A History of International Impact

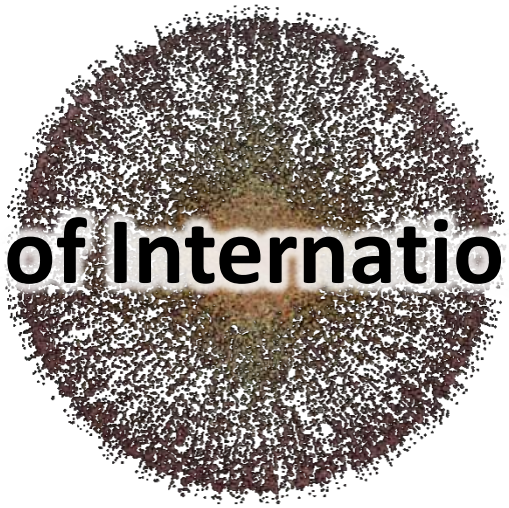
nature medicine

A placental clock controlling the length of human pregnancy

MARK MCLEAN[1], ANDREW BISITS[1], JOANNE DAVIES[1], RUSSELL WOODS[2], PHILIP LOWRY[2] & ROGER SMITH[1]

[1]*Maternal Health Research Centre, John Hunter Hospital, Locked Bag 1, Hunter Region Mail Centre, Newcastle, NSW 2310, Australia*
[2]*School of Animal and Microbial Sciences, University of Reading, Reading, UK*
Correspondence to R.S.

We report the existence of a 'placental clock', which is active from an early stage in human pregnancy and determines the length of gestation and the timing of parturition and delivery. Using a prospective, longitudinal cohort study of 485 pregnant women we have demonstrated that placental secretion of corticotropin-releasing hormone (CRH) is a marker of this process and that measurement of the maternal plasma CRH concentration as early as 16–20 weeks of gestation identifies groups of women who are destined to experience normal term, preterm or post-term delivery. Further, we report that the exponential rise in maternal plasma CRH concentrations with advancing pregnancy is associated with a concomitant fall in concentrations of the specific CRH binding protein in late pregnancy, leading to a rapid increase in circulating levels of bioavailable CRH at a time that coincides with the onset of parturition, suggesting that CRH may act directly as a trigger for parturition in humans.



A History of International Impact

The NEW ENGLAND JOURNAL of MEDICINE

MECHANISMS OF DISEASE

Parturition

Roger Smith, M.B., B.S., Ph.D.

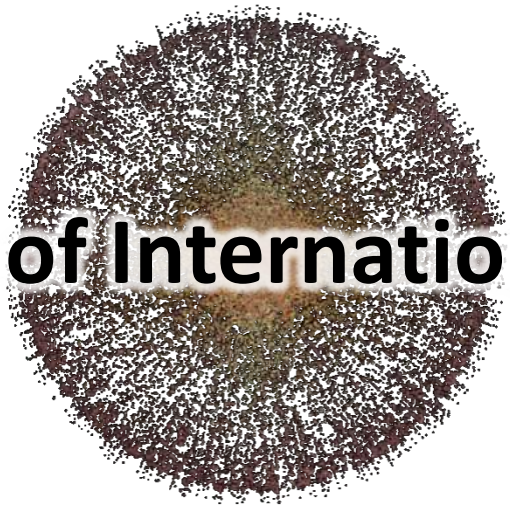
THE MECHANISMS THAT INSTIGATE PARTURITION IN HUMANS HAVE BEEN remarkably elusive, but some parts of the puzzle have begun to come together. A key change in the field was the realization that human parturition is a distinctly human event — animal models can reveal only limited insights. Consequently, investigators of human parturition have come to understand that they must focus on the pregnant woman, despite the ethical difficulties in conducting studies that involve women in labor.

Preterm birth occurs in 5 to 15% of pregnancies, depending on the population.[1] The rates are rising in many developed countries, and there is a particularly high incidence of preterm birth among black Americans. Assisted reproduction, which can increase the frequency of multiple gestations, is only a partial explanation.[2] Birth before 37 weeks of gestation is associated with 70% of neonatal deaths, and there is a strong inverse association between the perinatal death rate and the period of gestation.

Infant morbidity is also related to a short period of gestation. In a Swedish study, 50% of children with cerebral palsy had been born prematurely.[3] Although there has been no reduction in the incidence of preterm birth over the past 30 years, the development of neonatal intensive care has improved survival considerably. The short-term costs of neonatal intensive care are extremely high, and the long-term costs of medical and educational services for a child who was born prematurely make preterm birth particularly expensive.[4]

From the Mothers and Babies Research Centre, Hunter Medical Research Institute, John Hunter Hospital, Newcastle, Australia. Address reprint requests to Dr. Smith at the Mothers and Babies Research Centre, Hunter Medical Research Institute, John Hunter Hospital, Lookout Road, Newcastle NSW 2310, Australia, or at roger.smith@newcastle.edu.au.

N Engl J Med 2007;356:271-83.



nature COMMUNICATIONS

ARTICLE

Received 6 Feb 2014 | Accepted 13 May 2014 | Published 17 Jun 2014

DOI: 10.1038/ncomms5108

Diminished hERG K^+ channel activity facilitates strong human labour contractions but is dysregulated in obese women

Helena C. Parkington[1], Janet Stevenson[2], Mary A. Tonta[1], Jonathan Paul[3], Trent Butler[3], Kaushik Maiti[3], Eng-Cheng Chan[3], Penelope M. Sheehan[2], Shaun P. Brennecke[2,4], Harold A. Coleman[1] & Roger Smith[3]

Human ether-a-go-go-related gene (hERG) potassium channels determine cardiac action potential and contraction duration. Human uterine contractions are underpinned by an action potential that also possesses an initial spike followed by prolonged depolarization. Here we show that hERG channel proteins (α-conducting and β-inhibitory subunits) and hERG currents exist in isolated patch-clamped human myometrial cells. We show that hERG channel activity suppresses contraction amplitude and duration before labour, thereby facilitating quiescence. During established labour, expression of β-inhibitory protein is markedly enhanced, resulting in reduced hERG activity that is associated with an increased duration of uterine action potentials and contractions. Thus, changes in hERG channel activity contribute to electrophysiological mechanisms that produce contractions during labour. We also demonstrate that this system fails in women with elevated BMI, who have enhanced hERG activity as a result of low β-inhibitory protein expression, which likely contributes to the weak contractions and poor labour outcomes observed in many obese women necessitating caesarean delivery.

[1] Department of Physiology, Monash University, Clayton, Victoria 3800, Australia. [2] Department of Perinatal Medicine Pregnancy Research Centre, Royal Women's Hospital, Parkville, Victoria 3052, Australia. [3] Mothers and Babies Research Centre, University of Newcastle, Callaghan, New South Wales 2308, Australia. [4] Department of Obstetrics and Gynaecology, University of Melbourne, Parkville, Victoria 3010, Australia. Correspondence and requests for materials should be addressed to H.C.P. (email: helena.parkington@monash.edu).

A History of International Impact

USA TODAY

Scientists may have discovered the cause of stillbirths

Sonja Haller USA TODAY

Published 5:50 p.m. ET Sep. 17, 2017

Shot of a teddy bear sitting in a crib *Getty Images/iStockphoto*

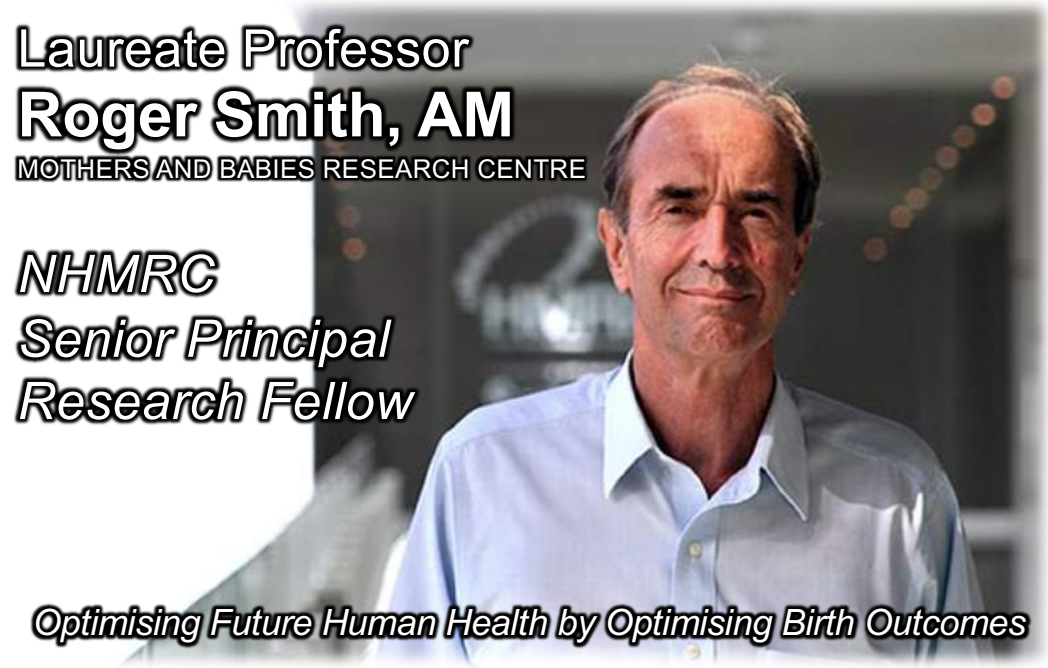
Major breakthrough

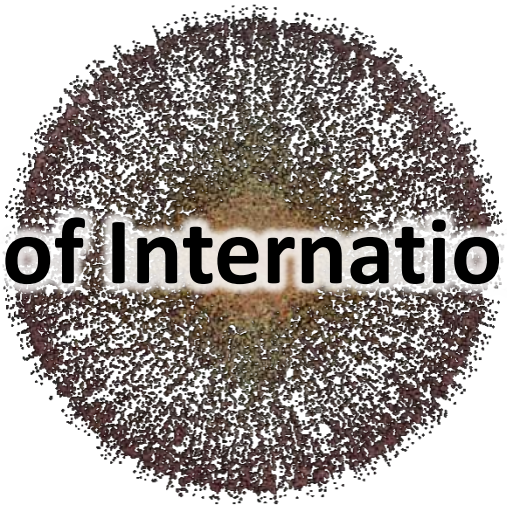
Australia's Hunter Medical Research Institute researchers report a major breakthrough in understanding the mystery.

Professor Roger Smith of the institute said researchers found that many stillbirths are triggered by an aging placenta, he told the Australia Broadcasting Corporation.

> "As you look around at everybody you know, you'll notice that different people age at different rates. And it's almost certainly the same with the placenta. Some placentas age more rapidly than others."

A History of International Impact





A History of International Impact

AJOG American Journal of Obstetrics & Gynecology

OBSTETRICS

Evidence that fetal death is associated with placental aging

Kaushik Maiti, PhD; Zakia Sultana, MPharm; Robert J. Aitken, PhD, ScD; Jonathan Morris, PhD, MBBS; Felicity Park, MBBS; Bronwyn Andrew, MBBS; Simon C. Riley, PhD; Roger Smith, PhD, MBBS

OBSTETRICS

Drug delivery to the human and mouse uterus using immunoliposomes targeted to the oxytocin receptor

Jonathan W. Paul, PhD[1]; Susan Hua, PhD[1]; Marina Ilicic, BSc (Hons); Jorge M. Tolosa, PhD; Trent Butler, BSc (Hons); Sarah Robertson, PhD; Roger Smith, MBBS, PhD

OBSTETRICS

A case for not adjusting birthweight customized standards for ethnicity: observations from a unique Australian cohort

Roger Smith, MB, BS, PhD; Lita Mohapatra, MSc; Mandy Hunter, MS; Tiffany-Jane Evans, PhD; Christopher Oldmeadow, PhD; Elizabeth Holliday, PhD; Alexis Hure, PhD; John Attia, MD, PhD

OBSTETRICS

What birthweight percentile is associated with optimal perinatal mortality and childhood education outcomes?

Ellie C. McEwen, BMedSci (Hons I); Steven L. Guthridge, MPhil; Vincent YF. He, PhD; John W. McKenzie, PhD; Thomas J. Boulton, MBChB, MD; Roger Smith, MBBS, PhD

A History of International Impact

AJOG American Journal of Obstetrics & Gynecology

OBSTETRICS

A first step to improving maternal mortality in a low-literacy setting; the successful use of singing to improve knowledge regarding antenatal care

Binod Bindu Sharma, MPH; Deborah Joanne Loxton, PhD; Henry Murray, DM; Giavanna Louise Angeli, PhD; Christopher Oldmeadow, PhD; Simon Chiu, DAppStat; Roger Smith, MB, BS, Hons, PhD

Is there a role for placental senescence in the genesis of obstetric complications and fetal growth restriction?

Zakia Sultana, MPharm; Kaushik Maiti, PhD; Lee Dedman, NHIL; Roger Smith, PhD, MBBS

Why the heart is like an orchestra and the uterus is like a soccer crowd

Roger Smith, MD, PhD; Mohammad Imtiaz, BSc (EE), PhD; David Banney, MB, BS, BMus (Hons); Jonathan W. Paul, BSc (Biotech)(Hons), PhD; Roger C. Young, MD, PhD

OBSTETRICS

Biochemical and biophysical predictors of the response to the induction of labor in nulliparous postterm pregnancy

Michela Torricelli, MD, PhD; Romina Novembri, Bsc; Chiara Voltolini, MD; Nathalie Conti, MD; Giulia Biliotti, MD; Enrico Piccolini, MD; Gabriele Cevenini, MD; Roger Smith, MD; Felice Petraglia, MD

Impacts in Indigenous Health

PERSONAL VIEW

Developing research in partnership with Aboriginal communities – strategies for improving recruitment and retention

K Rae[1], L Weatherall[1], K Hollebone[2], K Apen[2], M McLean[3], C Blackwell[4], S Eades[5], J Boulton[6], E Lumbers[1], R Smith[1]

BMJ Open

Improving smoking cessation care in pregnancy at Aboriginal Medical Services: 'ICAN QUIT in Pregnancy' step-wedge cluster randomised study

Yael Bar-Zeev,[1] Michelle Bovill,[1] Billie Bonevski,[1] Maree Gruppetta,[2] Christopher Oldmeadow,[3] Kerrin Palazzi,[3] Louise Atkins,[4] Jennifer Reath,[5] Gillian Sandra Gould,[1] the 'ICAN QUIT in Pregnancy' Pilot Group

Original Research ajog.org

OBSTETRICS

What birthweight percentile is associated with optimal perinatal mortality and childhood education outcomes?

Ellie C. McEwen, BMedSci (Hons I); Steven L. Guthridge, MPhil; Vincent YF. He, PhD; John W. McKenzie, PhD; Thomas J. Boulton, MBChB, MD; Roger Smith, MBBS, PhD

ORIGINAL ARTICLE ANZJOG

Post-traumatic stress disorder symptoms in pregnant Australian Indigenous women residing in rural and remote New South Wales: A cross-sectional descriptive study

Beth Mah[1,2], Loretta Weatherall[2], Julie Burrows[3], Caroline C. Blackwell[4], Josephine Gwynn[5,†], Pathik Wadhwa[6], Eugenie R. Lumbers[2,7,8], Roger Smith[2,8] and Kym M. Rae[3,8]

MOTHERS AND BABIES RESEARCH CENTRE

UNIVERSITY OF NEWCASTLE, AUSTRALIA

In partnership with the

HUNTER MEDICAL RESEARCH INSTITUTE