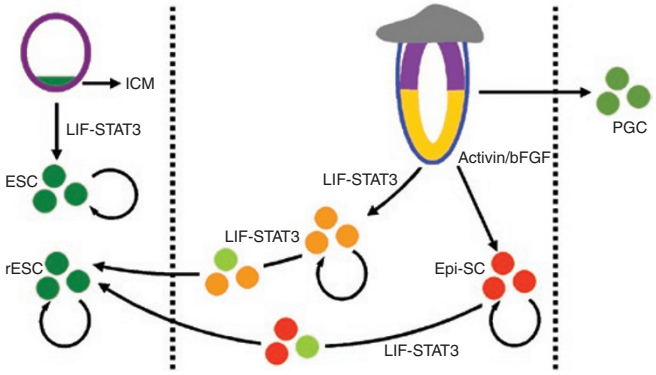

Schematic depicting pluripotent cell types that can be derived from the mouse embryo. ICM, inner cell mass; ESC, embryonic stem cell; rESC, reprogrammed ES cell-like cell; EpiSC, epi-stem cell; PGC, primordial germ cell. Image adapted from *Nature*.

could be useful to study the role of certain epigenetic mechanisms and other modifiers in the reprogramming process.

The work also has implications for studies of human embryonic stem cells (hESCs), which are thought to resemble mouse Epi-SCs. "There are a lot of people trying to revert hESCs to a more mESC-like state," Surani says. "Hopefully this might give some encouragement."

Natalie de Souza

RESEARCH PAPERS

Bao, S. *et al.* Epigenetic reversion of post-implantation epiblast to pluripotent embryonic stem cells. *Nature* **461**, 1292–1295 (2009).

and Genomes (KEGG)—the source for many of the substrates used on their array. However, they could also directly assign functions to dozens of hypothetical proteins whose existence had been predicted based solely on sequence data and to refine the functional annotations of many previously characterized enzymes.

Investigating the ecosystem in an environmental sample increases the metabolomic challenge by orders of magnitude. "One gram of soil can contain millions of reactions, enzymes and microbes," says Ferrer. However, because of its species-independence, the reactome chip proved useful for culling informative metagenomic data from diverse environments. For example, they found that a mineral-rich geothermal pool predominantly contained species with heightened enzymatic capacity for iron and sulfur oxidation whereas a sample of heavily polluted water from the Barents Sea was highly enriched for species with adaptations for efficient petroleum degradation and hydrocarbon use.

Other potential applications for this technology could include characterization of physiological changes resulting from cancer or infection, or analysis of metabolic alterations in transgenic plants, and Ferrer is keen to forge new collaborations. "We believe that the technology offers many possibilities for doing both basic and applied research," he says.

Michael Eisenstein

RESEARCH PAPERS

Beloqui, A. *et al.* Reactome array: forging a link between metabolome and genome. *Science* **326**, 252–257 (2009).

NEWS IN BRIEF

CELL BIOLOGY

3D cell culture on paper

Systems for three-dimensional (3D) cell culture exist, but controlling the distribution of oxygen and nutrients remains a challenge. Derda *et al.* now report a simple approach for constructing paper-supported 3D cell cultures. They added a hydrogel precursor solution containing suspended cells to a small piece of paper and gelled it in place. This allowed them to stack multiple layers of gelled paper to generate a 3D culture system. These stacks can also be readily destacked to examine the cells in the center of the culture.

Derda, R. *et al. Proc. Natl. Acad. Sci. USA* **106**, 18457–18462 (2009).

RNA INTERFERENCE

Predicting targets of microRNA

MicroRNAs regulate gene expression by binding to mRNAs and inhibiting translation. Algorithms for discovering microRNA-mRNA pairs have been developed but are prone to inaccuracies, so Ritchie *et al.* set out to develop an alternative approach for microRNA target discovery based on comparing the expression levels of microRNAs and mRNAs in mouse and in human, across multiple tissues. They used the conserved microRNA signatures to predict thousands of microRNA targets.

Ritchie, W. *et al. PLoS Comput. Biol.* **5**, e1000513 (2009).

GENOMICS

Human methylome at base pair resolution

After *Arabidopsis thaliana, Homo sapiens* is the second species to have its DNA methylome sequenced in its entirety. Lister *et al.* subjected bisulfite-converted genomic DNA to high-throughput sequencing and mapped all methylated cytosines in the genomes of human embryonic stem cells, where they found 25% of methylcytosine in non-(C+G) context, and in fetal lung fibroblasts, where non-(C+G) methylation had disappeared.

Lister, R. *et al. Nature* advance online publication (14 October 2009).

PROTEIN BIOCHEMISTRY

Site-specific histone acetylation

Modifications in the cores of histones have important roles in regulating the structure and function of chromatin. Neumann *et al.* describe an approach to recombinantly generate site-specifically acetylated histones using an evolved aminoacyl-tRNA synthetase and $tRNA_{CUA}$ pair that facilitates the incorporation of acetyl-lysine in response to an amber codon. This method allowed the researchers to investigate the mechanistic role of Lys56 acetylation, a highly conserved modification in histone H3, in detail.

Neumann, H. *et al. Mol. Cell* **36**, 153–163 (2009).

GENE REGULATION

Knocking down microRNA in chick embryos

There is great interest in studying the function of microRNAs in controlling gene expression during embryonic development. McGlinn *et al.* now describe an approach for knocking down microRNA function in developing chick embryos by using antagomiRs, engineered antisense oligonucleotides, to specifically target Hox genes. The researchers used this method to explore the function of miR-196 in regulating Hox genes central to axial skeletal patterning.

McGlinn, E. *et al. Proc. Natl. Acad. Sci. USA* **106**, 18610–18615 (2009).