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Dr Shiao-yng Chan B.A., PhD, MRCOG

Senior Clinical Research Fellow and Honorary Consultant Obstetrician

Reproduction, Genes and Development

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About

Shiao Chan is a practicing Consultant Obstetrician who heads the Endocrine Antenatal Clinic at the Birmingham Women's NHS Foundation Trust, UK. She is also a Health Foundation Clinician Scientist who runs a research program at the Institute of Biomedical Research, University of Birmingham, UK. Her particular research interest is in thyroid hormone action in the fetal brain and in placental development and function, including the pathophysiology of intrauterine growth-restriction.

She has many original research publications in scientific journals as well as reviews and book chapters in the fields of thyroid hormone action and thyroid dysfunction in pregnancy. She has also been invited to speak at international and national meetings.

She has received a Clinical Training Fellowship from the Medical Research Council followed by a Clinician Scientist Fellowship from the Health Foundation. She was awarded a Medical Research Council project grant as a New Investigator in 2006. With further research funding from charities including Action Medical Research, Wellbeing of Women and Birmingham Children's Hospital Charities, she has established a research team in laboratory sciences. She is a strong advocate of translational research and aims to build an effective bridge that enables scientific knowledge to be incorporated into improvements in the care of pregnant women and their developing fetus. She is part of the research team conducting the TABLET study, a randomised controlled clinical trial of levothyroxine treatment in TPO antibody positive women in pregnancy.

Qualifications

Post Graduate qualifications:

- PhD in Thyroid Status and Fetal Brain Development (University of Birmingham, July 2004)
- MRCOG (London, May 2000)

Basic Qualifications: Gonville & Caius College, University of Cambridge

- M.B. BChir. (1995)
- B.A.(Hons) in Developmental Biology and Neuroscience (1993)

Biography

Shiao Chan graduated in Medicine and Surgery from the University of Cambridge in 1995 and moved to the West Midlands to start training in Obstetrics and Gynaecology in 1997. Having obtained the MRCOG in 2000, she was awarded an MRC Clinical Training Fellowship to pursue a PhD, which she completed in 2004 from the University of Birmingham. After a short time as a Clinical Lecturer, she successfully obtained a prestigious five year Clinician Scientist Fellowship from the Health Foundation in 2006. She completed her clinical training in 2008 and is now an Honorary Consultant Obstetrician heading the Endocrine Antenatal Clinic at the Birmingham Women's NHS Foundation Trust. At the same time she manages a research group conducting laboratory science research in thyroid hormone action in placental and fetal brain development at the University of Birmingham.

Teaching

Teaching Programmes

- Reproductive and Endocrine module for Year 2 Medical students
- Obstetrics module for Year 5 Medical Students
- Basic Surgical Skills course (RCOG) for junior doctors
- Supervision of Intercalating BMedSci students

Postgraduate supervision

Shiao has successfully supervised a PhD student and an MPhil student who were both awarded degrees in 2010. She continues to mentor medical students and junior doctors and acts as Educational Supervisor to junior doctors in Obstetrics and Gynaecology.

Research

RESEARCH THEMES

- Thyroid hormones in normal placental and fetal central nervous system development
- Thyroid hormone action in intrauterine growth restriction
- Maternal thyroid dysfunction and pregnancy outcome

RESEARCH ACTIVITY

Shiao's research interest centers around thyroid hormones and thyroid dysfunction in pregnancy. Epidemiological reports have linked mild maternal thyroid hormone (TH) deficiency in early pregnancy with long-term neurodevelopmental delay in offspring. Both maternal hypothyroidism and hyperthyroidism are also associated with adverse pregnancy outcomes. Shiao's group seeks to investigate the underlying mechanisms for these effects. They aim to understand the role of thyroid hormones in normal fetal brain and placental development and function, as well as investigating alterations in thyroid hormone action in pregnancies complicated by intrauterine growth-restriction and the effects of abnormal maternal thyroid hormone levels upon placental development.

Fetal brain research:

The group has already demonstrated the biological plausibility for a direct maternal TH effect on the early human fetal brain. The developing human fetal brain, as early as the first trimester, expresses TH receptors (TRs) and exhibits mechanisms for pre-receptor control of TH supply in the form of deiodinases. The group continues to use a TH responsive model of human central nervous system (CNS) precursor cells, N-Tera-2 to study the effects of T3 in-vitro. They are also investigating the roles played by the different thyroid hormone transporters in human brain development.

Placental research:

The placenta is the only route of TH transfer from the mother to the fetus and the prime organ responsible for the pathophysiology of many adverse obstetric outcomes. Shiao's group has described the ontogeny of deiodinases and thyroid hormone transporters in the placenta throughout gestation. They continue to investigate the effects of thyroid hormones and the role of thyroid hormone transporters in trophoblast and decidual cell growth and differentiation. Their work of elucidating the mechanisms for transfer of TH from the maternal to fetal circulations (Loubiere et al. 2010) are consistent with the hypothesis that transplacental passage of TH occur from early gestation.

One aspect of our research has been to investigate TH action in placenta obtained from pregnancies complicated by intrauterine growth restriction (IUGR), a condition which affects 5-10% of all pregnancies. The group has recently reported that compared with normal, trophoblasts from IUGR placentae demonstrate increased T3 responsiveness associated with increased intracellular accumulation of T3 and increased MCT8 expression, resulting in decreased cell survival and increased apoptosis (Vasilopoulou et al. 2010). This raises the exciting and novel prospect that TH-mediated mechanisms could be a potential therapeutic target for malplacentation disorders such as IUGR. We are currently investigating this further.

TABLET trial:

Shiao's group is part of University of Birmingham's successful bid for an MRC/NIHR funded EME multicentred trial: Efficacy and mechanism of thyroxine treatment on pregnancy and neonatal outcomes in women with thyroid antibodies: A randomised, placebo-controlled, double-blind, multi-centre trial [The TABLET (Thyroid AntiBodies and LEvoThyroxine) Trial] due to commence in June 2011. Women will be screened preconception for the presence and TPO antibodies and randomised to levothyroxine or placebo to investigate effects on reducing miscarriage and preterm birth. They would also be investigating the underlying molecular mechanisms for these effects.

Other activities

- Member of the pregnancy project group of the British Thyroid Foundation aimed at raising awareness of the impact of thyroid dysfunction upon pregnancy amongst health care professionals, patients and the public.
- Member of the Academy of Medical Sciences Clinical Academic Careers Committee from 2008-2009.

Publications

S.Y.Chan, A. Martín-Santos, L.S. Loubière, A.M. González, B. Stieger, A. Logan, C.J. McCabe, J.A. Franklyn, M.D. Kilby. (2011) The expression of thyroid hormone transporters in the human fetal cerebral cortex during early development and in N-Tera-2 neurodifferentiation. **J Physiol** (in press).

S.Y. Chan. (2010) Early adjustment of levothyroxine treatment in pregnancy. **Nature Reviews Endocrinology** 6(10):537-8.

E. Vasilopoulou, L.S. Loubière, A. Martín-Santos, C.J. McCabe, J.A. Franklyn, M.D. Kilby, S-Y. Chan. (2010) Differential Triiodothyronine Responsiveness and Transport by Human Cytotrophoblasts from Normal and Growth-Restricted Pregnancies.**J Clin Endocrinol Metab**. 95(10):4762-70.

L.S. Loubière, E. Vasilopoulou, J.N. Bulmer, P.M. Taylor, B. Stieger, F. Verrey, C.J. McCabe, J.A. Franklyn, M.D. Kilby, S-Y. Chan. (2010) Expression of thyroid hormone transporters in the human placenta and changes associated with intrauterine growth restriction. **Placenta** 31(4):295-304.

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S.R. James, J.A. Franklyn, B.J. Reaves, V.E. Smith, S.Y. Chan, T.G. Barrett, M.D. Kilby, C.J. McCabe. (2009) Monocarboxylate transporter 8 in neuronal cell growth. **Endocrinology** 150(4):1961-9.

H.N. Pemberton, J.A. Franklyn, K. Boelaert, S.Y. Chan, D.S. Kim, C. Kim, S.Y. Cheng, M.D. Kilby, C.J. McCabe. (2007) Separase, securin and Rad21 in neural cell growth. **Journal of Cellular Physiology** 213(1):45-53.

S. Chan, C.J. McCabe, H. Pemberton, T. Visser, J. Bulmer, J.A. Franklyn, M.D. Kilby. (2006) Monocarboxylate transporter 8 expression in the human placenta: the effects of severe intrauterine growth restriction. **Journal of Endocrinology** 189(3): 465-71.

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