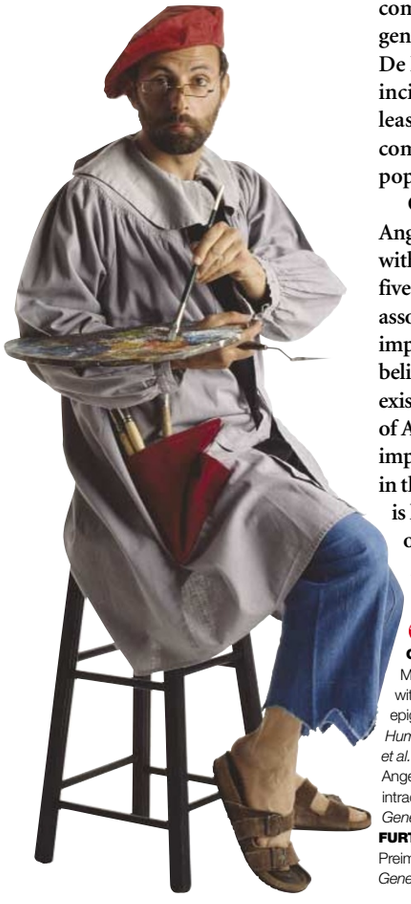
HUMAN GENETICS

The trouble with ART

Assisted reproductive technology (ART), which in its broadest sense encompasses all fertility treatments, has revolutionized reproductive medicine and dramatically changed the lives of many people. Nevertheless, recent reports of an increased incidence of Angelman syndrome following IVF raised the possibility that ART might bring about epigenetic changes in the early embryo and lead to birth defects. Now, in a collaborative study of families with Beckwith–Wiedemann syndrome (BWS), which also involves epigenetic modifications, DeBaun, Feinberg and colleagues show that it, too, might become more frequent following ART. In addition, in a letter to the Editor, Ørstavik and colleagues report another case of Angelman syndrome following ICSI (intracytoplasmic sperm injection) — a technique used to treat male infertility.



BWS, which is characterized by overgrowth and neoplasia, results from the loss of imprinting of a few specific loci, including *LIT1* and *H19*. Previous reports of an association between epigenetic disorders and ART, together with the similarity between the BWS phenotype and the large offspring syndrome — previously reported in cloned mammals — led DeBaun *et al.* to investigate the possibility of an association between ART and BWS incidence. Extending their existing study of BWS, which involved a registry of families with this syndrome, the authors designed a questionnaire to assess the method of conception for children with BWS. They found that six out of seven children with BWS were concieved as a result of IVF. The incidence of ART was 4.6% among those who participated in the study, compared with 0.76% in the general US population, leading De Baun *et al.* to suggest that the incidence of BWS increases at least sixfold after ART treatment, compared with the general population.

Given the previous reports of Angelman syndrome in association with ART, and the observation that five out of the six BWS cases were associated with classic BWS imprinting alterations, the authors believe that sufficient evidence now exists to suspect that some aspect of ART might interfere with imprinting either in the gametes or in the early embryo. So far, nothing is known about how this might occur, but one thing is certain — ART does not imitate life.

Magdalena Skipper

References and links

ORIGINAL RESEARCH PAPERS DeBaun, M. R. *et al.* Association of *in vitro* fertilization with Beckwith–Weidemann syndrome and epigenetic alterations of *LIT1* and *H19*. *Am. J. Hum. Genet.* **72**, 156–160 (2003) | Ørstavik, K. H. *et al.* Another case of imprinting defect in a girl with Angelman syndrome who was concieved by intracytoplasmic sperm injection. *Am. J. Hum. Genet.* **72**, 218–219 (2003)

FURTHER READING Braude, P. *et al.* Preimplantation genetic diagnosis. *Nature Rev. Genet.* **3**, 941–953 (2002)

IN BRIEF

TECHNOLOGY

Association testing by DNA pooling: an effective initial screen.

Bansal, A. *et al. Proc. Natl Acad. Sci. USA* **99**, 16871–16874 (2002)

High-throughput screening for evidence of association by using mass spectrometry genotyping on DNA pools.

Mohlke, K. L. *et al. Proc. Natl Acad. Sci. USA* **99**, 16928–16933 (2002)

Despite the increasing number of molecular markers that have become available, whole-genome scans for association between such markers and a disease are hindered by the number of genotyping reactions that need to be carried out and by the limiting amount of available DNA. These two studies provide evidence that DNA pooling — in which the case and control samples are genotyped as two large groups — is a valid alternative to sample-by-sample genotyping. Mohlke *et al.* have shown empirically that pooled SNP genotyping is comparable to individual genotyping in detecting differences in allelic frequency between cases and controls, whereas Bansal *et al.* have found a significant association between SNPs in the cholesterol ester transferase protein (*CETP*) gene and levels of serum HDL cholesterol.

POPULATION GENETICS

Genetics affinities of the Andaman Islanders, a vanishing human population.

Thangaraj, K. *et al. Curr. Biol.* 26 November 2002 (10.1016/S0960982202013362)

Disputes over the origin of the now nearly extinct inhabitants of the Andaman Islands have been laid to rest. Although they resemble African pygmies, the islanders have been considered to be more likely descendants of Southeast Asian settlers. The authors' analysis of mitochondrial DNA, RFLP and microsatellite markers from various local tribes showed that they are the descendants of the early Palaeolitic Southeast Asian colonizers, distinct from their neighbours on a separate, but near-by, group of islands.

ANIMAL MODELS

Zebrafish as a model organism for the identification and characterization of drugs and genes affecting p53 signaling.

Langheinrich, U. *et al. Curr. Biol.* **12**, 2023–2028 (2002)

The activity of the p53 gene is crucial in determining tumour progression as it mediates apoptosis and cell-cycle control. By using morpholinos to knockdown zebrafish gene activity, Langheinrich *et al.* show that the key components of p53 signalling are conserved between mammals and zebrafish. As cancer treatment drugs have a similar effect in both zebrafish and mammals, zebrafish could be a good system in which to carry out high-throughput screens for genes and compounds affecting p53 signalling. Results could then inform the development of new cancer therapies.