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## **Angiogenesis, proteases and angiogenic factors during the inception of pregnancy. Crucial contributors or trivial bystanders?**

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### **Citation**

Plaisier, G. M. (2008, May 7). *Angiogenesis, proteases and angiogenic factors during the inception of pregnancy. Crucial contributors or trivial bystanders?*. Retrieved from <https://hdl.handle.net/1887/12861>

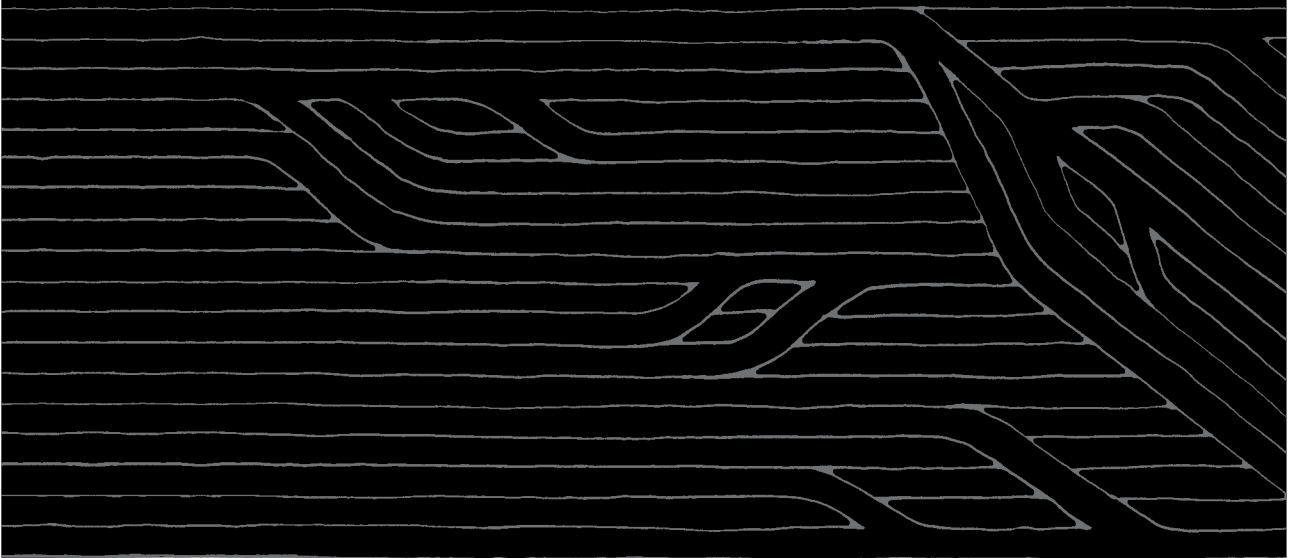
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# References





- Abberton KM, Rogers PA** (1995) Production of an endothelial cell migratory signal in rat endometrium during early pregnancy. *Cell Tissue Res* 279, 215-220.
- Adams RH, Alitalo K** (2007) Molecular regulation of angiogenesis and lymphangiogenesis. *Nat Rev Mol Cell Biol* 8, 464-478.
- Ahmad S, Ahmed A** (2004) Elevated placental soluble vascular endothelial growth factor receptor-1 inhibits angiogenesis in pre-eclampsia. *Cir Res* 95, 884-891.
- Ahmed A, Li XF, Dunk C, Whittle MJ, Rushton DI, Rollason T** (1995) Colocalisation of vascular endothelial growth factor and its Flt-1 receptor in human placenta. *Growth Factors* 12, 235-243.
- Ahmed A, Perkins J** (2000) Angiogenesis and intrauterine growth retardation. *Baill Best Pract Res Clin Obstet Gynaecol* 14, 981-998.
- Al-Atrash G, Kitson RP, Xue Y, Mazar AP, Kim MH, Goldfarb RH** (2001) uPA and uPAR contribute to NK cell invasion through the extracellular matrix. *Anticancer Res* 21, 1697-1704.
- Albertsson P, Kim MH, Jonges LE, Kitson RP, Kuppen PJ, Johansson BR, et al.** (2000) Matrix metalloproteinases of human NK cells. *In Vivo* 14, 269-276.
- Alfano D, Franco P, Vocca I, Gambi N, Pisa V, Mancini A, et al.** (2005) The urokinase plasminogen activator and its receptor: role in cell growth and apoptosis. *Thromb Haemost* 93, 205-211.
- Anand-Apte B, Pepper MS, Voest E, Montesano R, Olsen B, Murphy G, et al.** (1997) Inhibition of angiogenesis by tissue inhibitor of metalloproteinase-3. *Invest Ophthalmol Vis Sci* 38, 817-823.
- Aplin JD, Charlton AK, Ayad S** (1988) An immunohistochemical study of human endometrial extracellular matrix during the menstrual cycle and first-trimester of pregnancy. *Cell Tissue Res* 253, 231-240.
- Aplin JD** (2000) The cell biological basis of human implantation. *Baillieres Best Pract Res Clin Obstet Gynaecol* 14, 757-764.
- Armant DR, Wang J, Liu Z** (2000) Intracellular signaling in the developing blastocyst as a consequence of the maternal-embryonic dialogue. *Semin Reprod Med* 18, 273-287.
- Arroyo J, Torry RJ, Torry DS** (2004) Differential regulation of placenta growth factor (PLGF)-mediated signal transduction in human primary term trophoblast and endothelial cells. *Placenta* 25, 379-386.
- Asahara T, Chen D, Takahashi T, et al.** (1998) Tie2 receptor ligands, angiopoietin-1 and angiopoietin-2, modulate VEGF-induced postnatal neovascularization. *Circ Res* 83, 233-240.
- Athanassiades A, Lala PK** (1998) Role of PLGF in human extravillous trophoblast proliferation, migration and invasiveness. *Placenta* 19, 465-473.
- Bacharach E, Itin A, Keshet E** (1992) In vivo patterns of expression of urokinase and its inhibitor PAI-1 suggest a concerted role in regulating physiological angiogenesis. *Proc Natl Acad Sci U S A* 89, 10686-10690.
- Bai SX, Wang YL, Qin L, et al.** (2005) Dynamic expression of matrix metalloproteinases (MMP-2, -9 and -14) and the tissue inhibitors of MMPs (TIMP-1, -2 and -3) at the implantation site during tubal pregnancy. *Reproduction* 129, 103-113.
- Barker DJ, Winter PD, Osmond C, Margetts B, Simmonds SJ** (1993) Weight in infancy and death from ischemic heart disease in women. *BMJ* 306, 422-426.
- Bausero P, Cavaille F, Meduri G, Freitas S, Perrot-Appianat M** (1998) Paracrine action of vascular endothelial growth factor in the human endometrium: production and target sites, and hormonal regulation. *Angiogenesis* 2, 167-182.
- Bergers G, Benjamin LE** (2003) Tumorigenesis and the angiogenic switch. *Nat Rev Cancer* 3, 401-410.
- Bigg HF, Morrison CJ, Butler GS, Bogoyevitch MA, Wang Z, Soloway PD, Overall CM** (2001) Tissue inhibitor of metalloproteinases-4 inhibits but does not support the activation of gelatinase A via efficient inhibition of membrane type 1-matrix metalloproteinase. *Cancer Res* 61, 3610-3618.
- Birkedal-Hansen H, Taylor RE** (1982) Detergent-activation of latent collagenase and resolution of its component molecules. *Biochem Biophys Res Commun* 107, 1173-1178.
- Bjorn SF, Hastrup N, Lund LR, Dano K, Karsen JF, Pyke C** (1997) Co-ordinated expression of MMP-2 and its putative activator, MT1-MMP, in human placenta. *Mol Hum Reprod* 3, 713-723.
- Bjorn SF, Hastrup N, Larsen JF, Lund LR, Pyke C** (2000) Messenger RNA for Membrane-type 2 ma-

- trix metalloproteinase, MT2-MMP, is expressed in human placenta of first-trimester. *Placenta* 21, 170-176.
- Blasi F, Vassalli JD, Dano K** (1987) Urokinase plasminogen activator: pro-enzyme, receptor and inhibitors. *J Cell Biol* 104, 801-804.
- Blasi F, Carmeliet P** (2002) uPAR: a versatile signalling orchestrator. *Nat Rev Mol Cell Biol* 3, 932-943.
- Bosio PM, Wheeler T, Anthony F, Conroy R, O'herlihy C, McKenna P** (2001) Maternal plasma vascular endothelial growth factor concentrations in normal and hypertensive pregnancies and their relationship to peripheral vascular resistance. *AJOG* 184, 146-152.
- Boyd PJ, Doyle J, Gee E, Pallan S, Haas TL** (2004) Mitogen-activated protein kinase signaling regulates endothelial cell assembly into networks and the expression of MT1-MMP and MMP-2. *Am J Physiol Cell Physiol* 288, 659-668.
- Brosens I, Robertson WB, Dixon HG** (1967) The physiological response of the vessels of the placental bed to normal pregnancy. *J Pathol Bacteriol* 93, 569-579.
- Bulletti C, Galassi A, Jasonni VM, Martinelli G, Tabanelli S, Flamigni C** (1988) Basement membrane components in normal hyperplastic and neoplastic endometrium. *Cancer* 1, 142-149.
- Bulmer JN, Pace D, Ritson A** (1988) Immunoregulatory cells in human decidua: morphology, immunohistochemistry and function. *Reprod Nutr Dev* 28, 1599-1613.
- Bulmer JN, Morrison L, Longfellow M, Ritson A, Pace D** (1991) Granulated lymphocytes in human endometrium: histochemical and immunohistochemical studies. *Hum Reprod* 6, 791-798.
- Bulmer JN, Lash GE** (2005) Human uterine natural killer cells: a reappraisal. *Mol Immunol* 42, 511-521.
- Burrows TD, King A, Loke YW** (1996) Trophoblast migration during human placental implantation. *Hum Reprod Update* 2, 307-321.
- Burton GJ** (1997) On 'Oxygen and placental villous development: origins of fetal hypoxia. *Placenta* 18, 625-626.
- Burton GJ, Jauniaux E, Watson AL** (1999) Maternal arterial connections to the placental intervillous space during the first-trimester of human pregnancy: the Boyd collection revisited. *Am J Obstet Gynecol* 181, 718-724.
- Carmeliet P, Ferreira V, Breier G, Pollefeyt S, Kieckens L, Gertsenstein M, et al.** (1996) Abnormal blood vessel development and lethality in embryos lacking a single VEGF allele. *Nature* 380, 435-439.
- Carmeliet P, Moons L, Dewerchin M, Mackman N, Luther T, Breier G, et al.** (1997) Insights in vessel development and vascular disorders using targeted inactivation and transfer of vascular endothelial growth factor, the tissue factor receptor, and the plasminogen system. *Ann N Y Acad Sci* 811, 191-206.
- Carmeliet P, Moons L, Lutun A, Vincenti V, Compernelle V, De Mol M, et al.** (2001) Synergism between vascular endothelial growth factor and placental growth factor contributes to angiogenesis and plasma extravasation in pathological conditions. *Nat Med* 7, 575-583.
- Carmeliet P** (2003) Angiogenesis in health and disease. *Nat Med* 9, 653-660.
- Chakraborti S, Mandal M, Das S, Mandal A and Chakraborti T** (2003) Regulation of matrix metalloproteinases: an overview. *Mol Cell Biochem* 253, 269-285.
- Charnock-Jones S, Sharkey AM, Rajput-Williams J, Burch D, Schofield JP, Fountain SA, et al.** (1993) Identification and localization of alternately spliced mRNAs for vascular endothelial growth factor in human uterus and estrogen regulation in endometrial carcinoma cell lines. *Biol of Reprod* 48, 1120-1128.
- Charnock-Jones DS** (2002) Soluble flt-1 and the angiopoietins in the development and regulation of placental vasculature. *J Anat* 200, 607-615.
- Charnock-Jones DS, Kaufmann P, Mayhew TM** (2004) Aspects of human fetoplacental vasculogenesis and angiogenesis. I. Molecular regulation. *Placenta* 25, 103-113.
- Chegini N, Rhoton-Vlasak A, Williams RS** (2003) Expression of matrix metalloproteinase-26 and tissue inhibitor of matrix metalloproteinase-3 and -4 in endometrium throughout the normal menstrual cycle and alteration in users of levonorgestrel implants who experience irregular uterine bleeding. *Fertil Steril* 80, 564-570.

- Chen HF, Shew JY, Ho HN, Hsu WL, Yang YS** (1999) Expression of leukemia inhibitory factor and its receptor in preimplantation embryos. *Fertil Steril* 72, 713-719.
- Chi JT, Chang HY, Haraldsen G, Jahnsen FL, Troyanskaya OG, Chang DS, et al.** (2003) Endothelial cell diversity revealed by global expression profiling. *PNAS* 100, 10623-10628.
- Chomczynski P, Sacchi N** 1987 Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *Anal Biochem* 162:156-159.
- Chung HW, Lee JY, Moon HS, Hur SE, Park MH, Wen Y, Polan ML** (2002) Matrix metalloproteinase-2, membranous type 1 matrix metalloproteinase, and tissue inhibitor of metalloproteinase-2 expression in ectopic and eutopic endometrium. *Fertil Steril* 78, 787-795.
- Chung J, Song Y, Wang Y, Magness RR, Zheng J** (2004) Differential expression of vascular endothelial growth factor (VEGF), endocrine gland derived-VEGF, and VEGF receptors in human placentas from normal and preeclamptic pregnancies. *J Clin Endocrinol Metab* 89, 2484-2490.
- Clark DE, Smith SK, Sharkey AM, Charnock-Jones DS** (1996) Localization of VEGF and expression of its receptors flt and KDR in human placenta throughout pregnancy. *Hum Reprod* 11, 1090-1098.
- Clark DE, Smith SK, Licence D, Evans AL, Charnock-Jones DS** (1998a) Comparison of expression patterns for placenta growth factor, VEGF, VEGF-B and VEGF-C in the human placenta throughout gestation. *J of Endocrinol* 159, 459-467.
- Clark DE, Smith SK, He Y, Day KA, Licence DR, Corps AN, et al.** (1998b) A vascular endothelial growth factor antagonist is produced by the human placenta and released into the maternal circulation. *Biol of Reprod* 59, 1540-1548.
- Classen-Linke I, Alfer J, Krusche CA, Chwalisz K, Rath W, Beier HM** (2000) Progesterin, progesterone receptor modulators and progesterone antagonists change VEGF release of endometrial cells in culture. *Steroids* 65, 763-771.
- Clifford K, Flanagan AM, Regan L** (1999) Endometrial CD56+ natural killer cells in women with recurrent miscarriage: a histomorphometric study. *Hum Reprod* 14, 2727-2730.
- Collen A, Hanemaaijer R, Lupu F, Quax PH, van Lent N, Grimbergen J, et al.** (2003) Membrane-type matrix metalloproteinase-mediated angiogenesis in a fibrin-collagen matrix. *Blood* 101, 1810-1817.
- Cooper JC, Sharkey AM, McLaren J, Charnock-Jones DS, Smith SK** (1995) Localization of VEGF and its receptor, flt, in human placenta and decidua by immunohistochemistry. *J of Reprod Fert* 105, 205-213.
- Cooper JC, Sharkey AM, Charnock-Jones D, Palmer CR, Smith SK** (1996) VEGF mRNA levels in placentae from pregnancies complicated by pre-eclampsia. *Br J Obstet Gynaecol* 103, 1191-1996.
- Coulham CB** (1991) Epidemiology of recurrent spontaneous abortion. *Am J Reprod Imm* 26, 23-27.
- Craven CM, Morgan T, Ward K** (1998) Decidual spiral artery remodelling begins before cellular interaction with cytotrophoblasts. *Placenta* 19, 241-252.
- Craven CM, Chedwick LR, Ward K** (2002) Placental basal plate formation is associated with fibrin deposition in decidual veins at sites of trophoblast cell invasion. *Am J Obstet Gynecol* 186, 291-296.
- Critchley HO, Brenner RM, Henderson TA, Williams K, Nayak NR, Slayden OD, et al.** (2001) Estrogen receptor beta, but not estrogen receptor alpha, is present in the vascular endothelium of the human and nonhuman primate endometrium. *J Clin Endocrinol Metab* 86, 370-378.
- Curry TE Jr, Osteen KG** (2003) The matrix metalloproteinase system: changes, regulation, and impact throughout the ovarian and uterine reproductive cycle. *Endocr Rev* 24, 428-465.
- Das SK, Chakraborty I, Wang J, Dey SK, Hoffman LH** (1997a) Expression of vascular endothelial growth factor (VEGF) and VEGF-receptor messenger ribonucleic acids in the peri-implantation rabbit uterus. *Biol Reprod* 56, 1390-1399.
- Das S.K, Yano S, Wang J, Edwards D.R, Nagase H, Dey SK** (1997b) Expression of matrix metalloproteinases and tissue inhibitors of metalloproteinases in the mouse uterus during the peri-implantation period. *Dev Genet* 21, 44-54.
- Davis S, Aldrich TH, Jones PF, Acheson A, Compton DL, Jain V, et al.** (1996) Isolation of angiopoietin-1, a ligand for the TIE2 receptor, by secretion-trap expression cloning. *Cell* 87, 1161-1169.
- Defilippi P, van Hinsbergh VWM, Bertolotto A, Rossino P, Silengo L, Tarone G** (1991) Differential distribu-

- tion and modulation of expression of alpha 1/beta 1 integrin on human endothelial cells. *J Cell Biol* 114, 855-863.
- Deryugina EI, Bourdon MA, Jungwirth K, Smith JW, Strongin AY** (2000) Functional activation of integrin alpha V beta 3 in tumor cells expressing membrane-type 1 matrix metalloproteinase. *Int J Cancer* 86, 15-23.
- Dickey RP, Gasser RF, Olar TT, Taylor SN, Curole DN, Rye PH, et al.** (1994) Risk of recurrent abortion after appearance of a chorionic sac or heart rate on vaginal ultrasound. *Lancet* 344, 1442-1443.
- Dosiou C, Giudice LC** (2005) Natural killer cells in pregnancy and recurrent pregnancy loss: endocrine and immunologic perspectives. *Endocr Rev* 26, 44-62.
- Dunk C, Shams M, Nijjar S, Rhaman M, Qiu Y, Bussolati B, et al.** (2000) Angiopoietin-1 and angiopoietin-2 activate trophoblast Tie-2 to promote growth and migration during placental development. *Am J of Path* 156, 2185-2199.
- Dvorak HF, Brown LF, Detmar M, Dvorak AM** (1995) Vascular permeability factor/vascular endothelial growth factor, microvascular hyperpermeability, and angiogenesis. *Am J Pathol* 146, 1029-1039.
- Eekhout Y, Vaes G** (1977) Further studies on the activation of procollagenase, the latent precursor of bone collagenase. Effects of lysosomal cathepsin B, plasmin and kallikrein, and spontaneous activation. *Biochem J* 166, 21-31.
- Egeblad M, Werb Z** (2002) New functions for the matrix metalloproteinases in cancer progression. *Nat Rev Cancer* 2, 161-174.
- Erickson Hagen AS, Orbus RJ, Wilkening RB, Regnault TRH, Anthony RV** (2005) Placental expression of angiopoietin-1, angiopoietin-2 and Tie-2 during placental development in an ovine model of placental insufficiency- Fetal growth restriction. *Pediatr Res* 58, 1228-1232.
- Ferency A, Bertrand G, Gelfand MM** (1979) Proliferation kinetics of human endometrium during the normal menstrual cycle. *Am J Obstet Gynecol* 133, 859-867.
- Ferrara N, Winer J, Henzel WJ** (1992) Pituitary follicular cells secrete an inhibitor of aortic endothelial cell growth: identification as leukemia inhibitory factor. *Proc Natl Acad Sci USA* 89, 698-702.
- Ferrara N, Carver-Moore K, Chen H, Dowd M, Lu L, O'Shea KS, et al.** (1996) Heterozygous embryonic lethality induced by targeted inactivation of the VEGF gene. *Nature* 380, 439-442.
- Ferrara N** (2000) Vascular endothelial growth factor and the regulation of angiogenesis. *Recent Prog Horm Res* 55, 15-35.
- Ferrara N** (2001) Role of vascular endothelial growth factor in regulation of physiological angiogenesis. *Am J Physiol Cell Physiol* 280, C1358-1366.
- Ferrera N** (2004) VEGF: basic science and clinical progress. *Endocrine Reviews* 25, 581-611.
- Fisher SJ** (2004) The placental problem: linking abnormal cytotrophoblast differentiation to the maternal symptoms of preeclampsia. *Reprod Biol Endocrinol* 2, 53-57.
- Floridon C, Nielsen O, Holund B, Sunde L, Westergaard JG, Thomsen SG, et al.** (1999) Localization and significance of uPA and its receptor in placental tissue from intrauterine, ectopic and molar pregnancies. *Placenta* 20, 711-721.
- Folkman J** (1995) Angiogenesis in cancer, vascular, rheumatoid and other disease. *Nat Med* 1, 27-31.
- Freitas S, Meduri G, Le Nestour E, Bausero P, Perrot-Applanat M** (1999) Expression of metalloproteinases and their inhibitors in blood vessels in human endometrium. *Biol Reprod* 61, 1070-1082.
- Gambino LS, Wreford NG, Bertram JF, Dockery P, Lederman F, Rogers PA** (2002) Angiogenesis occurs by vessel elongation in proliferative phase human endometrium. *Hum Reprod* 17, 1199-1206.
- Galvez BG, Matias-Roman S, Albar JP, Sanchez-Madrid F, Arroyo AG** (2001) Membrane type 1-matrix metalloproteinase is activated during migration of human endothelial cells and modulates endothelial motility and matrix remodeling. *J Biol Chem* 276, 37491-37500.
- Galvez BG, Genis L, Matias-Roman S, Oblander SA, Tryggvason K, Apte SS, Arroyo AG** (2005) MT1-MMP is regulated by chemokines MCP-1/CCL2 and IL-8/CXCL8 in endothelial cells during angiogenesis. *J Biol Chem* 280, 1292-1298.
- Gargett CE, Lederman FL, Lau TM, Taylor NH, Rogers PA** (1999) Lack of correlation between vascular

- endothelial growth factor production and endothelial cell proliferation in the human endometrium. *Hum Reprod* 14, 2080-2088.
- Gargett CE, Rogers PA** (2001) Human endometrial angiogenesis. *Reproduction* 121, 181-186.
- Gendron RL, Adams LC, Paradis H** (2000) Tubedown-1, a novel acetyltransferase associated with blood vessel development. *Dev Dyn* 218, 300-315.
- Geva E, Jaffe RB** (2000) Role of angiopoietins in reproductive tract angiogenesis. *Obstet Gynecol Surv* 55, 511-519.
- Geva E, Ginzinger DG, Zaloudek CJ, Moore DH, Byrne A, Jaffe B** (2002) Human placental vascular development: vasculogenic and angiogenic (branching and non-branching) transformation is regulated by vascular endothelial growth factor-A, angiopoietin-1 and-2. *J Clin Endocrinol Metab* 87, 4213-4224.
- Giavazzi R, Albini A, Bussolino F, DeBraud F, Presta M, Ziche M, et al.** (2000) The biological basis for antiangiogenic therapy. *Eur J Cancer* 36, 1913-1918.
- Gibbons GH, Dzau VJ** (1994) The emerging concept of vascular remodeling. *N Engl J Med* 330, 1431-1438.
- Giudice LC** (1999) Genes associated with embryonic attachment and implantation and the role of progesterone. *J Reprod Med* 44, 165-172.
- Goffin F, Munaut C, Frankenne F, Perrier D'Hauterive S, Beliard A, Fridman V, et al.** (2003) Expression Pattern of Metalloproteinases and Tissue Inhibitors of Matrix-Metalloproteinases in Cycling Human Endometrium. *Biol Reprod* 69, 976-984.
- Goldman-Wohl DS, Ariel I, Greenfield C, Lavy Y, Yagel S** (2000) TIE-2 and angiopoietin-2 expression at the fetal-maternal interface: a receptor ligand model for vascular remodelling. *Mol Hum reprod* 6, 81-87.
- Gomez DE, Alomso DF, Yoshiji H, Thorgeirsson UP** (1997) Tissue inhibitors of metallo-proteinases: structure, regulation and biological functions. *Eur J of Cell Biol* 74, 111-122.
- Goodger AM, Rogers PA** (1993) Uterine endothelial cell proliferation before and after embryo implantation in rats. *J Reprod Fertil* 99, 451-457.
- Goodger AM, Rogers PA** (1994) Endometrial endothelial cell proliferation during the menstrual cycle. *Hum Reprod* 9, 399-405.
- Goodger AM, Rogers PA** (1995) Blood vessel growth in the endometrium. *Microcirculation* 2, 329-343.
- Greb RR, Heikinheimo O, Williams RF, Hodggen GD, Goodman AL** (1997) Vascular endothelial growth factor in primate endometrium is regulated by oestrogen-receptor and progesterone-receptor ligands in vivo. *Hum Reprod* 12, 1280-1292.
- Greene J, Wang M, Liu YE, Raymond LA, Rosen C, Shi YE** (1996) Molecular cloning and characterization of human tissue inhibitor of metalloproteinase 4. *J of Biol Chem* 271, 30375-30380.
- Greenwold N, Jauniaux E, Gulbis B, Hempstock J, Gervy C, Burton GJ** (2003) Relationship among maternal serum endocrinology, placental karyotype, and intervillous circulation in early pregnancy failure. *Fertil Steril* 79, 1373-1379.
- Greiss FC Jr, Anderson SG, Still JG** (1976) Uterine pressure-flow relationships during early gestation. *Am J Obstet Gynecol* 126, 799-808.
- Habara T, Nakatsuka M, Konishi H, Asagiri K, Noguchi S, Kudo T** (2002) Elevated blood flow resistance in uterine arteries of women with unexplained recurrent pregnancy loss. *Hum Reprod* 17,190-194.
- Haller H, Tedesco F, Rukavina D, Radillo O, Gudelj L, Beer AE** (1995) Decidual-trophoblast interactions: decidual lymphoid cell populations in basal and parietal decidua. *J Reprod Immunol.* 28, 165-171.
- Hanahan D, Folkman J** (1996) Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis. *Cell* 86, 353-364.
- Hanemaaijer R, Visser H, Konttinen YT, Koolwijk P, Verheijen JH** (1998) A novel and simple immunocapture assay for determination of gelatinase-B (MMP-9) activities in biological fluids: saliva from patients with Sjogren's syndrome contain increased latent and active gelatinase-B levels. *Matrix Biol* 17,657-665.
- Hanna J, Goldman-Wohl D, Hamani Y, Avraham I, Greenfield C, Natanson-Yaron S, et al.** (2006) Decidual



- NK cells regulate key developmental processes at the human fetal-maternal interface. *Nat Med* 12, 1065-1074.
- Hatzi E, Murphy C, Zoepfel A, Ahorn H, Tontsch U, Bamberger A, et al.** (2002) N-myc oncogene overexpression down-regulates leukemia inhibitory factor in neuroblastoma. *Eur J Biochem* 269, 3732-3741.
- Hayman R, Brockelsby J, Kenny L, Baker P** (1999) Preeclampsia: the endothelium, circulating factor (s) and vascular endothelial growth factor. *J Soc Gynecol Investig* 6, 3-10.
- Henderson TA, Saunders PT, Moffett-King A, Groome NP, Critchley HO** (2003) Steroid receptor expression in uterine natural killer cells. *J Clin Endocrinol Metab* 88, 440-449.
- Hernandez-Barrantes S, Bernardo M, Toth M, Fridman R** (2002) Regulation of membrane type-matrix metalloproteinases. *Semin Cancer Biol* 12, 131-138.
- Hewett P, Nijjar S, Shams M, Morgan S, Gupta J, Ahmed A** (2002) Down-regulation of angiotensin-1 in menorrhagia. *Am J of Path* 160,773-780.
- Heymans S, Luttun A, Nuyens D, Theilmeier G, Creemers E, Moons L, et al.** (1999) Inhibition of plasminogen activators or matrix metalloproteinases prevents cardiac rupture but impairs therapeutic angiogenesis and causes cardiac failure. *Nat Med* 5, 1135-1142.
- Hill JA, Melling GC, Johnson PM** (1995) Immunohistochemical studies of human uteroplacental tissues from first-trimester spontaneous abortion *Am J Obstet Gynecol* 173, 90-96.
- Hiraoka N, Allen E, Apel IJ, Gyetko MR, Weiss SJ** (1998) Matrix metalloproteinases regulate neovascularization by acting as pericellular fibrinolysins. *Cell* 95, 365-377.
- Hirchenhain J, Huse I, Hess A, Bielfield P, De Bryune F, Krussel JS** (2003) Differential expression of angiopoietins 1 and 2 and their receptor Tie-2 in human endometrium. *Mol Hum Reprod* 9, 663-669.
- Hoeben A, Landuyt B, Highley MS, Wildiers H, Van Oosterom AT, De Bruijn EA** (2004) Vascular endothelial growth factor and angiogenesis. *Pharmacol Rev* 56, 549-580.
- Hofmann GE, Glatstein I, Schatz F, Heller D, Deligdisch L** (1994) Immunohistochemical localization of urokinase-type plasminogen activator and the plasminogen activator inhibitors 1 and 2 in early human implantation sites. *Am J Obstet Gynecol* 170, 671-676.
- Hornung D, Lebovic DI, Shifren JL, Vigne JL, Taylor RN** (1998) Vectorial secretion of vascular endothelial growth factor by polarized human endometrial epithelial cells. *Fertil Steril* 69, 909-915.
- Hotary K, Allen E, Punturieri A, Yana I, Weiss SJ** (2000) Regulation of cell invasion and morphogenesis in a three-dimensional type I collagen matrix by membrane-type matrix metalloproteinases 1, 2, and 3. *J Cell Biol* 149, 1309-1323.
- Hotary KB, Yana I, Sabeh F, Li XY, Holmbeck K, Birkedal-Hansen H, et al.** (2002) Matrix metalloproteinases (MMPs) regulate fibrin-invasive activity via MT1-MMP-dependent and -independent processes. *J Exp Med* 195, 295-308.
- Hu ZY, Liu YX, Liu K, Byrne S, Ny T, Feng Q, Ockleford CD** (1999) Expression of tissue type and urokinase type plasminogen activators as well as plasminogen activator inhibitor type-1 and type-2 in human and rhesus monkey placenta. *J Anat* 194, 183-195.
- Huppertz B, Peeters LL** (2005) Vascular biology in implantation and placentation. *Angiogenesis* 8,157-167.
- Hurskainen T, Hoyhtya M, Tuuttila A, Oikarinen A, Autio-Harmainen H** (1996) mRNA expression of TIMP-1, -2 and -3 and 92kd type IV collagenase in early human placenta and decidual membrane as studied by in situ hybridisation. *J of Histochem Cytochem* 44, 1379-1388.
- Hurskainen T, Seiki M, Apte SS, Syrjakallio-Ylitalo M, Sorsa T, Oikarinen A, et al.** (1998) Production of Membrane-type matrix metalloproteinase 1 (MT-MMP1) in early human placenta: a possible role in placental implantation. *J of Histochemistry and Cytochemistry* 46, 221-229.
- Hyder SM, Stancel GM** (1999) Regulation of angiogenic growth factors in the female reproductive tract by estrogens and progestins. *Mol Endocrinol* 13, 806-811.
- Hyder SM, Stancel GM** (2000) Regulation of VEGF in the reproductive tract by sex-steroid hormones. *Histol Histopathol* 15, 325-334.
- Inagaki N, Ung L, Otani T, Wilkinson D, Lopata A** (2003a) Uterine cavity matrix metalloproteinases and

- cytokines in patients with leiomyoma, adenomyosis or endometrial polyp. *Eur J Obstet Gynecol Reprod Biol* 111, 197-203.
- Inagaki N, Stern C, McBain J, Lopata A, Kornman L, Wilkinson D** (2003b) Analysis of intra-uterine cytokine concentration and matrix-metalloproteinase activity in women with recurrent failed embryo transfer *Hum Reprod* 18, 608-615.
- Iwahashi M, Muragaki Y, Ooshima A, Yamoto M, Nakano R** (1996) Alterations in distribution and composition of the extracellular matrix during decidualization of the human endometrium. *J Reprod Fertil* 108, 147-155.
- Iruela-Arispe ML, Rodriguez-manzanaque JC, Abujawdeh G** (1999) Endometrial endothelial cells express estrogen and progesterone receptors and exhibit a tissue response to angiogenic growth factors. *Microcirculation* 6, 127-140.
- Jackson MR, Carney EW, Lye SJ, Ritchie JW** (1994) Localization of two angiogenic growth factors (PDECGF and VEGF) in human placentae throughout gestation. *Placenta* 15, 341-353.
- Jaffe R, Woods JR Jr** (1993) Color Doppler imaging and in vivo assessment of the anatomy and physiology of the early uteroplacental circulation. *Fertil Steril* 60, 293-297.
- Jauniaux E, Watson AL, Hempstock J, Bao YP, Skepper JN, Burton GJ** (2000) Onset of maternal arterial blood flow and placental oxidative stress. A possible factor in human early pregnancy failure. *Am J Pathol* 157, 2111-2122.
- Jauniaux E, Burton GJ** (2005) Pathophysiology of histological changes in early pregnancy loss. *Placenta* 26, 114-123.
- Jokimaa V, Oksjoki S, Kujari H, Vuorio E, Anttila L** (2002) Altered expression of genes involved in the production and degradation of endometrial extracellular matrix in patients with unexplained infertility and recurrent miscarriages. *Mol Hum Reprod* 8, 1111-1116.
- Joswig A, Gabriel HD, Kibschull M, Winterhager E** (2003) Apoptosis in uterine epithelium and decidua in response to implantation: evidence for two different pathways. *Reprod Biol Endocrinol* 1, 44-52.
- Kam EP, Gardner L, Loke YW, King A.** (1999) The role of trophoblast in the physiological change in decidual spiral arteries. *Hum Reprod* 14, 2131-2138.
- Kapiteijn K, Koolwijk P, Van Der Weiden R, Helmerhorst F, Kooistra T, Van Hinsbergh VW** (2001) Steroids and cytokines in endometrial angiogenesis. *Anticancer Res* 21, 4231-4242.
- Kapiteijn K, Koolwijk P, van der Weiden RM, van Nieuw Amerongen G, Plaisier M, van Hinsbergh VW, et al.** (2006) Human embryo-conditioned medium stimulates in vitro endometrial angiogenesis. *Fertil Steril* 85, Suppl 1, 1232-1239.
- Kavaliar F** (2005) Investigation of recurrent miscarriages, a successful pregnancy is the most likely outcome. *BMJ* 331: 122-123.
- Kayisli UA, Luk J, Guzeloglu-Kayisli O, Seval Y, Demir R, Arici A** (2004) Regulation of angiogenic activity of human endometrial endothelial cells in culture by ovarian steroids. *J Clin Endocrinol Metab* 89, 5794-5802.
- Khaliq A, Li XF, Shams M, Sisi P, Acevedo CA, Whittle MJ, et al.** (1996) Localisation of placenta growth factor (PlGF) in human term placenta. *Growth Factors* 13, 243-250.
- Khaliq A, Dunk C, Jiang J, Shams M, Li XF, Acevedo C, et al.** (1999) Hypoxia downregulates placenta growth factor, whereas fetal growth restriction up-regulates placenta growth factor expression: molecular evidence for "placental hyperoxia" in intrauterine growth restriction. *Lab Invest* 79, 151-170.
- Khong TY, De Wolf F, Robertson WB, Brosens I** (1986) Inadequate maternal vascular response to placentation in pregnancies complicated by pre-eclampsia and by small-for-gestational age infants. *Br J Obstet Gynaecol* 93, 1049-1059.
- Khong TY** (1987) Immunohistologic study of the leukocytic infiltrate in maternal uterine tissues in normal and preeclamptic pregnancies at term. *Am J Reprod Immunol Microbiol.* 15, 1-8.
- Kim MH, Kitson RP, Albertsson P, Nannmark U, Basse PH, Kuppen PJ, et al.** (2000) Secreted and membrane-associated matrix metalloproteinases of IL-2-activated NK cells and their inhibitors. *J Immunol* 164, 5883-5889.

- Kimber SJ** (2000) Molecular interactions at the maternal-embryonic interface during the early phase of implantation. *Semin Reprod Med* 18,237-253.
- Kindzelskii AL, Amhad I, Keller D, Zhou MJ, Haugland RP, Garni-Wagner BA, et al.** (2004) Pericellular proteolysis by leukocytes and tumor cells on substrates: focal activation and the role of urokinase-type plasminogen activator. *Histochem Cell Biol* 121, 299-310.
- King A, Gardner L, Loke YW** (1996) Evaluation of oestrogen and progesterone receptor expression in uterine mucosal lymphocytes. *Hum Reprod* 11, 1079-1082.
- King A, Burrows T, Verma S, Hiby S, Loke YW** (1998) Human uterine lymphocytes. *Hum Reprod Update* 4, 480-485.
- King A** (2000) Uterine leucocytes and decidualisation. *Hum Reprod Update* 6, 28-36.
- Kingdom JCP, Kaufmann P** (1997) Oxygen and placental villous development: origins of fetal hypoxia. *Placenta* 18, 613-621.
- Kleemann R, Gervois PP, Verschuren L, Staels B, Princen HM, Kooistra T** (2003) Fibrates down-regulate IL-1-stimulated C-reactive protein gene expression in hepatocytes by reducing nuclear p50-NFkappa B-C/EBP-beta complex formation. *Blood* 101, 545-551.
- Kloosterman GJ** (1969) Over intra-uteriene groei en de intra-uteriene groeicurve. [Intrauterine growth and intrauterine growth curves]. *Ned Tijdschr Verloskd Gynaecol* 69, 349-365.
- Koolwijk P, van Erck MG, de Vree WJA, Vermeer MA, Weich HA, Hanemaaijer R, et al.** (1996) Cooperative effect of TNFalpha, bFGF, and VEGF on the formation of tubular structures of human microvascular endothelial cells in a fibrin matrix. Role of urokinase activity. *J Cell Biol* 132, 1177-1188.
- Koolwijk P, Kapiteijn K, Molenaar B, van Spronsen E, van Der Vecht B, Helmerhorst FM, et al.** (2001) Enhanced angiogenic capacity and urokinase-type plasminogen activator expression by endothelial cells isolated from human endometrium. *J Clin Endocrinol Metab* 86, 3359-3367.
- Korgun ET, Celik-Ozenci C, Acar N, Cayli S, Desoye G, Demir R** (2006) Location of cell cycle regulators cyclin B1, cyclin A, PCNA, Ki67 and cell cycle inhibitors p21, p27 and p57 in human first-trimester placenta and deciduas. *Histochem Cell Biol* 125, 615-624.
- Krikun G, Schatz F, Finlay T, Kadner S, Mesia A, Gerrets R, Lockwood CJ** (2000) Expression of angiopoietin-2 by human endometrial endothelial cells: regulation by hypoxia and inflammation. *Biochem Biophys Res Commun* 275, 159-163.
- Krikun G, Schatz F, Lockwood CJ** (2004a) Endometrial angiogenesis: from physiology to pathology. *Ann N Y Acad Sci* 1034, 27-35.
- Krikun G, Sakkas D, Schatz F, Buchwalder L, Hylton D, Tang C, Lockwood CJ** (2004b) Endometrial angiopoietin expression and modulation by thrombin and steroid hormones: a mechanism for abnormal angiogenesis following long-term progestin-only contraception. *Am J Pathol* 164, 2101-2107.
- Krikun G, Schatz F, Taylor R, Critchley HO, Rogers PA, Huang J, et al.** (2005) Endometrial endothelial cell steroid receptor expression and steroid effects on gene expression. *J Clin Endocrinol Metab* 90, 1812-1818.
- Kroon ME, Koolwijk P, van Goor H, Weidle UH, Collen A, van der Pluijm G, et al.** (1999) Role and localization of urokinase receptor in the formation of new microvascular structures in fibrin matrices. *Am J Pathol* 154, 1731-1742.
- Krüssel JS, Casan E, Raga F, Hirchenhain J, Wen Y, Huang H, et al.** (1999) Expression of mRNA for VEGF transmembrane receptors flt-1 and KDR and the soluble receptor sflt in cycling humane endometrium. *Mol Hum Reprod* 5, 452-458.
- Krüssel JS, Huang HY, Hirchenhain J, Bielfeld P, Cupisti S, Jeremias L, et al.** (2000a) Is there a place for biochemical embryonic preimplantational screening? *J Reprod Fertil Suppl* 55,147-59.
- Krüssel JS, Behr B, Hirchenhain J, Wen Y, Milki AA, Cupisti S, et al.** (2000b) Expression of vascular endothelial growth factor mRNA in human preimplantation embryos derived from tripronuclear zygotes. *Fertil Steril* 74, 1220-1226.
- Krüssel JS, Behr B, Milki AA, Hirchenhain J, Wen Y, Bielfeld P, et al.** (2001) Vascular endothelial growth

- factor (VEGF) mRNA splice variants are differentially expressed in human blastocysts. *Mol Hum Reprod* 7, 57-63.
- Krüssel JS, Bielfeld P, Polan ML, Simon C** (2003) Regulation of embryonic implantation. *Eur J Obstet Gynecol Reprod Biol* 110 S: S2-9.
- Kutteh WH** (1999) Recurrent pregnancy loss: an update. *Curr Opin Obstet Gynecol* 11, 435-439.
- Lafleur MA, Handsley MM, Knauper V, Murphy G, Edwards DR** 2002 Endothelial tubulogenesis within fibrin gels specifically requires the activity of membrane-type-matrix metalloproteinases (MT-MMPs). *J Cell Sci* 115, 3427-3438.
- Lam C, Lim KH, Karumanchi SA** (2005) Circulating angiogenic factors in the pathogenesis and prediction of preeclampsia. *Hypertension* 46, 1077-1085.
- Lamfers ML, Grimbergen JM, Aalders MC, Havenga MJ, de Vries MR, Huisman LG, et al.** (2002) Gene transfer of the urokinase-type plasminogen activator receptor-targeted matrix metalloproteinase inhibitor TIMP-1.ATF suppresses neointima formation more efficiently than tissue inhibitor of metalloproteinase-1. *Circ Res* 91, 945-952.
- Lash GE, Schiessl B, Kirkley M, Innes BA, Cooper A, Searle RF, et al.** (2006) Expression of angiogenic growth factors by uterine natural killer cells during early pregnancy. *Leukoc Biol* 80, 572-580.
- Lessey BA** (2000) Endometrial receptivity and the window of implantation. *Baillieres Best Pract Res Clin Obstet Gynaecol* 14, 775-788.
- Lessey BA** (2003) Two pathways of progesterone action in the human endometrium: implications for implantation and conception. *Steroids* 68, 809-815.
- Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Lu KF, et al.** (2004) Circulating angiogenic factors and the risk of preeclampsia. *N Eng J Med* 350, 672-683.
- Li TC, Warren MA, Hill CJ, Saravelos H** (1994) Morphology of the human endometrium in the peri-implantation period. *Ann N Y Acad Sci* 734, 169-184.
- Li XF, Charnock-Jones DS, Zhang E, Hiby S, Malik S, Day K, et al.** (2001a) Angiogenic growth factor messenger ribonucleic acids in uterine natural killer cells. *J Clin Endocrinol Metab* 86, 1823-1834.
- Li H, Lindenmeyer F, Grenet C, Opolon P, Menashi S, Soria C, et al.** (2001b) AdTIMP-2 inhibits tumor growth, angiogenesis, and metastasis, and prolongs survival in mice. *Hum Gene Ther* 12, 515-526.
- Licht P, Russu V, Wildt L** (2001) On the role of human chorionic gonadotropin (hCG) in the embryonic endometrial microenvironment: implications for differentiation and implantation. *Semin Reprod Med* 19, 37-47.
- Licht P, von Wolff M, Berkholz A, Wildt L** (2003) Evidence for cycle-dependent expression of full-length human chorionic gonadotropin/luteinizing hormone receptor mRNA in human endometrium and decidua. *Fertil Steril* 79 Suppl 1, 718-723.
- Lindhard A, Bentin-Ley U, Ravn V, Islin H, Hviid T, Rex S, et al.** (2002) Biochemical evaluation of endometrial function at the time of implantation. *Fertil Steril* 78, 221-233.
- Lisman BA, Boer K, Bleker OP, van Wely M, van Groningen K, Exalto N** (2004) Abnormal development of the vasculosyncytial membrane in early pregnancy failure. *Fertil Steril* 82, 654-660.
- Llano E, Pendas AM, Freije JP, Nakano A, Knauper V, Murphy G, et al.** (1999) Identification and characterization of human MT5-MMP, a new membrane-bound activator of progelatinase a overexpressed in brain tumors. *Cancer Res* 59, 2570-2576.
- Lockwood CJ, Krikun G, Hausknecht VA, Papp C, Schatz F** (1998) Matrix metalloproteinase and matrix metalloproteinase inhibitor expression in endometrial stromal cells during progestin-initiated decidualization and menstruation-related progestin withdrawal. *Endocrinology* 139, 4607-4613.
- Lopata A** (1996) Blastocyst-endometrial interaction: an appraisal of some old and new ideas. *Mol Hum Reprod* 2, 519-525.
- Lunell NO, Sarby B, Lewander R, Nylund L** (1979) Comparison of uteroplacental blood flow in normal and intrauterine growth retarded pregnancy. *Gynaecol Obstet Invest* 10, 106-118.
- Luttun A, Tjwa M, Moons L, Wu Y, Angelillo-Scherrer A, Liao F, et al.** (2002) Revascularization of ischemic

- tissues by PlGF treatment, and inhibition of tumor angiogenesis, arthritis and atherosclerosis by anti-Flt1. *Nat Med* 8, 831-840.
- Luttun A, Carmeliet P** (2003) Soluble VEGF receptor Flt1: the elusive preeclampsia factor discovered? *J Clin Invest* 111, 600-602.
- Lyall F** (1997) Placental expression of VEGF in placentae of preeclampsia and intrauterine growth restriction does not support placental hypoxia at delivery. *Placenta* 18, 269-276.
- Maas JW, Groothuis PG, Dunselman GA, de Goeij AF, Struyker Boudier HA, et al.** (2001) Endometrial angiogenesis throughout the human menstrual cycle. *Hum Reprod* 16, 1557-1561.
- Maatta M, Soini Y, Liakka A, Autio-Harminen H** (2000) Localization of MT1-MMP, TIMP-1, TIMP-2, and TIMP-3 messenger RNA in normal, hyperplastic, and neoplastic endometrium. Enhanced expression by endometrial adenocarcinomas is associated with low differentiation. *Am J Clin Pathol* 114, 402-411.
- Maciag T, Cerundolo J, Ilsley S, Kelley PR, Forand R** (1979) An endothelial cell growth factor from bovine hypothalamus: identification and partial characterization. *Proc Natl Acad Sci U S A* 76, 5674-5678.
- Macklon NS, Geraedts JPM, Fauser BCJM** (2002) Conception to ungoing pregnancy: "the black box" of early pregnancy loss. *Hum Reprod Update* 8, 333-343.
- Maisonpierre PC, Suri C, Jones PF, Bartunkova S, Wiegand SJ, Radziejewski C, et al.** (1997) Angiopoietin-2, a natural antagonist for Tie2 that disrupts in vivo angiogenesis. *Science* 277, 55-60.
- Marx L, Arck P, Kapp M, Kieslich C, Dietl J** (1999) Leukocyte populations, hormone receptors and apoptosis in eutopic and ectopic first-trimester human pregnancies. *Hum Reprod* 14, 1111-1117.
- Maynard SE, Min J, Merchan J, Lim KH, Li J, Mondal S, et al.** (2003) Excess placental soluble fms-like tyrosine kinase 1 (sflt-1) may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia. *J Clin Invest* 111, 649-658.
- Meduri G, Bausero P, Perrot-Applanat M** (2000) Expression of vascular endothelial growth factor receptors in the human endometrium: modulation during the menstrual cycle. *Biol Reprod* 62, 439-447.
- Meegdes BH, Ingenhoes R, Peeters LL, Exalto N** (1988) Early pregnancy wastage: relationship between chorionic vascularization and embryonic development. *Fertil Steril* 49, 216-220.
- Michimata T, Ogasawara MS, Tsuda H, Suzumori K, Aoki K, Sakai M, et al.** (2002) Distributions of endometrial NK cells, B cells, T cells, and Th2/Tc2 cells fail to predict pregnancy outcome following recurrent abortion. *Am J Reprod Immunol* 47, 196-202.
- Moller B, Rasmussen C, Lindblom B, Olovsson M** (2001) Expression of the angiogenic growth factors VEGF, EGF, FGF-2 and their receptors in normal endometrium during the menstrual cycle. *Mol Hum Reprod* 7, 65-72.
- Morgan KG, Wilkinson N, Buckley CH** (1996) Angiogenesis in normal, hyperplastic, and neoplastic endometrium. *J Pathol* 179, 317-320.
- Multhaupt HA, Mazar A, Cines DB, Warhol MJ, McCrae KR** (1994) Expression of urokinase receptors by human trophoblast. A histochemical and ultra-structural analysis. *Lab Invest* 71, 392-400.
- Mutter G, Ferenczy A.** (2002) Anatomy and histology of the uterine corpus. In Kurman R (Ed.). *Blaustein's Pathology of the Female Genital Tract* (Springer-Verlag, New York, NY), 383-419.
- Nagy JA, Dvorak AM, Dvorak HF** (2003) VEGF-A (164/165) and PlGF: roles in angiogenesis and arteriogenesis. *Trends Cardiovasc Med* 13, 169-175.
- Nakano M, Hara T, Hayama T, Obara M, Yoshizato K, Ohama K** (2001) Membrane-type 1 matrix metalloproteinase is induced in decidual stroma without direct invasion of trophoblast. *Mol Hum Reprod* 7, 271-277.
- Nap AW, Dunselman GA, de Goeij AF, Evers JL, Groothuis PG** (2004) Inhibiting MMP activity prevents the development of endometriosis in the chicken chorioallantoic membrane model. *Hum Reprod* 19, 2180-2187.
- Nardo LG, Nikas G, Makrigiannakis A** (2003) Molecules in blastocyst implantation. Role of matrix metalloproteinases, cytokines and growth factors. *J Reprod Med* 48, 137-147.
- Nawrocki B, Polette M, Marchand V, Maquoi E, Beorchia A, Tournier JM, et al.** (1996) Membrane-type Matrix metalloproteinase-1 expression at the site of human placentation. *Placenta* 17, 565-572.

- Nelen WL, Bulten J, Steegers EA, Blom HJ, Hanselaar AG, Eskes TK** (2000) Maternal homocysteine and chorionic vascularization in recurrent early pregnancy loss. *Hum Reprod* 15, 954-960.
- Norwitz ER, Schust DJ, Fisher SJ** (2001) Implantation and the survival of early pregnancy. *New Engl J Med* 345, 1400-1408.
- Noyes RW, Hertig AT, Rock J** (1975) Dating the endometrial biopsy. *Am J Obstet Gynecol* 122, 262-263.
- Okada Y, Asahina T, Kobayashi T, Goto J, Terao T** (2001) Studies on the mechanism of edematous changes at the endometrial stroma for implantation. *Semin Thromb Hemost* 27, 67-77.
- Ong S, Lash G, Baker PN** (2000) Angiogenesis and placental growth in normal and compromised pregnancies. *Baillieres Best Pract Res Clin Obstet Gynaecol* 14, 969-980.
- O'Shea JD, Kleinfeld RG, Morrow HA** (1983) Ultrastructure of decidualization in the pseudopregnant rat. *Am J Anat* 166, 271-298.
- Parhar RS, Yagel S, Lala PK** (1989) PGE<sub>2</sub>-mediated immunosuppression by first-trimester human decidual cells blocks activation of maternal leukocytes in the decidua with potential anti-trophoblast activity. *Cell Immunol* 120, 61-74.
- Pei D** (1999) Identification and characterization of the fifth membrane-type matrix metalloproteinase MT<sub>5</sub>-MMP. *J Biol Chem* 274, 8925-8932.
- Pepper MS, Belin D, Montesano R, Orci L, Vassalli JD** (1990) Transforming growth factor-beta 1 modulates basic fibroblast growth factor-induced proteolytic and angiogenic properties of endothelial cells in vitro. *J Cell Biol* 111, 743-755.
- Pepper MS, Ferrara N, Orci L, Montesano R** (1995) Leukemia inhibitory factor (LIF) inhibits angiogenesis in vitro. *J Cell Sci* 108, 73-83.
- Pepper MS** (1997) Manipulating angiogenesis. From basic science to the bedside. *Arterioscler Thromb Vasc Biol* 17, 605-619.
- Pepper MS** (2001a) Role of the matrix metalloproteinase and plasminogen activator-plasmin systems in angiogenesis. *Arterioscler Thromb Vasc Biol* 21, 1104-1117.
- Pepper MS** (2001b) Extracellular proteolysis and angiogenesis. *Thromb Haemost* 86, 346-355.
- Perrot-Appinat M, Ancelin M, Buteau-Lozano H, Meduri G and Bausero P** (2000) Ovarian steroids in endometrial angiogenesis. *Steroids* 65, 599-603.
- Pierleoni C, Samuelsen GB, Graem N, Ronne E, Nielsen BS, Kaufmann P, et al.** (1998) Immunohistochemical identification of the receptor for uPA associated with fibrin deposition in normal and ectopic human placenta. *Placenta* 19, 501-508.
- Pijnenborg R, Bland JM, Robertson WB, Brosens I** (1983) Uteroplacental arterial changes related to interstitial trophoblast migration in early human pregnancy. *Placenta* 4, 397-413.
- Pijnenborg R, Anthony J, Davey DA, Rees A, Tiltman A, Vercruyse L** (1991) Placental bed spiral arteries in the hypertensive disorders of pregnancy. *Br J Obstet Gynaecol* 98, 648-655.
- Pijnenborg R** (1998) The origin and future of placental bed research. *Eur J Obstet Gynecol Reprod Biol* 81, 185-190.
- Plaisier M, Kapiteijn K, Koolwijk P, Fijten C, Hanemaaijer R, Grimbergen JM, et al.** (2004) Involvement of Membrane-Type Matrix Metalloproteinases (MT-MMPs) in Capillary Tube Formation by Human Endometrial Microvascular Endothelial Cells: Role of MT<sub>3</sub>-MMP. *J.Clin.Endocrinol.Metab* 89, 5828-5836.
- Plaisier M, Koolwijk P, Hanemaaijer R, Verwey A, Weiden RM, Risse KJ, et al.** (2006) Membrane-type matrix metalloproteinases and vascularization in human endometrium during the menstrual cycle. *Mol Hum Reprod* 12, 11-18.
- Plaisier M, Rodrigues S, Willems F, Koolwijk P, van Hinsbergh VW, Helmerhorst FM** (2007) Different degree of vascularisation and its relation to the expression of VEGF, PlGF, angiopoietins and their receptors in first-trimester decidua. *Fertility Sterility* 88, 176-187.
- Plaisier M, Koolwijk P, Willems F, van Hinsbergh VWM, Helmerhorst FM** (2008) The expression of pericellular acting proteases in human first-trimester decidua. *Mol Hum Reprod* 14, 41-51.
- Quack K, Vassiliadou N, Pudney J, Anderson DJ, Hill JA** (2001) Leucocyte activation in the decidua of

- chromosomally normal and abnormal fetuses from women with recurrent abortion. *Human Reprod* 16, 949-955.
- Quax PH, Lamfers ML, Lardenoye JH, Grimbergen JM, de Vries MR, Slomp J, et al.** (2001) Adenoviral expression of a urokinase receptor-targeted protease inhibitor inhibits neointima formation in murine and human blood vessels. *Circulation* 103, 562-569.
- Quenby S, Bates M, Doig T, Brewster J, Lewis-Jones DI, Johnson PM, et al.** (1999) Pre-implantation endometrial leukocytes in women with recurrent miscarriage. *Hum Reprod* 14, 2386-2391.
- Quenby S, Farquharson R** (2006) Uterine natural killer cells, implantation failure and recurrent miscarriage. *Reprod Biomed Online* 13, 24-28.
- Rai R, Regan L** (2006) Recurrent miscarriage. *The Lancet* 368, 601-611.
- Ranheim T, Staff AC, Henriksen T** (2001) VEGF mRNA is unaltered in decidual and placental tissues in preeclampsia at delivery. *Acta Obstet Gynecol Scand* 80, 93-98.
- Red-Horse K, Zhou Y, Genbacev O, Prakobphol A, Foulk R, McMaster M, et al.** (2004) Trophoblast differentiation during embryo implantation and formation of the maternal-foetal interface. *J Clin Invest* 114: 744-754.
- Regnault TRH, de Vrijer B, Galan HL, Davidsen ML, Trembler KA, Battaglia FC, et al.** (2003) The relationship between transplacental O<sub>2</sub> diffusion and placental expression of PlGF, VEGF, and their receptors in a placental insufficiency model of fetal growth restriction. *J Physiol* 550, 641-656.
- Reshef E, Lei ZM, Rao CV, Pridham DD, Chegini N, Luborsky JL** (1990) The presence of gonadotropin receptors in non-pregnant human uterus, human placenta, fetal membranes and decidua. *J Clin Endocrinol Metab* 70, 421-430.
- Reuning U, Sperl S, Kopitz C, Kessler H, Kruger A, Schmitt M, et al.** (2003) Urokinase-type plasminogen activator (uPA) and its receptor (uPAR): development of antagonists of uPA/uPAR interaction and their effects in vitro and in vivo. *Curr Pharm Des* 9, 1529-1543.
- Rey JM, Pujol P, Dechaud H, Edouard E, Hedon B, Maudelonde T** (1998) Expression of oestrogen receptor-alpha splicing variants and oestrogen receptor-beta in endometrium of infertile patients. *Mol Hum Reprod* 4, 641-647.
- Rijnders PM, Jansen CA** (1998) The predictive value of day 3 embryo morphology regarding blastocyst formation, pregnancy and implantation rate after day 5 transfer following in-vitro fertilization or intracytoplasmic sperm injection. *Hum Reprod* 13, 2869-2873.
- Robb AO, Mills NL, Newby DE, Denison FC** (2007) Endothelial progenitor cells in pregnancy. *Reproduction*. 133, 1-9.
- Roberts JM, Cooper DW** (2001) Pathogenesis and genetics of pre-eclampsia. *The Lancet* 357, 53-56.
- Roberts JM, Lain KY** (2002) Recent Insights into pathogenesis of pre-eclampsia. *Placenta* 23, 359-372.
- Rodgers WH, Matrisian LM, Giudice LC, Dsupin B, Cannon P, Svitek C, et al.** (1994) Patterns of matrix metalloproteinase expression in cycling endometrium imply differential functions and regulation by steroid hormones. *J Clin Invest* 94, 946-953.
- Rogers PA, Au CL, Affandi B** (1993) Endometrial microvascular density during the normal menstrual cycle and following exposure to long-term levonorgestrel. *Hum Reprod* 8, 1396-1404.
- Rogers PA, Gargett CE** (1998) Endometrial angiogenesis. *Angiogenesis* 2, 287-294.
- Sakkas D, Lu C, Zulfikaroglu E, Neuber E, Taylor HS** (2003) A soluble molecule secreted by human blastocysts modulates regulation of HOXA10 expression in an epithelial endometrial cell line. *Fertil Steril* 80, 1169-1174.
- Salamonsen LA** (1994) Matrix metalloproteinases and endometrial remodelling. *Matrix Cell Biol Int* 18, 1139-1144.
- Salamonsen LA., Woolley DE** (1996) Matrix metalloproteinases in normal menstruation. *Hum Reprod* 11 S2,124-133.
- Salamonsen LA, Butt AR, Hammond FR, Garcia S, Zhang J** (1997) Production of endometrial MMPs, but not their tissue inhibitors, is modulated by progesterone withdrawal in an in vitro model for menstruation. *J Clin Endocrin Metab* 82, 1409-1415.

- Salamonsen LA.** (1999) Role of proteases in implantation. *Reviews of Reproduction* 4, 11-22.
- Salamonsen LA, Dimitriadis E, Robb L** (2000) Cytokines in implantation. *Semin Reprod Med* 18, 299-310.
- Salamonsen L.A., Nie G, Findlay JK** (2002) Newly identified endometrial genes of importance for implantation. *J Reprod Immunol* 53, 215-225.
- Salamonsen LA, Dimitriadis E, Jones RL, Nie G** (2003) Complex regulation of decidualization: a role for cytokines and proteases, a review. *Placenta* 24 Suppl A: S76-85.
- Seiki M, Yana I** (2003) Roles of pericellular proteolysis by membrane type-1 matrix metalloproteinase in cancer invasion and angiogenesis. *Cancer Sci* 94, 569-574.
- Sengupta J, Lalitkumar PGL, Najwa AR, Charnock-Jones DS, Evans AL, Sharkey AM, et al.** (2007) Immunoneutilization of vascular endothelial growth factor inhibits pregnancy establishment in the rhesus monkey. *Reproduction* 133, 1199-1211.
- Sgambati E, Marini M, Zappoli Thyron GD, Paretti E, Mello G, Orlando C, et al.** (2004) VEGF expression in the placenta from pregnancies complicated by hypertensive disorders. *Br J Obstet Gyn* 111, 564-570.
- Sharkey AM, Charnock-Jones DS, Boocock CA, Brown KD, Smith SK** (1993) Expression of mRNA for VEGF in human placenta. *J of Reprod Fert* 99, 609-615.
- Sharkey AM, Day K, McPherson A, Malik S, Licence D, Smith SK, et al.** (2000) Vascular endothelial growth factor expression in humane endometrium is regulated by hypoxia. *J Clin Endocrinol Metab* 85, 402-409.
- Sherer DM, Abulafia O** (2001) Angiogenesis during implantation, and placental and early embryonic development. *Placenta* 2001 22, 1-13.
- Shifren JL, Tseng JF, Zaloudek CJ, Ryan IP, Meng YG, Ferrara N, et al.** (1996) Ovarian steroid regulation of vascular endothelial growth factor in the human endometrium: implications for angiogenesis during the menstrual cycle and in the pathogenesis of endometriosis. *J Clin Endocrinol.Metab* 81, 3112-3118.
- Shimada S, Kato EH, Morikawa M, Iwabuchi K, Nishida R, Kishi R, et al.**(2004) No difference in natural killer or natural killer T-cell population, but aberrant T-helper cell population in the endometrium of women with repeated miscarriage. *Hum Reprod* 19, 1018-1024.
- Shimada S, Nishida R, Takeda M, Iwabuchi K, Kishi R, Onoe K, et al.** (2006) Natural killer, natural killer T, helper and cytotoxic T cells in the decidua from sporadic miscarriage. *Am J Reprod Immunol* 56, 193-200.
- Shofuda KI, Hasenstab D, Kenagy R, Shofuda T, Li ZY, Lieber A, et al.** (2001) Membrane-type matrix metalloproteinase-1 and -3 activity in primate smooth muscle cells. *FASEB J* 15, 2010-2012.
- Shore VH, Wang TH, Wang CL, Torry RJ, Caudle MR, Torry DS** (1997) Vascular endothelial growth factor, placenta growth factor and their receptors in isolated human trophoblast. *Placenta* 18, 657-665.
- Skinner JL, Riley SC, Gebbie AE, Glasier AF, Critchley HO** (1999) Regulation of matrix metalloproteinase-9 in endometrium during the menstrual cycle and following administration of intrauterine levonorgestrel. *Hum Reprod* 14, 793-799.
- Simoncini T, Mannella P, Fornari L, Caruso A, Varone G, Genazzani AR** (2003) In vitro effects of progesterone and progestins on vascular cells. *Steroids* 68, 831-836.
- Simpson JL, Gray RH, Queenan J, Barbato M, Perez A, Mena P, et al.** (1994) Risk of recurrent spontaneous abortion for pregnancies discovered in the fifth week of gestation. *Lancet* 344, 964.
- Sindram-Trujillo AP, Scherjon SA, van Hulst-van Miert PP, van Schip JJ, Kanhai HH, Roelen DL, et al.** (2003) Differential distribution of NK cells in decidua basalis compared with decidua parietalis after un-complicated human term pregnancy. *Hum Immunol* 64, 921-929.
- Singer CF, Marbaix E, Lemoine P, Courtoy PJ, Eeckhout Y** (1999) Local cytokines induce differential expression of matrix metalloproteinases but not their tissue inhibitors in human endometrial fibroblasts. *Eur J Biochem* 259, 40-45.
- Smith SK** (1998) Angiogenesis, vascular endothelial growth factor and the endometrium. *Hum Reprod Update* 4, 509-519.

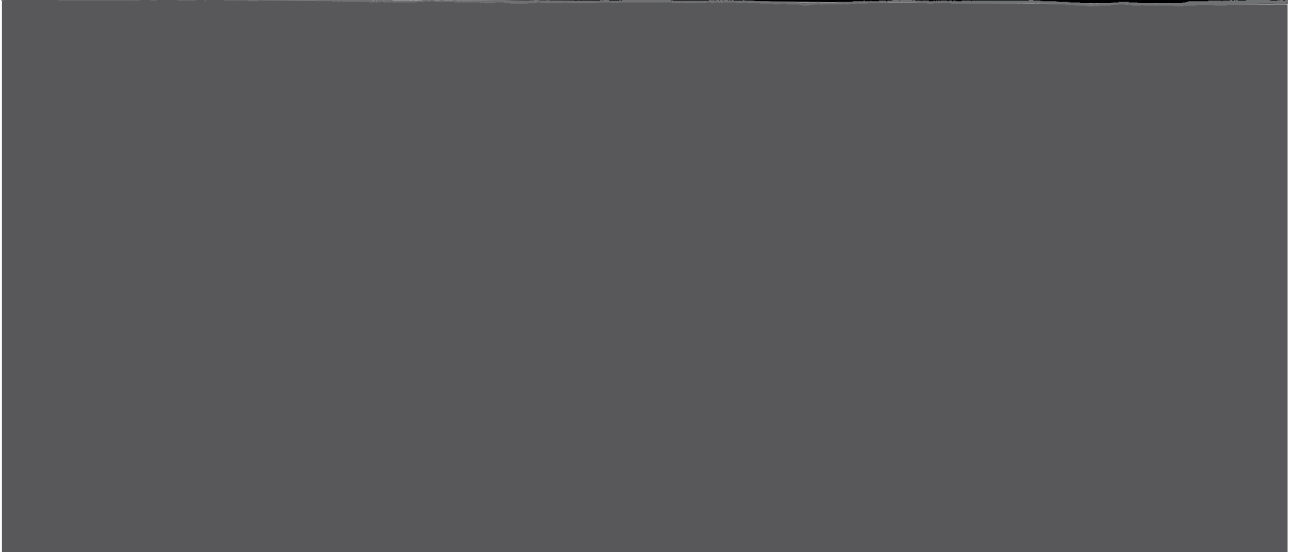
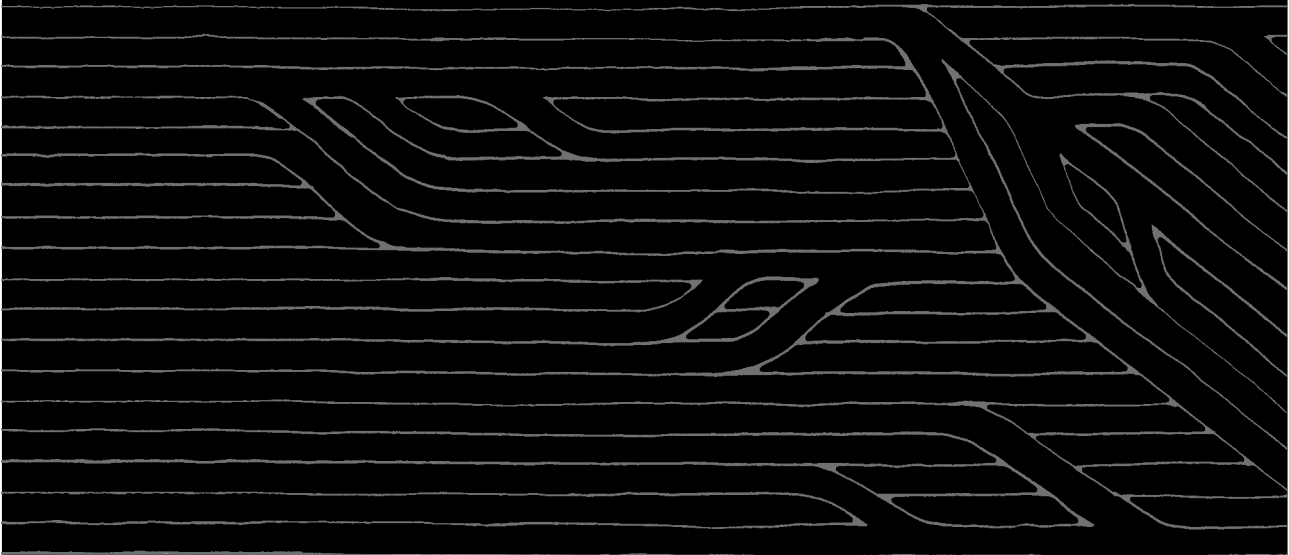


- Smith SK** (2000) Angiogenesis and implantation. *Hum Reprod* 15 Suppl 6, 59-66.
- Smith SK** (2001) Regulation of angiogenesis in the endometrium. *Trends Endocrinol Metab* 12, 147-151.
- Solberg H, Rinkenberger J, Dano K, Werb Z, Lund LR** (2003) A functional overlap of plasminogen and MMPs regulates vascularisation during placental development. *Development* 130, 4439-4450.
- Sounni NE, Devy L, Hajitou A, Frankenne F, Munaut C, Gilles C, et al.** (2002) MT1-MMP expression promotes tumor growth and angiogenesis through an up-regulation of vascular endothelial growth factor expression. *FASEB J* 16, 555-564.
- Specht K, Richter T, Muller U, Walch A, Werner M, Hofer H** (2001) Quantitative gene expression analysis in microdissected archival formalin-fixed and paraffin-embedded tumor tissue. *Am J Pathol* 158, 419-429.
- Spengers ED, Kluff C** (1987) Plasminogen activator inhibitors. *Blood* 69, 381-387.
- Stetler-Stevenson W** (1999) Matrix metalloproteinases in angiogenesis: a moving target for therapeutic intervention. *J Clin Invest* 103, 1237-1241.
- Stewart CL, Kaspar P, Brunet LJ, Bhatt H, Gadi I, Kontgen F, et al.** (1992) Blastocyst implantation depends on maternal expression of leukaemia inhibitory factor. *Nature* 359, 76-79.
- Sugimoto H, Hamano Y, Charytan D, Cosgrove D, Kieran M, Sudhakar A, et al.** (2003) Neutralization of circulating vascular endothelial growth factor (VEGF) by anti-VEGF antibodies and soluble VEGF receptor 1 (sFlt-1) induces proteinuria. *J Biol Chem* 278, 12605-12608.
- Sugino N, Kashida S, Karube-Harada A, Takiguchi S, Kato H** (2002) Expression of VEGF and its receptors in human endometrium throughout the menstrual cycle and in early pregnancy. *Reproduction* 123, 379-387.
- Sunder S, Lenton EA** (2000) Endocrinology of the peri-implantation period. *Baillieres Best Pract Res Clin Obstet Gynaecol* 14, 789-800.
- Suri C, Jones PF, Patan S, Bartunkova S, Maisonpierre PC, Davis S, et al.** (1996) Requisite role of angiopoietin-1, a ligand for the TIE2 receptor, during embryonic angiogenesis. *Cell* 87, 1171-1180.
- Suri C, McClain J, Thurston G, McDonald DM, Zhou H, Oldmixon EH, et al.** (1998) Increased vascularization in mice overexpressing angiopoietin-1. *Science* 282, 468-471.
- Tabibzadeh S, Babaknia A.** (1995) The signals and molecular pathways involved in implantation, a symbiotic interaction between blastocyst and endometrium involving adhesion and tissue invasion. *Hum Reprod* 10, 1579-1602.
- Tabibzadeh S, Babaknia A** (1996) The signals and molecular pathways involved in human menstruation, a unique process of tissue destruction and remodelling. *Mol Hum Reprod* 2, 77-92.
- Tanaka SS, Togooka Y, Sato H, Seiki M, Tojo H, Tachi C** (1998) Expression and localisation of membrane type matrix metalloproteinase-1 (MT1-MMP) in trophoblast cells of cultured mouse blastocysts and ectoplacental cones. *Placenta* 19, 41-48.
- Tarabozetti G, D'Ascenzo S, Borsotti P, Giavazzi R, Pavan A, Dolo V** (2002) Shedding of the matrix metalloproteinases MMP-2, MMP-9, and MT1-MMP as membrane vesicle-associated components by endothelial cells. *Am J Pathol* 160, 673-680.
- Taylor RN, Grimwood J, Taylor RS, McMaser MT, Fisher SJ, North RA** (2003) Longitudinal serum concentrations of PlGF: evidence for abnormal placental angiogenesis in pathologic pregnancies. *AJOG* 188, 177-182.
- Tjoa ML, Levine RJ, Karumanchi SA** (2007) Angiogenic factors in preeclampsia. *Front Biosci* 112, 2395-2402.
- Torry DS, Torry RJ** (1997) Angiogenesis and the expression of vascular endothelial growth factor in endometrium and placenta. *Am J Reprod Immunol* 37, 21-29.
- Torry DS, Wang HS, Wang TH, Caudle MR, Torry RJ** (1998) Preeclampsia is associated with reduced serum levels of placenta growth factor. *Am J Obstet Gynecol* 179, 1539-1544.
- Torry DS, Ahn H, Barnes EL, Torry RJ** (1999) Placenta growth factor: potential role in pregnancy. *Am J Reprod Immunol* 41, 79-85.
- Torry DS, Hinrichs M, Torry RJ** (2004) Determinants of placental vascularity. *Am J of Reprod Immunol* 51, 257-268.

- Toth P, Li X, Rao CV, Lincoln SR, Sanfilippo JS, Spinnato JA, et al.** (1994) Expression of functional human chorionic gonadotropin/human luteinizing hormone receptor gene in human uterine arteries. *J Clin Endocrinol Metab* 79, 307-315.
- Toth P, Lukacs H, Gimes G, Sebestyen A, Pasztor N, Paulin F, et al.** (2001) Clinical importance of vascular LH/hCG receptors-a review. *Reprod Biol* 1, 5-11.
- Trundley A, Moffett A** (2004) Human uterine leucocytes and pregnancy. *Tissue Antigens* 63, 1-12.
- Tsatsaris V, Goffin F, Munaut C, Brichant JF, Pignon MR, Noel A, et al.** (2003) Overexpression of the soluble vascular endothelial growth factor receptor in preeclamptic patients: pathological consequences. *J Clin Endocrinol Metab* 88, 5555-5563.
- Tuckerman E, Laird SM, Prakash A, Li TC** (2007) Prognostic value of the measurement of uterine natural killer cells in the endometrium of women with recurrent miscarriage. *Hum Reprod* 22, 2208-2213.
- Vagnoni KE, Zheng J, Magness RR** (1998) Matrix metalloproteinases-2 and -9, and tissue inhibitor of metalloproteinases-1 of the sheep placenta during the last third of gestation. *Placenta* 19:447-455
- Vailhe B, Dietl J, Kapp M, Toth B, Arck P** (1999) Increased blood vessel density in decidua parietalis is associated with spontaneous human first-trimester abortion. *Hum Reprod* 14, 1628-1634.
- Van Boheemen PA, Van den Hoogen CM and Koolwijk P** (1995) Comparison of the inhibition of urokinase-type plasminogen activator (u-PA) activity by monoclonal antibodies specific for u-PA as assessed by different assays. *Fibrinolysis* 9, 343-349.
- Van den Heuvel MJ, Horrocks J, Bashar S, Taylor S, Burke S, Hatta K, et al.** (2005a) Menstrual cycle hormones induce changes in functional interactions between lymphocytes and decidual vascular endothelial cells. *J Clin Endocrinol Metab* 90, 2835-2842.
- Van den Heuvel MJ, Chantakru S, Xuemei X, Evans SS, Tekpetey F, Mote PA, et al.** (2005b) Trafficking of circulating pro-NK cells to the decidualizing uterus: regulatory mechanisms in the mouse and human. *Immunol Invest* 34 (3):273-293.
- Van der Laan WH, Quax PH, Seemayer CA, Huisman LG, Pieterman EJ, Grimbergen JM, et al.** (2003) Cartilage degradation and invasion by rheumatoid synovial fibroblasts is inhibited by gene transfer of TIMP-1 and TIMP-3. *Gene Ther* 10, 234-242.
- Van der Weiden RM, Helmerhorst FM, Keirse MJ** (1991) Influence of prostaglandins and platelet activating factor on implantation. *Hum Reprod* 6, 436-442.
- Van der Weiden RM, Wisse LJ, Helmerhorst FM, Keirse MJ, Poelmann RE** (1996) Immunohistochemical and ultrastructural localization of prostaglandin H synthase in the preimplantation mouse embryo. *J Reprod Fertil* 107, 161-166.
- Van Hinsbergh VWM, Sprengers ED, Kooistra T** (1987) Effect of thrombin on the production of plasminogen activators and PA inhibitor-1 by human foreskin microvascular endothelial cells. *Thromb Haemost* 57, 148-153.
- Van Hinsbergh VWM, Engelse MA, Quax PHA** (2006) Pericellular proteases in angiogenesis and vasculogenesis. *Arterioscler Thromb Vasc Biol* 26, 716-728.
- Vasse M, Pourtau J, Trochon V, Muraine M, Vannier J, Lu H, et al.** (1999) Oncostatin M induces angiogenesis in vitro and in vivo. *Arterioscler Thromb Vasc Biol* 19, 1835-1842.
- Vernon RB, Lara SL, Drake CJ, Angello JC, Little CD, Wight TN, et al.** (1995) Organized type I collagen influences endothelial patterns during "spontaneous angiogenesis in vitro": planar cultures as models of vascular development. *In Vitro Cell Dev Biol Anim* 31, 120-131.
- Visse R, Nagase H** (2003) Matrix metalloproteinases and tissue inhibitors of metalloproteinases: structure, function, and biochemistry. *Circ Res* 92, 827-839.
- Von Rango U, Krusche CA, Kertschanska S, Alfer J, Kaufmann P, Beier HM** (2003) Apoptosis of extravillous trophoblast cells limits the trophoblast invasion in uterine but not in tubal pregnancy during first-trimester. *Placenta* 24, 929-940.
- Vuorela P, Hatva E, Lymboussaki A, Kaipainen A, Joukov V, Persico MG, et al.** (1997) Expression of vascular endothelial growth factor and placental growth factor in human placenta. *Biol of Reprod* 56, 489-494.

- Vuorela P, Carpen O, Tulppala M, Halmesmaki E** (2000) VEGF, its receptors and the tie receptors in recurrent miscarriage. *Mol Hum Reprod* 6, 276-282.
- Wang X, Chen C, Wang L, Chen D, Guang W, French J** (2003) Conception, early pregnancy loss, and time to clinical pregnancy: a population based prospective study. *Fert Ster* 79, 577-584.
- Werb Z** (1997) ECM and cell surface proteolysis: regulating cellular ecology. *Cell* 91, 439-442.
- Weston G, Rogers PA** (2000) Endometrial angiogenesis. *Baillieres Best Pract Res Clin Obstet Gynaecol* 14, 919-936.
- Wilcox AJ, Weinberg CR, O'Connor JF, Baird DD, Schlatterer JP, Canfield RE, et al.** (1988) Incidence of early loss of pregnancy. *New Eng J Med* 319, 189-194.
- Will H, Atkinson SJ, Butler GS, Smith B, Murphy G** (1996) The soluble catalytic domain of membrane type 1 matrix metalloproteinase cleaves the propeptide of progelatinase A and initiates autoprolytic activation. *J of Biol Chem* 271, 17119-17123.
- Woessner JFJ** (2001) That impish TIMP: the tissue inhibitor of metalloproteinases-3. *J Clin Invest* 108, 799-800.
- Wulff C, Wilson H, Largue P, Duncan WC, Armstrong DG, Fraser HM** (2000) Angiogenesis in the human corpus luteum: localization and changes in angiopoietins, tie-2, and vascular endothelial growth factor messenger ribonucleic acid. *J Clin Endocrinol Metab* 85, 4302-4309.
- Yagel S, Geva TE, Solomon H, Shimonovitz S, Reich R, Finci-Yeheskel Z, et al.** (1993) High levels of human chorionic gonadotropin retard first-trimester trophoblast invasion in vitro by decreasing urokinase plasminogen activator and collagenase activities. *J Clin Endocrinol Metab* 77, 1506-1511.
- Yuan HT, Haig D, Karumanchi SA** (2005) Angiogenic factors in the pathogenesis of preeclampsia. *Curr Top Dev Biol* 71, 297-312.
- Zhang J, Hampton AL, Nie G, Salamonsen LA** (2000) Progesterone inhibits activation of latent matrix metalloproteinase (MMP)-2 by membrane-type 1 MMP: enzymes coordinately expressed in human endometrium. *Biol Reprod* 62, 85-94.
- Zhang EG, Smith SK, Baker PN, Charnock-Jones DS** (2001) The regulation and localization of angiopoietin-1, -2, and their receptor Tie2 in normal and pathologic human placentae. *Mol Med* 7, 624-635.
- Zhang EG, Burton GJ, Smith SK, Charnock-Jones DS** (2002) Placental vessel adaptation during gestation and to high altitude: changes in diameter and perivascular cell coverage. *Placenta* 23, 751-762.
- Zhang J, Salamonsen LA.** (2002) In vivo evidence for active matrix metalloproteinases in human endometrium supports their role in tissue breakdown at menstruation. *J Clin Endocrinol Metab* 87, 2346-2351.
- Zhou Y, Damsky CH, Fisher SJ** (1997) Preeclampsia is associated with failure of human cytotrophoblasts to mimic a vascular adhesion phenotype. One cause of defective endovascular invasion in this syndrome? *J Clin Invest* 99, 2152-2164.
- Zhou Z, Apte SS, Soininen R, Cao R, Baaklini GY, Rauser RW, et al.** (2000) Impaired endochondral ossification and angiogenesis in mice deficient in membrane-type matrix metalloproteinase 1. *Proc Natl Acad Sci U S A* 97, 4052-4057.
- Zhou Y, McMaster M, Woo K, Janatpour M, Perry J, Karpanen, et al.** (2002) Vascular endothelial growth factor ligands and receptors that regulate human cytotrophoblast survival are dysregulated in severe preeclampsia and hemolysis, elevated liver enzymes, and low platelets syndrome. *Am J Pathol* 160, 1405-1423.
- Zhou Y, Bellingard V, Feng K, McMaster M, Fisher S** (2003) Human cytotrophoblasts promote endothelial survival and vascular remodelling through secretion of Ang-2, PlGF and VEGF-C. *Dev Biol* 263, 114-125.
- Zygmunt M, Herr F, Keller-Schoenwetter S, Kunzi-Rapp K, Munstedt K, Rao CV, et al.** (2002) Characterization of human chorionic gonadotropin as a novel angiogenic factor. *J Clin Endocrinol Metab* 87, 5290-5296.
- Zygmunt M, Herr F, Munstedt K, Lang U, Liang OD** (2003) Angiogenesis and vasculogenesis in pregnancy. *Eur. J Obstet Gynecol Reprod Biol* 110 Suppl, S10-S18.

# Abbreviations

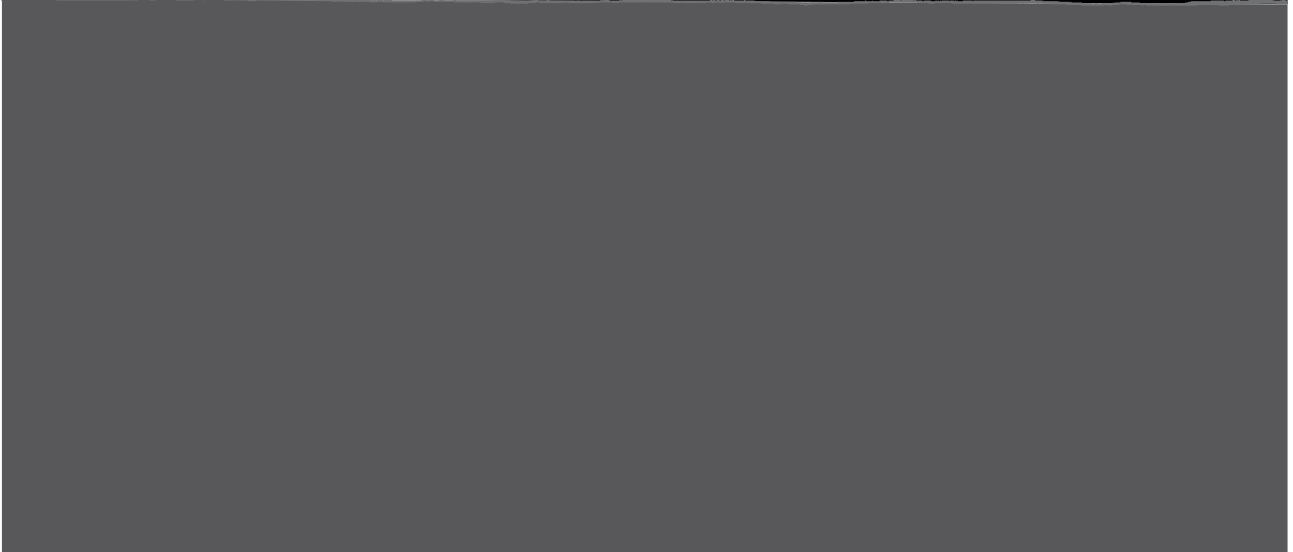
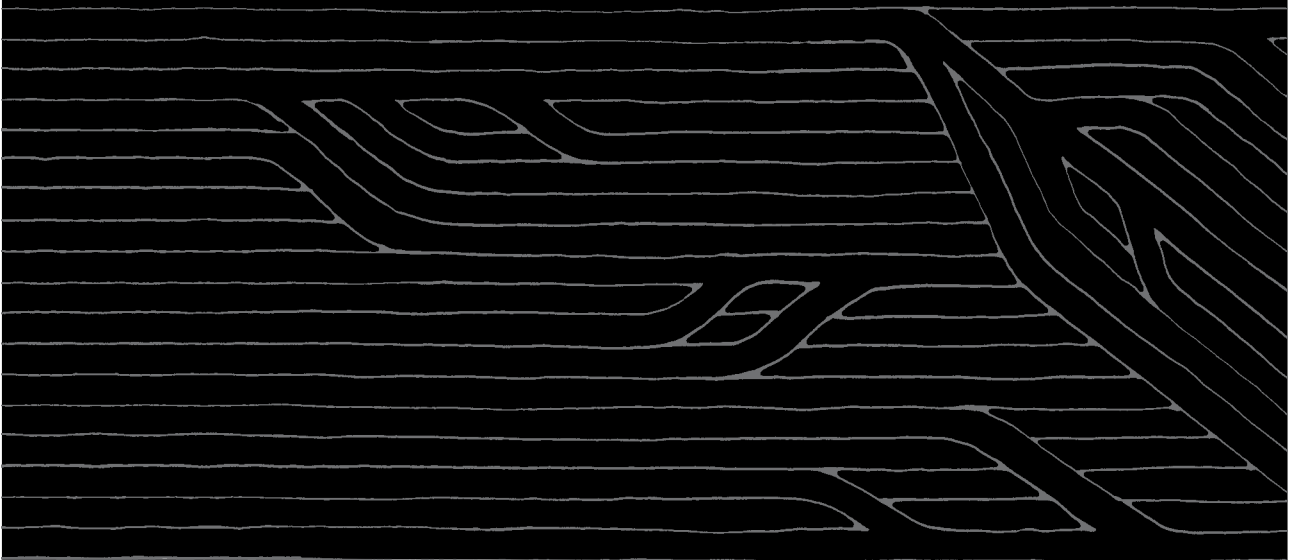




Ang-1	Angiopoietin-1
Ang-2	Angiopoietin-2
ANOVA	Analysis of Variance
APLA	Abortus Provocatus Lege Artis
BP	Blood pressure
cDNA	complementary DNA
CSF-1	Colony stimulating factor-1
Ct	Cycle threshold
CVS	Chorion villous sampling
dCt	Difference in Ct values
$\Delta$ dCt	Difference in $\Delta$ dCt values
DB	Decidua Basalis
DP	Decidua Parietalis
DSE	Decidual Secretory Endometrium
EC	Endothelial cell
ECGF	Endothelial cell growth factor
ECM	Extracellular matrix
EGF	Epidermal growth factor
ELISA	Enzyme-linked immunosorbent Assay
ER	Estrogen receptor
EP	Early proliferative
ES	Early secretory
EVT	Extra-villous trophoblast
FAM	6-carboxyfluorescein
FGR	Foetal growth restriction
Flt-1	Fms-related Tyrosine Kinase-1 or VEGF-Receptor 1
GA	Gestational age
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
GPI	Glycosyl-phosphatidylinositol
hCG	Human chorionic gonadotropin
hEEC	Human endometrial epithelial cells
HELLP	Haemolysis, elevated liver enzymes, low platelets
hEMVEC	Human endometrial micro-vascular endothelial cells
hESC	Human endometrial stromal cells
hFMVEC	Human foreskin microvascular endothelial cells
HPS	Haematoxylin phloxin safrane
HRT	Hormonal replacement therapy
HS	Human serum
IFN	Interferon
IGF	Insulin-like growth factor
IgG	Immunoglobulin
IL	Interleukin
IVF	In vitro fertilisation
KDR	Kinase insert Domain Receptor or VEGF-Receptor 2
LIF	Leukaemia inhibitory factor
LP	Late proliferative
LS	Late secretory
M	Menstruation
MAPK	Mitogen-activated protein kinase
MMP	Matrix metalloproteinase
mRNA	Messenger ribonucleic acid

MSI	Mean staining index
MT-MMP	Membrane-type matrix metalloproteinase
NBSC	Newborn calf serum
PDGF	Platelet-derived growth factor
PE	Preeclampsia
PI <sub>3</sub> K	Phosphatidyl-Inositol-3-kinase
PIGF	Placental Growth Factor
PSMC	Perivascular smooth muscle cell
SC	Stromal cell
SD	Standard deviation
SEM	Standard error of mean
S-Flt-1	Soluble Flt-1
SI	Staining Index
RT-PCR	Real time polymerase chain reaction
TAMRA	tetramethyl-6-carboxyrhodamin
TGF	Transforming growth factor
TIE-2	Tyrosine protein kinase receptor for Ang-1 and Ang-2
TIMP	Tissue inhibitor of matrix metalloproteinase
TNF	Tumour Necrosis Factor
tPA	Tissue-type plasminogen activator
TSI	Total staining index
VEGF	Vascular endothelial growth factor
vWF	Van Willebrand Factor
uNK	Uterine Natural Killer cells
uPA	Urokinase-type plasminogen activator
uPAR	Urokinase-type plasminogen activator receptor

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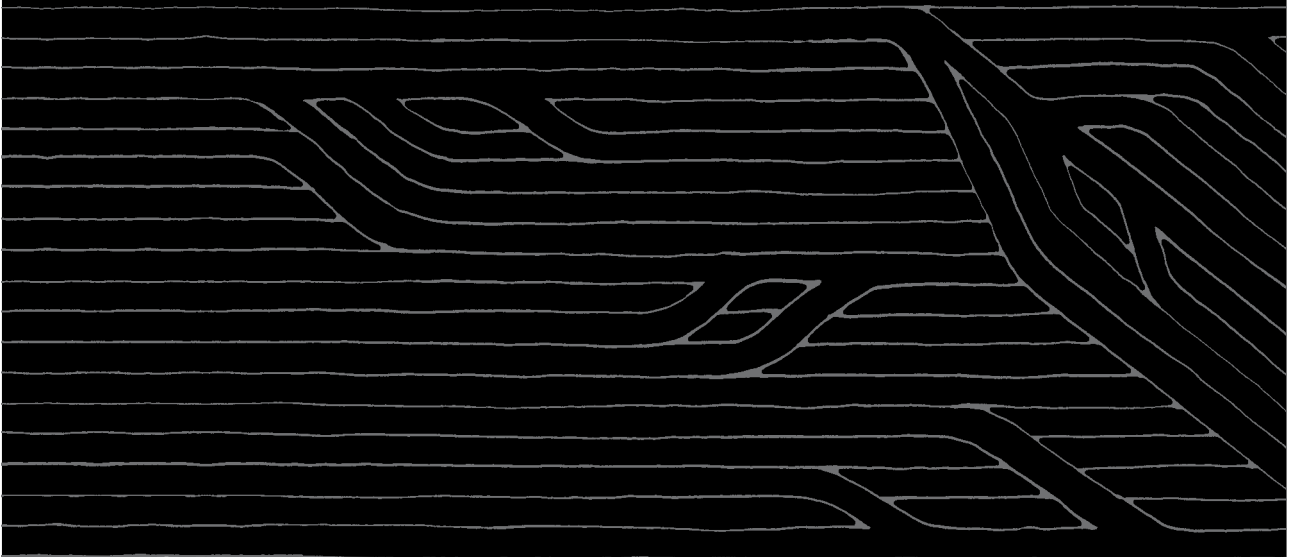
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# Curriculum Vitae





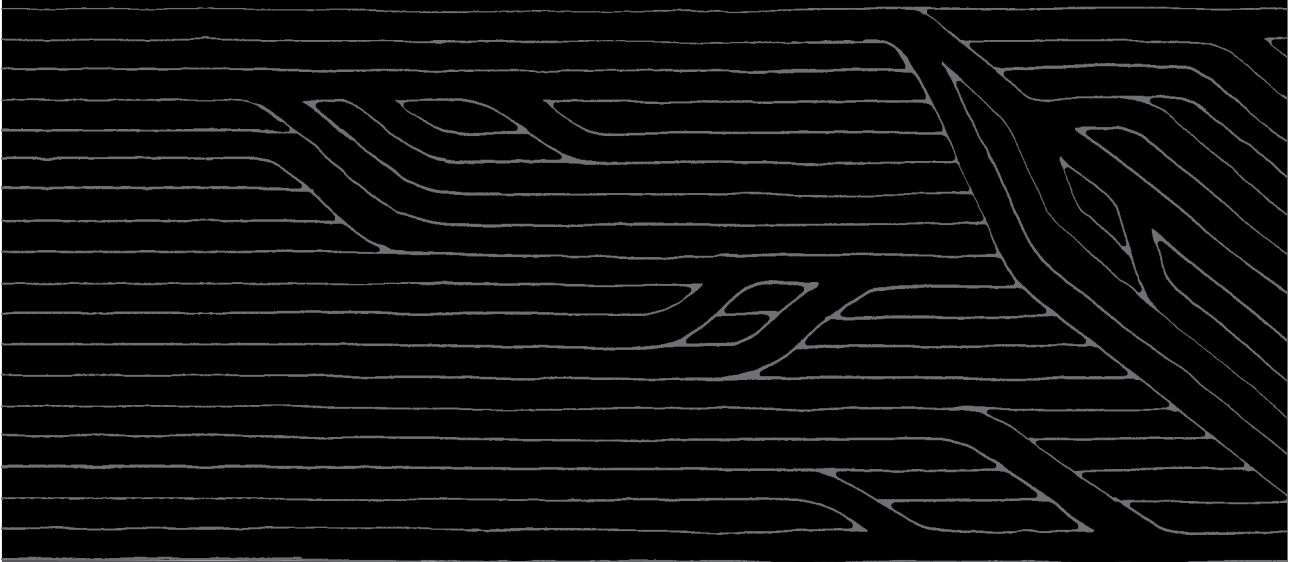
De schrijfster van dit proefschrift werd geboren op 15 december 1975 te Dordrecht. Haar jeugd bracht zij door in Puttershoek, Zuid-Holland. Na het behalen van het eindexamen atheneum aan de Willem van Oranje Scholengemeenschap, te Oud-Beijerland, startte zij in 1994 met de studie Biomedische Wetenschappen aan de Universiteit Leiden. In 1996 werd begonnen met de studie geneeskunde aan dezelfde universiteit. Tijdens de studie geneeskunde werkte zij als student-assistent bij de vakgroep Fysiologie. In 1998 verbleef zij enkele maanden in Bolgatanga, Ghana, en werkte daar aan een onderzoek naar *Oesophagostomum Bifurcum*. Tevens was zij betrokken bij het onderzoek naar de rol van het immuunsysteem bij herhaalde miskramen, onder leiding van Prof. Dr. F.M. Helmerhorst en Prof. Dr. T. Huizinga in het Leids Universitair Medisch Centrum (LUMC). Het doctoraal examen van beide studies behaalde zij in 2000, gevolgd door het artsexamen in 2002.

Na het behalen van haar artsexamen werd in 2002 aangevangen met wetenschappelijk onderzoek in het kader van een AGIKO-aanstelling op de afdeling Gynaecologie (LUMC) en de afdeling Biomedical Research van TNO Kwaliteit van Leven te Leiden. Zij deed onderzoek naar de rol van angiogenese in de jonge zwangerschap, onder begeleiding van Prof. Dr. V.W.M. van Hinsbergh (Vrije Universiteit Medisch Centrum) en Prof. Dr. F.M. Helmerhorst (LUMC). De resultaten van dit onderzoek staan beschreven in dit proefschrift.

In 2005 startte zij met de opleiding tot gynaecoloog in het LUMC (opleiders Prof. Dr. H.H.H. Kanhai en Prof. Dr. G.G. Kenter) en het Bronovo Ziekenhuis (opleider Dr. C.A.G. Holleboom). Margreet woont in Den Haag samen met Roger Froklage en hun zoon Matthijs.



# Acknowledgements







**Dank...**

Mijn voorgangers in onderzoek, voor jullie aanstekelijk enthousiasme  
*Frédérique en Kitty*



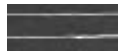
De secretaresses, voor jullie onmisbare werk  
*Wil en Bea*



Vriendinnen van vroeger, omdat jullie er nog steeds zijn  
*Corine, Simone, Miranda en Marjolein*



“Mijn” studenten, voor hun vele werk  
*Sharon, Indra en Ellen*



Mijn nieuw gevonden familie  
*Jaap, Tine en Irving*



Ghana girls, voor jullie aandacht en vriendschap  
*Petra, Marieke, Nicole, Minke en Jutte*



Medewerkers van de STIMEZO-plus kliniek Scheveningen, het Bronovo ziekenhuis,  
het Spaarne Ziekenhuis, het UMC Groningen en het Leids Univeristair Medisch Centrum  
voor hun bijdrage aan het verzamelen van weefsel

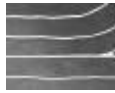


*Jutte*, omdat je als paranimf naast me staat



“Oud”-kamergenoten, voor de noodzakelijke lach

*Bea en Claudia*



Medewerkers TNO en de angiogenese club, voor alle gezelligheid en geleende expertise

*Margreet, Erna, Adri, Jos, Erik, Abbey, Marten, Nancy, Martine, Daniël,*

*Kees, Vincent, Karin, Roeland, Natasja, Monique,*

*Linda, Lars, Robert en Eric*



Lieve vriendinnen, voor de leuke momenten van afleiding

*Eiskje, Cindy, Madlenka en Cecile*

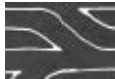


Mede-auteurs, voor hun waardevolle bijdrage



Medewerkers van de afdeling Gynaecologie en Obstetrie van het

Bronovo Ziekenhuis



*Leendert-Jan*, grote broer en paranimf, omdat je er altijd voor me bent



Mijn bovenstebeste schoonzus en neefjes

*Arienne, Luc en Jesse*



Ylang, Ylang, lieve cordial-genootjes, voor jullie gezelligheid en aandeel in zoveel mooie herinneringen

*Marjolein, Marion, Susanna, Michele, Myrna, Nicole, Marijke, Karen en Marjolein*



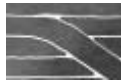
Arts-assistenten Gynaecologie en Obstetrie Cluster Leiden



Mede-AGIKO-ers, voor een luisterend oor en de kroketten  
*Marjon, Wendela, Huib, Elles, Esther, Marieke, Ellen, Muriël, Sabrina, Joost,  
Peggy, Heleen, Jessica, Quirine en Henry*



Waar het allemaal begon, dank voor alles .....!  
*Pap en Mam*



Mijn allerliefste thuishaven  
*Roger en Matthijs*



“We must not forget that when radium was discovered no one knew that it would prove useful in hospitals. The work was one of pure science. And this is a proof that scientific work must not be considered from a point of view of the direct usefulness of it. It must be done for itself, for the beauty of science. And then, there is always the chance that a scientific discovery may become like the radium.”

**By Marie Curie (1867 - 1934)**