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

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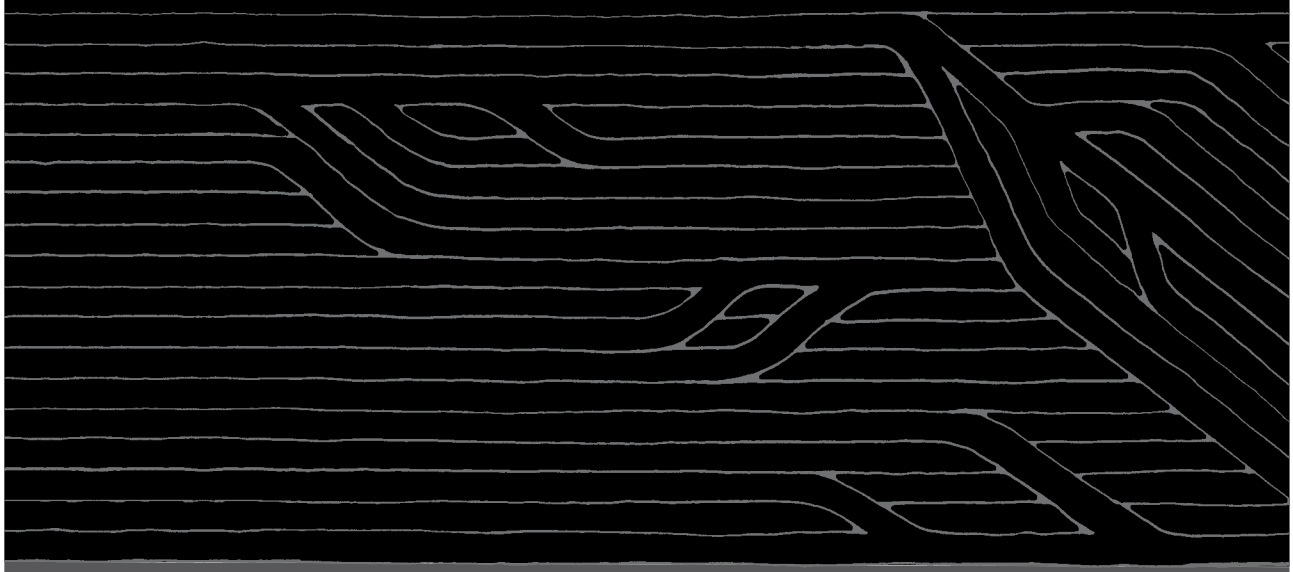

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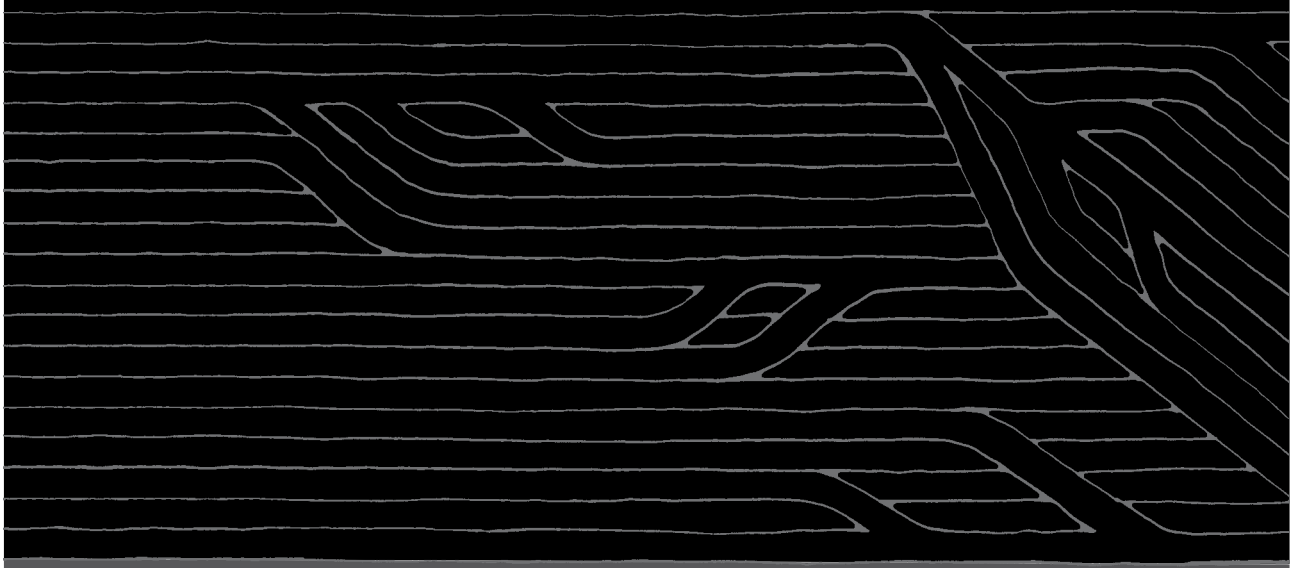
Abbreviations



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
ΔdCt	Difference in ΔdCt 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	Glycerylaldehyde-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
PI3K	Phosphatidyl-Inositol-3-kinase
PlGF	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	tetremethyl-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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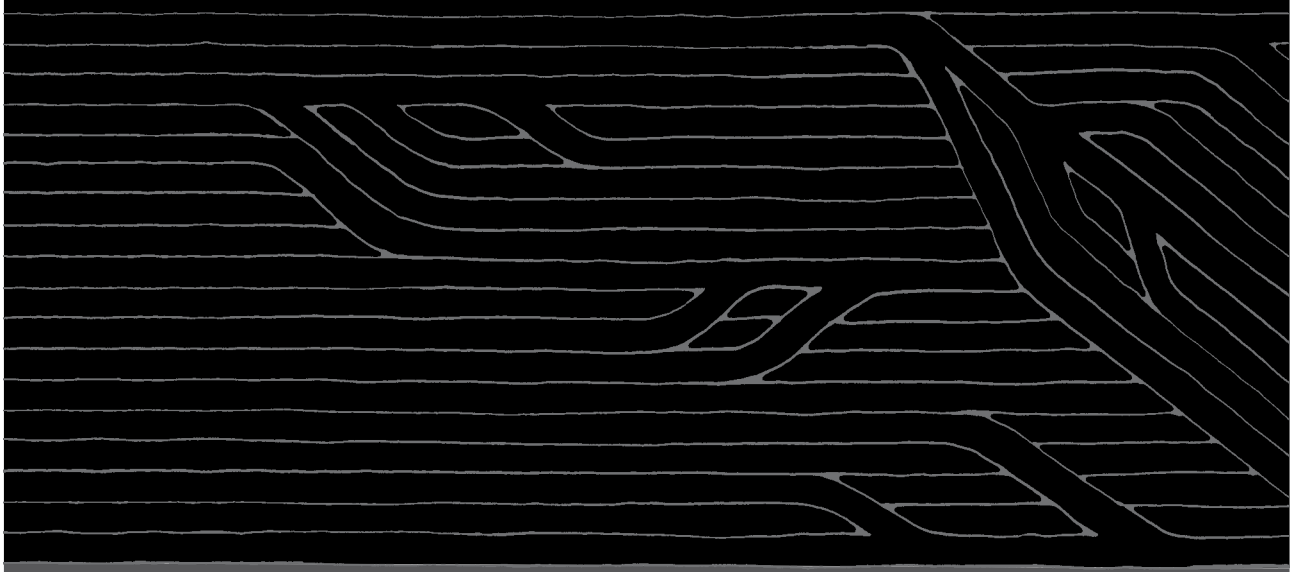

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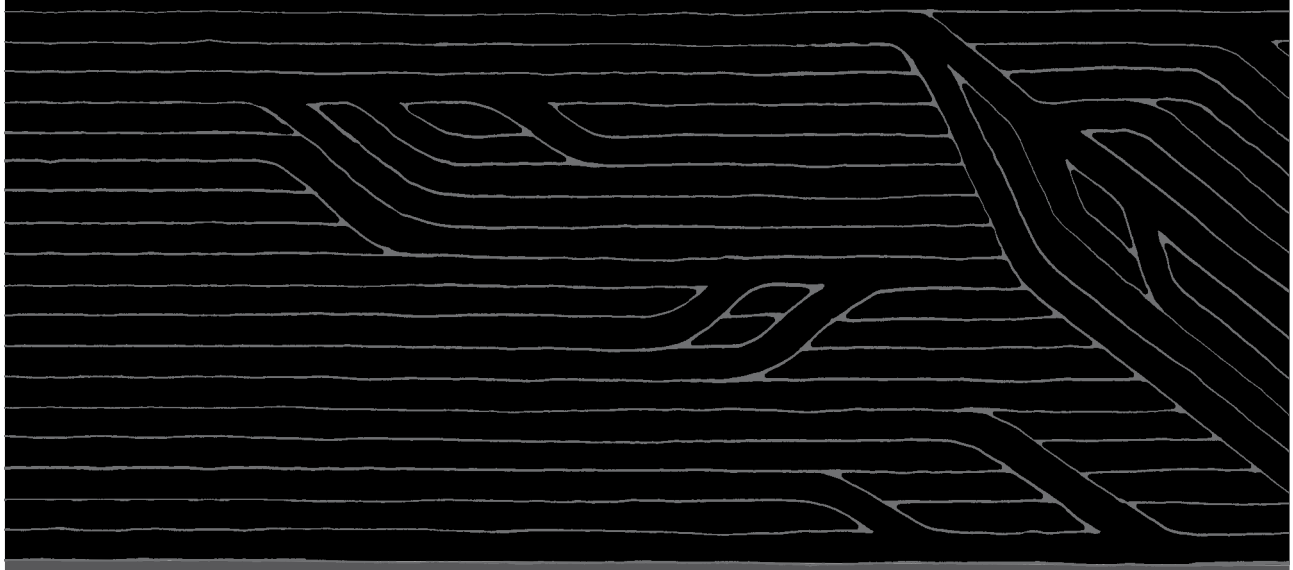

De schrijfster van dit proefschrift werd geboren op 15 december 1975 te Dordrecht. Haar jeugd bracht zij door in Puttershoek, Zuid-Holland. Na het behalen van het eindexamen atheneum aan de Willem van Oranje Scholengemeenschap, te Oud-Beijerland, startte zij in 1994 met de studie Biomedische Wetenschappen 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.

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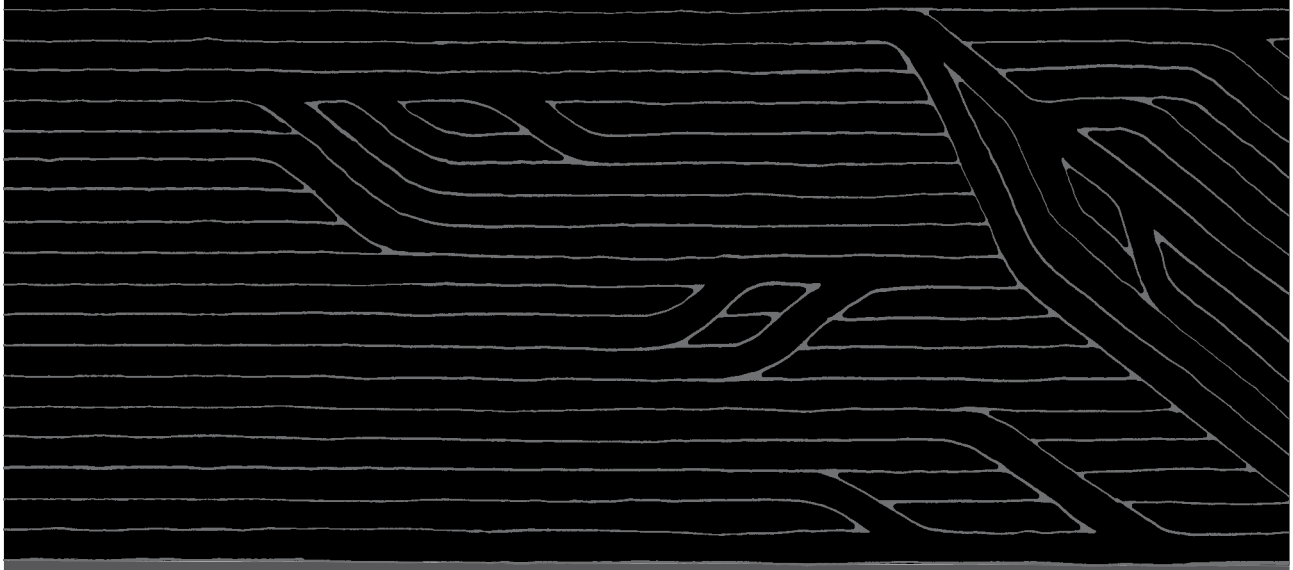

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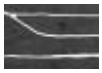

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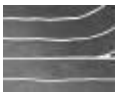

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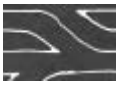

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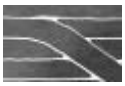

Mijn allerliefste thuishaven
Roger en Matthijs

"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)