

Identification and manipulation of signalling pathways that control growth and differentiation of human auditory stem cells using small molecules

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Project description:

Deafness is a condition that affects over 270 million people worldwide and for which there is no medical treatment. During the past few years, our laboratory has isolated populations of human auditory stem cells, either from foetal cochleae or from hESCs, which could be the basis for a future therapeutic solution. The translation of a stem cell approach into a clinical therapy would be greatly facilitated by understanding the signalling pathways involved in proliferation and differentiation of these stem cells. The ability to control these pathways using small molecules would allow their production in vitro in a safe and reliable manner.

Small compound libraries that contain hundred of thousands of chemicals targeting different molecules and signalling pathways, are excellent tools for screening. Combined with well-defined in vitro systems and specific assays, they have been successfully applied to identify signalling pathways that regulate important stem cell properties. For instance, Chen et al (1) using a phenotype-based screening, identified pluripotin as a promoter of self-renewal in mES cells.

The proposed project aims to identify small compounds that could be used:

1. to improve the culture conditions to maintain human auditory stem cells in vitro and
2. to better control their differentiation into the main sensory lineages i.e. hair cells and neurons.

This project is jointly supported by the MRC and Pfizer Ltd through a CASE studentship awarded to M. Rivolta. Prospective candidates should apply to http://www.shef.ac.uk/bms/prospective_pg/how_to_apply.

References

1. Chen, S. et al. (2006) *Self-renewal of embryonic stem cells by a small molecule*. Proc Natl Acad Sci U S A 103 (46), 17266-17271.
2. Chen, W; Cacciabue-Rivolta, D; Moore, HD and Rivolta, MN. *The human fetal cochlea can be a source for auditory progenitors/stem cells isolation*. Hearing Res 233: 23-29, 2007.
3. Chen, W; Johnson, SL; Marcotti, W; Andrews, PW; Moore, HD and Rivolta, MN. *Human Fetal Auditory Stem Cells (hFASCs) can be expanded in vitro and differentiate into functional auditory neurons and hair cell-like cells*. Stem Cells, 27:1196-1204, 2009.

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<http://www.shef.ac.uk/bms/research/rivolta>

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