

1. **Institution:** University of Nottingham

2. **Principal investigator and contact person:** Kevin D Sinclair, PhD, DSc

3. Key personnel

NAME	EMAIL	RESEARCH AREA DETAILS
Lydia Kwong	sbzwyk@exmail.nottingham.ac.uk	Embryology, molecular biology

4. Research profile

Metabolic programming during early mammalian development, where epigenetic outcomes are determined in embryonic cells and tissues, and long-term developmental consequences assessed in offspring. First to discover that developmental anomalies following mammalian embryo culture were due to errors in genomic imprinting (*Nature Genetics*, **27**: 153-154). Similar phenomena have since been reported in human IVF pregnancies. First to demonstrate that reductions in folate and vitamin B₁₂ in the diets of intending mothers (rat and sheep) lead to epigenetic modifications to DNA methylation and adult offspring with increased body fat and blood pressure, altered immune function and insulin resistance (showcased to the NICHD Advisory Council in Washington DC in January 2007; *PNAS*, **104**: 19351-19356).

5. Key technologies and tools

- Whole animal studies (Sheep, cow, pig and mouse)
- Bioimaging equipment
 - Computed Tomography
 - MRI
 - Scintigraphy
 - DEXA
- Mammalian embryo culture (Sheep, cow, pig, mouse)
- Cell culture – primary and cell lines
- Quantitative RT-PCR, GeXP
- Proteomics
- Metabolomics (HPLC/GC-MS)
- Pyrosequencing/Bisulphite sequencing

6. Selected publications (max. 5)

1. **Sinclair KD**, Allegrucci A, Singh R, Gardner DS, Sebastian S, Bispham J, Thurston A, Huntley JF, Rees WD, Maloney CA, Lea RG, Craigon J, McEvoy TG, Young LE (2007). DNA methylation, insulin resistance and blood pressure in offspring determined by maternal periconceptional B vitamin and methionine status. *Proc. Nat. Acad. Sci. (USA)* **104**: 19351.
2. Twigt JM, Hammiche F, **Sinclair KD**, Beckers NG, Lindemans J, de Jong FH, Laven JSE, Steegers-Theunissen RP. (2011). Preconception folic acid modulates estradiol and follicular responses to ovarian stimulation in women. *J Clin Endocrinol Metab* **96**: E322.
3. Kwong WY, Adamiak SJ, Gwynn A, Singh R and **Sinclair KD** (2010). Endogenous folates and single-carbon metabolism in the ovarian follicle, oocyte and pre-implantation embryo. *Reprod.* **139**: 1.
4. Adamiak SJ, Mackie K, Watt RG, Webb, R and **Sinclair, KD** (2005). Impact of nutrition on oocyte quality: Cumulative effects of body composition and diet leading to hyperinsulinemia in cattle. *Biol Reprod* **73**: 918.
5. Powell, K; Rooke, J; McEvoy, T; Ashworth C; Robinson, J; Wilmut, I; Young, LE & **Sinclair, KD** (2006). Zygote donor nitrogen metabolism and in vitro embryo culture perturbs in utero development and *IGF2R* expression in ovine fetal tissues. *Theriogenology* **66**: 1901.