. *Proc. Natl. Acad. Sci.* (USA) 1991;88:4855-4859.

16. HindIII-polymorphism in the LPL-gene detected by PCR. T. Bruin, P.W.A. Reymer, B.E. Groenemeyer, P.J. Talmud and **J.J.P. Kastelein**. *Nucl. Acids. Res* 1991;19:6346.

1992

17. Hemostase, Thrombose en Perifere Vaatziekten. A. Sturk, H.R. Büller, **J.J.P. Kastelein**, J.W. ten Cate. Hoofdstuk in *Leerboek Interne Geneeskunde* 1992, Eds. G.J. den Ottolander. 10e herziene druk. Bohn, Stafleu, van Loghum, Houten/Zeventer.

18. Two naturally occuring mutations at the first and second base of codon Asp^{156} in the proposed catalytic triad of human lipoprotein lipase - in vivo evidence that Asp^{156} is

essential for catalysis. Y. Ma, S. Tuzgöl, T. Bruin, J.D. Brunzell, **J.J.P. Kastelein** and M.R. Hayden. *J. Biol. Chem.* 1992;267(3):1918-1923

19. Lipoproteine Lipase. Caput Selectum. **J.J.P. Kastelein**, T. Bruin, J.W. ten Cate. *Ned. Tijdschr. Geneesk.* 1992;15:727-730

20. High-Density Lipoproteine. Caput Selectum. **J.J.P. Kastelein**, R.P.G. Peters en J.W. ten Cate. *Ned. Tijdschr. Geneeskd.* 1992;136:723-726

21. De behandeling van Familiaire Hypercholesterolemie. Caput Selectum. P.J. Lansberg, **J.J.P. Kastelein**, J.C. Defesche en J.W. ten Cate. *Ned. Tijdschr. Geneeskd.* 1992;136:734-738

22. Familial high-density lipoprotein deficiency causing corneal opacities (fish eye disease) in a family of Dutch descent. **J.J.P. Kastelein**, P.H. Pritchard, D.W. Erkelens, J.J. Albers, J.J. Frohlich. *J. Int. Med.* 1992;231:413-419

23. Postmenopausale oestrogeen substitutie en het risico voor atherosclerotische hart- en vaatziekten. Caput Selectum. Commentaar. E. Dekker, H.R. Büller and **J.J.P. Kastelein**. *Ned. Tijdschr. Geneeskd.* 1992;25:1197-1200.

24. A missense mutation (Asp^{250} Asn) in exon 6 of the human lipoprotein lipase gene causes hyperchylomicronemia in patients of different ancestries. Y. Ma, B.I. Wilson, S. Bijvoet, H.E. Henderson, E. Cramb, G. Roederer, M.R. McMurthy, P. Julien, H. Bakker, **J.J.P. Kastelein**, J.D. Brunzell, M.R. Hayden. *Genomics*. 1992;13:649-653.

25. Absence of mutations in the promoter region of the low density lipoprotein receptor gene in a large number of Familial Hypercholesterolemia patients as revealed by denaturing gradient gel electrophoresis. B. Top, A.G. Uiterlinden, A. v.d. Zee, **J.J.P. Kastelein**, J.A. Gevers Leuven, L.M. Havekes and R.R. Frants. *Hum. Genet.* 1992;89:561-565.

26. The familial hyperchylomicronaemia syndrome. S.M. Bijvoet, T. Bruin, **J.J.P. Kastelein**. *Neth. J. Med.* 1992;42:36-44.

27. Molecular Geography of Inherited Disorders of Lipoprotein Metabolism: Lipoprotein Lipase Deficiency and Familial Hypercholesterolemia. Hayden M.R., De Braekeleer M., Henderson H.E., and **Kastelein J.J.P.** Chapter in: *Genetic Factors in Atherosclerosis-Candidate Genes and Processes.* Eds. A.J. Lusis, J.I. Rotter and R.S. Sparkes. Monogr. Hum. Genet. Basel, Karger 1992;14:350-362.

28. A missense mutation ($Pro^{157} \rightarrow Arg$) in lipoprotein lipase ($LPL_{nijmegen}$) resulting in loss of catalytic activity. T. Bruin, **J.J.P. Kastelein**, D.E. van Diermen, Y. Ma, H.E. Henderson, P.M.J. Stuyt, A.F.H. Stalenhoef, A. Sturk, J.D. Brunzell, M.R. Hayden. *Eur. J. Biochem.* 1992;208:267-272.

29. Detection of the $Pro^{664} \rightarrow$ Leu mutation in the low-density lipoprotein-receptor gene and its relation to lipoprotein(a) levels in patients with familial hypercholesterolemia

of Dutch ancestry from the Netherlands and Canada. J.C. Defesche, M.A. van de Ree, **J.J.P. Kastelein**, D.E. van Diermen, N.W.E. Janssens, J.J. van Doormaal and M.R. Hayden. *Clin. Genet.* 1992;42:273-280.

30. Efficacy and tolerability of simvastatin and pravastatin in patients with primary hypercholesterolemia (a multicenter comparative study). The European Study group. *Am. J. Cardiol.* 1992;70:1281-1286.

1993

31. Analysis of the Afrikaner mutation in exon 9 of the low-density lipoprotein receptor gene in a large Dutch kindred suffering from Familial Hypercholesterolemia. J.C. Defesche, P.J. Lansberg, P.W. Reymer, R.J. Lamping, **J.J.P. Kastelein**. *Neth. J. Med.* 1993; 42: 53-60.

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33. Comparison of the efficacy, safety and tolerability of Simvastatin and Pravastatin for Hypercholesterolemia. The Simvastatin Pravastatin Study Group. *Am. J. Cardiol.* 1993; 71: 1408-1414.

34. Treatment of primary hypercholesterolaemia. Short-term efficacy and safety of increasing doses of simvastatin and pravastatin: a double-blind comparative study. A.F.H. Stalenhoef, P.J. Lansberg, A.A. Kroon, B. Kortmann, A.F.J. de Haan, P.M.J. Stuyt and **J.J.P. Kastelein**. *J. Intern. Med.* 1993; 234; 77-82.

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