

NAME Gerard Pasterkamp

POSITION TITLE Professor of experimental Cardiology, Division Heart and Lungs, UMCU

EDUCATION/TRAINING

August 1998-2001 MSc, Clinical Epidemiology. NIHES, Erasmus University, Rotterdam.
1992-June 1995 PhD, Department of Cardiology, Laboratory of Experimental Cardiology (promotor prof. dr. C. Borst). Title Thesis: "Applications of Intravascular Ultrasound". June 8, 1995"
1982-1990: MD, Free University, Amsterdam.



Research achievements

Gerard Pasterkamp has done several original research observations in the field of vascular biology that, at that time, were considered counterintuitive. He made the following innovative contributions that resulted in new concepts in the pathogenesis of atherosclerotic disease progression and biomarker discovery, Project number 3 can be considered as the main project that is relevant for the current proposal:

- 1- In 1987 it was demonstrated that arteries are capable of expansive remodeling when atherosclerotic disease develops (NEJM 1987). Subsequently, the concept of arterial compensatory enlargement was widely studied post mortem and using in vivo intravascular ultrasound imaging studies. In 1995 Gerard Pasterkamp was the first to report that not all arteries undergo expansive remodeling and that many arterial sites undergo constrictive remodeling during atherogenesis (Circulation 1995).
- 2- In the clinical arena it was already appreciated that luminal thrombosis in the coronary artery could occur at sites that were not significantly narrowed, which was demonstrated when an angiogram was available at a time point preceding the event. Gerard Pasterkamp was the first to show that this phenomenon could be explained by an association between the mode of geometrical remodeling and the stability of the atherosclerotic plaque (JACC 1998). At present researchers now use the variability of geometrical remodeling as a surrogate measure for atherosclerotic plaque stability in clinical IVUS studies.
- 3- It is not possible to predict on an individual level which patients will suffer from plaque rupture and a subsequent stroke or a myocardial infarction. Since 2002 Gerard Pasterkamp has been working on an ambitious project with an original approach to discover local plaque biomarkers that are predictive for adverse events. He is the initiator and the program leader of Athero-Express study and together with Frans Moll and Dominique de Kleijn he has now built world's largest atherosclerotic plaque biobank. At present more than 2500 patients have been included. The unique aspect of this study is that all patients who donate plaques undergo a follow up. The group has discovered a wide range of proteins in plaques that have a predictive value for events. The discovery of these plaque biomarkers will help to select the discovery and validation of biomarkers in plasma and circulating cells and will also facilitate drug development programs (JAMA 2008). The discovery of these plaque derived biomarkers resulted in the launch of a startup company Cavadis.

Cavadis

Gerard Pasterkamp is one of the founders of this biotech company. At present he is a temporary member of the management team and acts as advisor. Cavadis started her activities in 2007 as an academic startup funded by the Erasmus sees fund and the UU holding. In 2009 an A-round was closed and activities will be continued at least until 2012. Cavadis is a growing biomarker company and will bring its first plaque biomarker kit to the market in 2010. The company has several collaborations with global operating Pharma companies.

Activities

- Past chairman and member of the nucleus of the European Society of Cardiology (ESC) working group of pathogenesis of Atherosclerosis
- Member of the Program Committee of the annual scientific sessions of the European Society of cardiology.
- Member of the Basic science council of the European Society of cardiology.
- Board member of the Dutch Atherosclerosis Society.
- Board of the Scientific Committee of the Interuniversity Cardiology Institute of the Netherlands.
- Member of the MT of the Durrer Centre: a Cardiovascular Genetics biobank installed by the ICIN/KNAW.
- Member of the WAC "Pathogenesis" of the Dutch Heart Foundation.
- Coordinator of multi centre STREP-SME research consortia: a- Immunath (EU KP6, 2.5 mEuro), b- Circulating Cells (CTMM, 18 mEuro).
- "Trekker" Focus and massa area Cardiovascular research of the University Utrecht.

Educational activities

- One of the program leaders of the Papendal courses of the NHS (Vascular Biology).
- Responsible for the PhD educational track Cardiovascular research at the University Utrecht.
- Coordinator of several courses in the Bachelor and Master curriculum of Biomedical sciences and medicine at the UMCU.

Selected peer-reviewed key publications

- *Pasterkamp G, Wensing PJ, Post MJ, Hillen B, Mali WP, Borst C. Paradoxical arterial wall shrinkage may contribute to luminal narrowing of human atherosclerotic femoral arteries. *Circulation* 1995;91:1444-9.*
- *Pasterkamp G, Borst C, Post MJ, Mali WP, Wensing PJ, Gussenhoven EJ, Hillen B. Atherosclerotic arterial remodeling in the superficial femoral artery. Individual variation in local compensatory enlargement response. *Circulation* 1996;93:1818-25.*
- *Pasterkamp G, Schoneveld AH, van der Wal AC, Haudenschild CC, Clarijs RJ, Becker AE, Hillen B, Borst C. Relation of arterial geometry to luminal narrowing and histologic markers for plaque vulnerability: the remodeling paradox. *J Am Coll Cardiol* 1998;32:655-62*
- *Pasterkamp G, Schoneveld AH, van der Wal AC, Hijnen DJ, van Wolveren WJ, Plomp S, Teepen HL, Borst C. Inflammation of the atherosclerotic cap and shoulder of the plaque is a common and locally observed feature in unruptured plaques of femoral and coronary arteries. *Arterioscler Thromb Vasc Biol* 1999;19:54-8.*
- *Sierevogel MJ, Pasterkamp G, Velema E, de Jaegere PP, de Smet BJ, Verheijen JH, de Kleijn DP, Borst C. Oral matrix metalloproteinase inhibition and arterial remodeling after balloon dilation : an intravascular ultrasound study in the pig. *Circulation* 2001;103:302-307.*
- *Rotmans JI, Heyligers JM, Verhagen HJ, Velema E, Nagtegaal MM, de Kleijn DP, Groot FG, Stroes ES, Pasterkamp G. In vivo cell seeding with anti-CD34 antibodies successfully accelerates endothelialization but stimulates intimal hyperplasia in porcine arteriovenous expanded polytetrafluoroethylene grafts. *Circulation* 2005;112:12-8.*
- *Timmers L, Sluijter JP, Verlaan CW, Steendijk P, Cramer MJ, Emons M, Strijder C, Gründeman PF, Sze SK, Hua L, Piek JJ, Borst C, Pasterkamp G, de Kleijn DP. Cyclooxygenase-2 inhibition increases mortality, enhances left ventricular remodeling, and impairs systolic function after myocardial infarction in the pig. *Circulation* 2007;115:326-32.*
- *Rodriguez-Feo JA, Hellings WE, Moll FL, De Vries JP, van Middelaar BJ, Algra A, Sluijter J, Velema E, van der Broek T, Sessa WC, De Kleijn DP, Pasterkamp G. Caveolin-1 influences vascular protease activity and is a potential stabilizing factor in human atherosclerotic disease. *PLoS ONE* 2008 2;3:e2612.*
- *Hellings WE, Moll FL, De Vries JP, Ackerstaff RG, Seldenrijk KA, Met R, Velema E, Derksen WJ, De Kleijn DP, Pasterkamp G. Atherosclerotic plaque composition and occurrence of restenosis after carotid endarterectomy. *JAMA* 2008 6;299:547-54.*
- *Peeters W, Hellings WE, de Kleijn DP, de Vries JP, Moll FL, Vink A, Pasterkamp G. Carotid atherosclerotic plaques stabilize after stroke: insights into the natural process of atherosclerotic plaque stabilization. *Arterioscler Thromb Vasc Biol* 2009;29:128-33.*
- *Taleb S, Romain M, Ramkhalawon B, Uyttenhove C, Pasterkamp G, Herbin O, Esposito B, Perez N, Yasukawa H, Van Snick J, Yoshimura A, Tedgui A, Mallat Z. Loss of SOCS3 expression in T cells reveals a regulatory role for interleukin-17 in atherosclerosis. *J Exp Med*. 2009 Sep 8. [Epub ahead of print, co-author on paper and mentioned here as example of relevance contribution athero-express biobank for international collaborations]*

C. Research Support (projects in Italics have been completed)

- Coordinator Circulating Cells, CTMM, 2008, total consortium 18 mEuro
- Participating in consortium Toll Like Receptors, TI Pharma, (1 PhD student)
- Coordinator "Immunath". A STREP-SME consortium EU, KP6. (2.5mEuro)
- "Athero-Express: an atherosclerotic plaque biobank study". Support funded by the Bekalis Foundation, 2004 (20kE) and the ICIN, 2005 (60kE), industrial support (>1.0mE).
- Collaborations in projects funded by Industry in large animal models (ischemia reperfusion and stem cell research (+/- 1.0 mEuro)
- Projects coordinated by postdocs within the laboratory and within the responsibility of Gerard Pasterkamp, have not been listed here.
- *"Bone marrow derived cells as a therapeutic means to influence post ischemic myocardial damage". Collaboration project with prof. dr. J.J. Piek (AMC) sponsored by the Board of Directors of AMC and UMC 04-07) (250kE).*
- *"The role of proinflammatory bacterial wall antigen peptidoglycan in atherosclerotic plaque formation and vulnerability." Funded by the Dutch Heart Foundation 2001. (226kE).*
- *"Inhibition of constrictive arterial remodeling after balloon dilation." Program, Accepted and funded by the Dutch Heart Foundation 1999 (900kE).*