S 12

Lorraine E. Young

Associate Professor
University of Nottingham

2006-present	Professor of Molecular Embryology
	Director of Centre for Stem Cells and Tissue Engineering
	University of Nottingham
2001-2005	Reader in Molecular Embryology, University of Nottingham
2000-2001	Molecular Embryology Project Leader, Roslin Institute
1999-2001	Consultant to Geron Biomed (US Human ES Cell Company).
1994-2000	Postdoctoral Researcher, Roslin Institute
1992-1994	Postdoctoral Researcher University of Liverpool
1988-1992	PhD University of Aberdeen
1984-1988	BSc University of Aberdeen
	Zoology (Physiology) BSc First Class Honours

Epigenetic Issues for Embryos and Embryonic Stem Cells

Lorraine E. Young

University of Nottingham, UK

The epigenetic reprogramming in DNA methylation that occurs in the preimplantation embryo appears vulnerable to disruption when *in vitro* embryo production technologies are applied and may also be influenced by maternal nutrition *in vivo*. Thus we reasoned that blastocyst-derived, human embryonic stem cells isolated and cultured through a diverse range of protocols in different laboratories (hESC), may also be subject to epigenetic instability and variation, providing a novel model for the human embryo (Allegrucci et al., 2004. Lancet 364:206-20). In order to define the degree of epigenetic variation between independently-derived hESC lines we have employed Restriction Landmark Genome Scanning (RLGS) to examine the genome-wide methylation profiles of gene-rich CpG islands in hESC. Using NotI/EcoRV/HinfI digestion, our comparisons of hESC CpG islands to a normal human lymphocyte profile (comprising 2025 fragments for which a genomic NotI/EcoRVlagenase passage all resulted in altered RLGS profiles. Overall, a high proportion of the loci with variable DNA methylation between and within cultures were in genes either previously reported as expressed in hESC, expressed only in more differentiated lineages or as hypermethylated in a variety of human tumours. The phenotypic and therapeutic consequences now require further investigation and our data suggest that further optimisation and standardization of hESC culture conditions is urgently required to develop a safe therapeutic product to which tissue-specific differentiation protocols can be generically applied.

Since the environmental factors implicated in altering DNA methylation in hESC cultures are in common with a range of human embryo culture media, hESCs might provide a novel model system to optimise culture conditions for assisted reproduction technologies. Furthermore, identification of key nutrients which can predispose early embryonic cells to programmed epigenetic change might uncover mechanisms pertinent to the developmental origins of adult disease. The potential use of human embryonic stem cells to inform key medical aspects of early pregnancy will therefore be discussed, in addition to their use in cell-based therapies.

57% clones comprised 5 CpG island 46% contained LINE and / or SINE elements represented 18 chromosomes, 7, 12 and 22 (3 spots), 2 and 17 (4 spots) 62.9% previously identified in hESC gene expression databases