Progesterone utilizes distinct membrane pools of tissue factor to increase coagulation and invasion and these effects are inhibited by TFPI

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Tissue factor (TF) serving as the receptor for coagulation factor VII (FVII) initiates the extrinsic coagulation pathway. We previously demonstrated that progesterone increases TF, coagulation and invasion in breast cancer cell lines. Herein, we investigated if tissue factor pathway inhibitor (TFPI) could down-regulate progesterone-increased TF activity in these cells. Classically, TFPI redistributes TF-FVII-FX-TFPI in an inactive quaternary complex to membrane associated lipid raft regions. Herein, we demonstrate that TF increased by progesterone is localized to the heavy membrane fraction, despite progesterone-increased coagulation originating almost exclusively from lipid raft domains, where TF levels are extremely low. The progesterone increase in coagulation is not a rapid effect, but is progesterone receptor (PR) dependent and requires protein synthesis. Although a partial relocalization of TF occurs, TFPI does not require the redistribution to lipid rafts to inhibit coagulation