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

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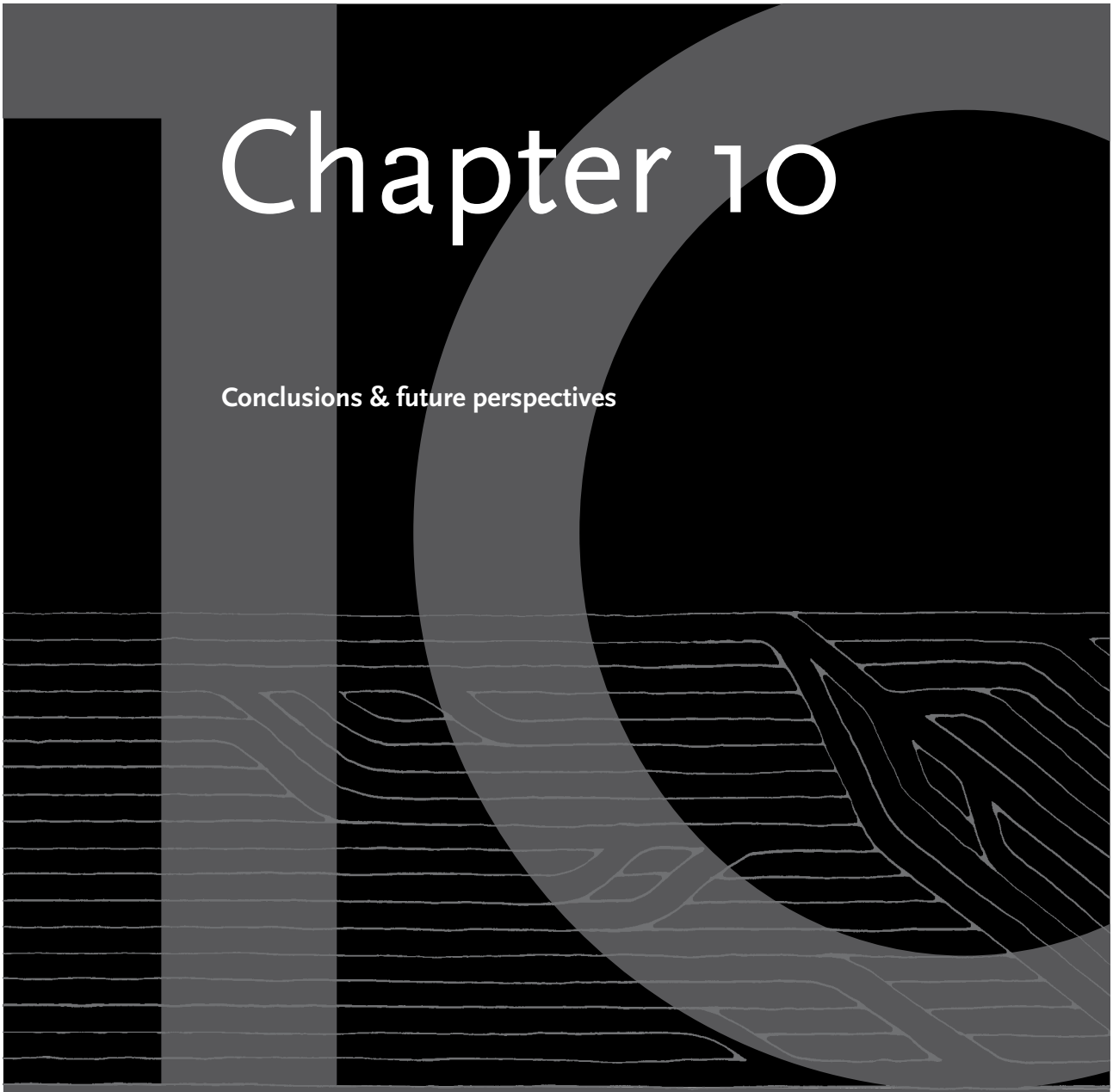
Chapter 10

Conclusions & future perspectives



Angiogenesis and pericellular proteases in cycling endometrium

- Tube formation by endometrial endothelial cells depends on uPA/plasmin and MMPs (**Ch. 2**).
- MT3-MMP is a potential regulator of endometrial angiogenesis *in vitro* (**Ch. 2**).
- MT-MMPs are expressed in endometrium in a cycle-dependent pattern (**Ch. 3**).
- MT2- and MT3-MMP appear associated with endometrial angiogenesis *in vivo*, which is a confirmation of earlier *in vitro* data (**Ch. 3**).

Contributors to the formation of first-trimester decidua

- Pregnancy induced hormones, i.e. oestradiol, progesterone and hCG, uterine NK cells and the extra-villous trophoblast are the main regulators of decidual development (**Ch. 5, 6**).

Vascularisation patterns in first-trimester decidua

- The extra-villous trophoblast (EVT), the pregnancy-induced hormones (oestradiol, progesterone and hCG), and uterine NK cells contribute to vascular regulation (**Ch. 5**).
- Vasculature at the implantation site displays fewer vessels with greater circumference and an enlarged total vascular area (**Ch. 5**).

Angiogenic factors in first-trimester decidua

- The human embryo is able to stimulate decidual angiogenesis via VEGF-A (**Ch. 4**).
- VEGF-A is probably involved in vascularisation in all decidual tissues (**Ch. 5**).
- PlGF, via Flt-1, and the angiopoietins appear to be related to decidual angiogenesis at the implantation site (**Ch. 5**).

Pericellular proteases in first-trimester decidua

- The pericellular proteases, uPA (and uPAR), MT1-, MT2-, MT3- and MT5-MMP were differentially regulated by the EVT, pregnancy-induced hormones, and uterine NK cells (**Ch. 6**).
- All MT-MMPs might be involved in trophoblast and uNK cell invasion, whereas MT2- and MT3-MMP also appear to contribute to decidual vascularisation (**Ch. 6**).

Angiogenesis, proteases and angiogenic factors in late first-trimester pregnancy

- Decidual vascularisation is altered as gestation progresses, showing less but larger vessels (**Ch. 5**).
- This altered vascularisation correlated with elevated expression of VEGF and PlGF and decreased expression of MT1, MT2- and MT3-MMP in endothelium and in general (**Ch. 5/6**).

Vascularisation and miscarriage, pre-eclampsia and foetal growth restriction

- Decidual vascularisation appears to adapt too rapidly to embryonic implantation in miscarriage (**Ch. 7**).
- The disturbed vascular development correlated with differential expression of angiogenic factors and proteases (**Ch. 7**).
- Altered expression of angiogenic factors in first-trimester decidua appears correlated with the pathogenesis of pre-eclampsia of foetal growth retardation later in pregnancy (**Ch. 8**).