CDB SEMINAR

Martin Leeb

Wellcome Trust - Medical Research Council Cambridge Stem Cell Institute, University of Cambridge

Monday, December 10, 2012
16:00~17:00 C1F Auditorium

Haploid ES cells as a tool for forward genetic approaches in mammals

Summary

Forward genetics is a powerful and unbiased approach to identify key factors that underlie biological processes. However, diploid genomes of complex organisms limit forward genetic approaches in biomedical model species such as in mice. Mammalian haploid cells are only present in the germ line and in some tumour derived cell lines. Near haploid mammalian tumour cell lines have been used successfully in forward genetic approaches. However, genomic rearrangements and a transformed phenotype limit their use in a developmentally relevant context.

We have established haploid mouse ES cell lines from several genetic backgrounds by parthenogenetic activation of oocytes. Haploid ES cells can stably be maintained in culture for over 35 passages and have a stable karyotype. Their authentic ES cell identity was confirmed by immunostaining and global gene expression analysis. Furthermore, haploid ES cells retain developmental potential and can contribute efficiently to germ line competent chimeras after diploidization.

We have successfully tested their applicability in forward genetic approaches in a proof-of-principle loss of function screen to identify genes involved in mismatch repair. Currently, haploid ES cells are used in a piggyBac based screen for regulators of the exit from pluripotency. We believe that haploid ES cells will provide a useful platform for forward genetic approaches in mammalian cells.

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