hESC – iPSC equivalence: a genetic, epigenetic, functional and immunogenic comparison.

Chevallard Navarro, Pablo
Universitat Autònoma de Barcelona

Introduction
ESC: Embryonic Stem Cell  iPSC: induced Pluripotency Stem Cell
iPSC are very similar to ESC, but are they equivalent? Our goals are to determine which are the differences and similarities between this cell groups at different levels, enunciate the fields of future investigations and to obtain some conclusions that may help in better understanding of the hESC-iPSC equivalence question.

Genetic
Small number of genes differently expressed (Chin et al., 2010). Guenther et al.,(2010) objected differences are due to laboratorial and statistic methods, and not consistent through different cellular lines (due to line variability). Cellular lines heterogeneity and differences between early and late passages of iPSC might be the cause for some of the observed differences.

Epigenetic
iPSC have to acquire an ESC-alike histone open methylation pattern. Xie et al (2009) identified 71 Different Methylated Regions (DMR) between ESC and iPSC. Most were related to epigenetic memory, but some were exclusive from iPSC. High levels of ARNmi. Pluripotent context.: low H3K27me3 and high H3K4me3 in promotors of actively transcribed genes. Alike at both cell types.

Functional
Proteomics: differences in less than 1% of proteins and fosforilation sites; no common functionality observed. The number of differences between IPS-ESC were the same than between ESC lines.
Epigenetic memory has been detected at high passages. It might affect long term.

Inmunogenic
Supposedly, iPSC does not generate immune response. But it depends on the method of generation. Retrovirus can insert in transcriptionally active locations related with immune mediators. Immune response has been observed in murines. With lentivirus and plasmids no immune response has ever been observed. This is one of the main advantages of iPSC. ESC depends of compatibility or syngeneic donators. Immunogeneicity in human iPSC has not been deeply studied yet. As each cell involves different proteins, further studies need to be made.

Conclusions
Genetic: no concrete and recurrent differences.
Epigenetic: the most controverted field. Differences observed, particularly regarding lysine methylation pattern, whose effects are not clear. Might affect cell functions.
Proteomic: negligible differences, with no common functionality. No distinction possible.
Functional: high number of study limitations. Very similar differentiation potential, ESC’s seems slightly higher.
Immunogenic: iPSC do not produce immunogenic response (some exceptions with retrovirus method). Cells obtained from ESC can produce IR if there is no HLA compatibility.

Methods
Bibliographic search at NCBI’s PubMed. Articles comparison.4 months stage at Human Genetics lab at E.O. Ospedale Galliera (Genoa, IT) practising iPSC obtention from fibroblasts and neural differentiaton.

Bibliography