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Neural differentiation of murine androgenetic embryonic stem cells

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Introduction:

Zygotes with two genomes from the same sex generated by the exchange of paternal (androgenetic; AG) or maternal (gynogenetic; GG) pronuclei are not competent to develop into viable offspring. Despite the restricted developmental potential of uniparental cells probably reflecting the different roles of maternal and paternal genomes during development, uniparental zygotes develop into blastocyst from which embryonic stem cells (ESC) can be generated. The neural differentiation potential of GG ESCs is well characterised while the developmental potential of AG ES cells is less clear.

Materials and Methods:

Our study investigates the potential of murine AG ESCs in comparison to GG and biparental (normal fertilised; N) ESCs to differentiate into neural progenitor/stem cells utilizing an *in vitro* and an *in vivo approach*. Firstly, AG, GG and N ESCs were *in vitro* differentiated into pan-neural progenitor cells and subsequently into neuronal and glial cell types. Secondly, after blastocyst injection of AG, GG and N ESCs and isolation of donor cells from

chimeric fetal brains, the multi-lineage neural differentiation potential of donor cells was analysed.

Results:

We observe that AG ESCs similar to GG and N ESCs differentiate *in vitro* into cells with neuronal and glial morphology that express neuronal- and glial-specific markers. In addition, following blastocyst injection and analysis of donor cells in E12.5 chimeric brains we observe similar brain seeding patterns of uniparental and biparental cells. Likewise, FACS-sorted cells from E12.5 chimeric brains show comparable frequencies of neurosphere-initiating and neural multilineage-differentiation potentials.

Discussion and Conclusions:

Our data show that uni- and bi-parental ESCs do not differ in their *in vitro* neural differentiation potentials. Furthermore, uni- and bi-parental ES cells generate similar seeding patterns and neural progenitor/stem cells in E12.5 chimeric brain. These *in vivo* data suggest that the previously described differences in the *in vivo* engraftment pattern

of uniparental cells in late fetal and adult brains is not due to limitations in the proliferation or differentiation properties of uniparental neural progenitor/stem cells.

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