

NRSF is a repressor of a subset of neural specific genes. While this observation alone supports the hypothesis that NRSF acts as a repressor *in vivo*, the most surprising observation, however, is that in the absence NRSF activity, no ectopic neural tissue is observed. In other words, although neural specific genes are induced in non-neural cells, this expression does not make those cells neuron. As courageously acknowledged by the authors, the fact that the knockout mice have a grossly normal nervous system demonstrates that NRSF does not play a role in the process of cell fate determination (assuming that redundancy of NRSF function is not an issue). Just as all masters are eventually stripped of their masterhood, the study by Chen *et al.* demonstrates that NRSF is not, in fact, a master negative regulator of neurogenesis.

The idea of derepression of a repressor is at the heart of the prediction of the default model. As NRSF does not seem to be the key player in cell fate determination, does this mean that such regulatory (instead of master) transcription factors don't exist? Are there other candidates for the role

originally suggested for NRSF? What is the link between the early inhibitory signals that operate in the embryonic ectoderm and neurogenic genes? These questions are far from being answered, but several recent studies provide possible clues to the transcription factors involved that may comprise such a link. First, it has been shown that proteins encoded by the immediate early-response genes whose transcription is triggered by BMPs inhibit neural induction and induce epidermis in amphibian ectodermal explants during gastrulation. These proteins include *Msx1* (the vertebrate homologue of the *Drosophila msh* gene; ref. 10), *PV.1* (ref. 11) and *GATA-1* (ref. 12). It has been shown that *SoxD* is the earliest known transcription factor induced following extracellular inhibition of the BMP pathway and appears to be an endogenous activator of neurogenic genes, a few hours later, in the neural plate¹³. If *Msx1* is a direct repressor of *SoxD* expression—which has yet to be proven—then it is possible, at least theoretically, to make the link between the organizer-specific inhibitors of the BMP pathway operating

outside of the cell to the transcription factors that carry the baton down the line.

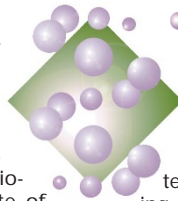
Although the study by Chen *et al.* suggests that the role of NRSF during early vertebrate embryonic neural induction can be put to rest, it does not mean, of course, that the molecule does not carry out important functions that are unrelated to cell-type specification. On the contrary; the requirement of NRSF for the repression of neural-specific genes in non-neuronal cells has now been proven masterfully *in vivo*. □

1. Harland, R. & Gerhart, J. *Annu. Rev. Cell Dev. Biol.* **13**, 611–667 (1997).
2. Chang, C. & Hemmati Brivanlou, A. *J. Neurobiol.* **36**, 128–151 (1998).
3. Schoenherr, C.J. & Anderson, D. *Science* **267**, 1360–1363 (1995).
4. Chong, J.A. *et al. Cell* **80**, 949–957 (1995).
5. Tapia-Ramirez, J. *et al. Proc. Natl Acad. Sci.* **94**, 1177–1182 (1997).
6. Schoenherr, C.J. *et al. Proc. Natl Acad. Sci.* **93**, 9881–9886 (1996).
7. Scholl, T. *et al. J. Immunol.* **156**, 1448–1457 (1996).
8. Palm, K. *et al. J. Neurosci.* **18**, 1280–1296 (1998).
9. Chen, Z.-F., Paquette, A.J. & Anderson, D.J. *Nature Genet.* **20**, 136–142 (1998).
10. Suzuki, A. *et al. Development* **124**, 3037–3044 (1997).
11. Ault, K.T. *et al. Dev. Biol.* **192**, 162–171 (1997).
12. Xu, R.H. *et al. Mol. Cell Biol.* **17**, 436–443 (1997).
13. Mizuseki, M. *et al. Neuron* **21**, 77–85 (1998).

TOUCHINGbase

● Ellison funds ageing research

Research into the biology of ageing has received a financial boost through the philanthropic interests of Larry Ellison, CEO of the software giant, Oracle Corporation. Ellison's long standing interest in biomedical research resulted last year in the establishment of the Ellison Medical Foundation, a private non-profit organization and the second largest funding agency of basic biomedical research on ageing after the National Institute of Aging (NIA). Ellison is seeking to fund innovative biomedical ageing research that is currently funded inadequately, perhaps because of perceived risk of failure or because it is outside traditional research interests. Richard Sprott, Executive Director of the foundation (formerly Associate Director of Biology of Aging programs at NIA) explains that they are working closely with the NIA to ensure that their efforts complement, rather than compete. The current activities of the foundation include a New Scholars program, a Senior Scholars program and sponsorship of a series of conferences focusing on specific areas of ageing research. Ellison has given financial commitment for five years, after which time he will evaluate whether the research activities supported by the Foundation warrant his continued investment. Joshua Lederberg, Chairman of the Scientific Advisory Board, notes that Ellison's interests in biomedical research are broad and that, if successful, the foundation's activities may inspire Ellison to support other fields in the future.



● CSHL workshop online

Cold Spring Harbor Laboratory (CSHL) kicked off its series of workshops on Emerging Technologies for Cancer Research with the "Conditional Genetics Technologies in the Mouse" workshop (August 31–September 2). Organized by Allan Bradley, Klaus Rajewsky and Janet Rossant, the meeting embraced the latest technology for creating conditional mouse mutants, including updates on Cre and Flp recombination, ligand-induced dimerization and hormone-modulated systems. In the wake of the National Institutes of Health and the Jackson Laboratory signing an agreement with DuPont to use *Cre/loxP* technology last month (see September's editorial), the workshop concluded with a presentation by Daniel Curran, a representative from DuPont, outlining the conditions under which researchers can access the patented technology. For those who couldn't attend the workshop, there is an opportunity to peruse the material online at <http://www.leadingstrand.org>. The website features a slideshow of 32 of the 34 lectures, with audio accompaniment, although the discussions that followed the talks are not available. Access to the online material is free for workshop attendees and available to academic non-attendees for US\$25. This is the first time that the contents of a CSHL meeting are available online. According to David Stewart, director of meetings and courses at the Laboratory, who arranged the online workshop, "this is a one-off trial for the Laboratory to assess the level of interest in this scientific resource".

● Eugenia Spanopoulou (1960-1998)

The scientific community was saddened last month by the untimely passing of Eugenia Spanopoulou, an Assistant Professor at the Mount Sinai School of Medicine in New York and recently appointed Howards Hughes Medical Institute Investigator. Dr. Spanopoulou was among those who perished in the Swissair 111 crash on September 3, as were her husband, Andrew Hodtsev, and son, Platon. Her scientific achievements included the characterization of the *Thy-1* gene and its role in thymic oncogenesis as a graduate student with Frank Grosveld at the University of London; as a postdoctoral associate with David Baltimore, at MIT and the Rockefeller University, and later as an independent investigator, she was instrumental in characterizing the roles of the RAG-1 and RAG-2 proteins in V(D)J recombination, the fundamental mechanism by which animals generate diversity in antigen receptors on B and T cells. More recently, she participated in demonstrating that Omenn syndrome, a severe immunodeficiency, results from defects in the V(D)J recombination process. "She really enjoyed the intellectual process, the whole puzzle, trying to move the pieces around and seeing where they would fit in," said colleague and collaborator Dr. David Schatz of Yale University. "She was just hitting her stride."