



## Abstract

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**PI Title:** ASSOCIATE PROFESSOR

**Project Title:** ESTROGEN/PLATELET INTERACTION IN CEREBRAL ISCHEMIA

**Abstract:** *Platelet activation in the cerebrovasculature has been implicated as a mediator of tissue injury following stroke or other ischemic events. Data suggest that pre-menopausal women are at lower risk than men for cardiovascular diseases including stroke and transient ischemic attacks, conceivably due to the effects of estrogenic hormones on platelet biology or vascular function. Many women make a choice to receive hormone replacement therapy, but controversy surrounds the risks versus the benefits of estrogen therapy. Recent studies indicate that increasing estrogen levels promotes expression of the antiaggregant vasodilator, nitric oxide (NO), while depressing platelet elaboration of the adhesion molecule, P-selectin. We propose to study the effects of elevated estrogen on platelet biology to determine if the hormone moderates alterations in pre and post-ischemic platelet function or microvascular vasodilator capacity via the expression of vasoconstrictive platelet products. In Aim 1 we will determine if chronic estrogen in two physiologic doses modulates platelet biologic via a P-selectin mediated mechanism at baseline or after global cerebral ischemia. In Aim 2 we will test if chronic estrogen in two physiologic doses modulates changes in post-ischemia pial vessel vasodilatory capacity via attenuation of the release of adhesive or vasoactive platelet products. In Aim 3 we study the interrelationship between NO and P-selectin expression. We will determine, if the effects of chronic estrogen treatment in two physiologic doses improves microvascular perfusion by depressing post-ischemic platelet and endothelial P-selectin as a result of increased nitric oxide production. We will use whole blood platelet aggregometry, intravital microscopy, immunological and biochemical techniques to ascertain how estrogen affects platelet biology and microvascular endothelial function.*

*The studies proposed in this project will clarify the contribution of exogenous estrogen therapy in ischemic brain injury both mechanistically and according to dosage. These are important considerations which impact nursing therapeutics given the controversy surrounding the safety and efficacy of estrogen replacement regimens.*

***Thesaurus Terms:***

*cerebral ischemia /hypoxia, estrogen, hormone regulation /control mechanism, platelet activation*

*dosage, gene expression, nitric oxide, selectin, vascular endothelium, vasodilation female, intravital microscopy, laboratory rabbit*

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