

Reducing the risk of preterm birth will involve both complex biological and environmental factors. Innovative models of prenatal care and interventions will be developed and tested based on our discoveries. We will use this new knowledge to inform community interventions, with results being applicable to decrease preterm birth rate and improve health outcomes in Alberta and beyond.

Group prenatal care will be compared to standard physician delivered prenatal care, and both environmental and biological data will be incorporated into the Data Repository. Understanding of uterine transition from active quiescence to preparation for labour will help define new approaches for pharmacological interventions to delay labour. The Tissue and Bio Core will provide tissues for testing. An animal models core will also be used to mimic environmental challenges that may affect development after preterm birth.

Detailed Research Strategies

Project 1: Group Prenatal Care to Improve Outcomes

Leaders: Dr. Tough

Researchers: Dr. McNeil

Group prenatal care appears to show promise for improved health outcomes for both mother and baby, with a decrease in preterm birth rates due to factors such as health promotion and social support. We will perform a randomized control trial (RCT) in our Calgary communities to determine whether group care improve infant outcomes at birth and maternal well-being during late pregnancy and at four months postpartum. This information will influence policy, program and decision makers.

Project 2: Mechanisms and Tocolytics in Interventions for Preterm Birth

Leader: Dr. Slater

Researchers: Dr. Guilbert, Dr. Mitchell, Dr. Olson, Dr. Wood

The process of delivery is complex, with an interplay between relaxatory and contractile mechanisms that result in the uterine transitioning from a quiescent state to one undergoing active contractions. The cellular events remain to be understood, and this information will help us identify new interventions for pregnancy maintenance. It will also help in the development of effective tocolytic (contraction arresting) interventions for prevention of preterm labour.

Signalling mediators will be studied in human myometrial smooth muscle cells, and decidual explants will be studied as well. The Tissue and Bio Core will provide such biological tissue samples.

The following projects have already been funded by CIHR but are integrated into the overall theme strategy:

- Projects 2A (PGE₂ and the EP receptors in the human uterus during pregnancy and parturition)
(Leader: Dr. Slater; Researcher: Dr. Wood)

This project will investigate effects of agonists and antagonists of the EP₁₋₄ receptors in maintaining active myometrial quiescence in late gestation.

- 2B (Calcium sensitization mechanisms in uterine activation and parturition)

(Leader: Dr. Mitchell)

This project is an analysis of transition of calcium sensitization mechanisms that maintain quiescence and those that activate the myometrium.

- 2C (PGF_{2α} and FP Receptors)

(Leader: Dr. Olson; Researcher: Dr. Mitchell, Dr. Slater)

This project will study ways to suppress FP (the receptor to prostaglandin F_{2α}), a key element in birth at full term and preterm birth.

Project 2D (Orphan nuclear receptors and uterine relaxation), led by Dr. Mitchell, will study receptors which are similar to the progesterone (P4) receptor but which are activated by metabolites of P4. These receptors are pregnane X receptor (PXR) and constitutive androstane receptor (CAR). Both of these receptors can, in turn, regulate the expression of the enzyme inducible nitric oxide synthase (iNOS), thereby producing a potent uterine relaxant, nitric oxide. Studying how these receptors or metabolites bring about the onset of labour will help develop more effective strategies for preterm labour.

Project 3: Animal Models of Preterm Birth and Interventions to Prolong Pregnancy

Leader: Dr. Metz

Researchers: Dr. Benzie, Dr. Guilbert, Dr. Mitchell, Dr. Olson, Dr. Slater

Stress and stress hormones are critical in determining gestational length and maternal behaviour. Furthermore, exposure to chronic or severe stress may lead to adverse health outcomes in both mother and offspring. Using a rodent model, we will examine the influence of stress and experience on pregnancy outcomes.

Project 3A: The role of stress and co-factors in preterm birth in the rat model (Leader: Dr. Metz)

A series of models will be developed that will help identify the role of stress, with comparison of stress exposure during early and late pregnancy in normal and pregnant rats.

Project 3B: Stress interventions in the model of preterm birth (Leader: Dr. Metz)

We will examine whether experiential and pharmacological treatments can alter gestational physiological and behavioural markers, reduce the effects of stress on pregnancy and prevent stress-induced preterm birth. Our findings will help inform the analysis of data from the Group Prenatal Care study. Better environments may help reduce birth risk and optimize child development after delivery. Neuro-imaging will help generate hypotheses for neuro-mechanisms of human interactions. The expression profiles of key signalling genes in rat uterine tissue will be examined longitudinally throughout gestation and compared to those in human studies.