RESEARCH HIGHLIGHTS

HIGHLIGHT ADVISORS

NANCY ANDREASEN

UNIVERSITY OF IOWA, IA, USA

ALLAN BASBAUM

UNIVERSITY OF CALIFORNIA
SAN FRANCISCO, CA, USA

RANDY BUCKNER

WASHINGTON UNIVERSITY,
MO, USA

DAVID CLAPHAM

HARVARD MEDICAL SCHOOL,
MA, USA

PIETRO DE CAMILLI

YALE UNIVERSITY SCHOOL OF
MEDICINE, CT, USA

BARRY EVERITT

UNIVERSITY OF CAMBRIDGE,
UK

GORDON FISHELL

SKIRBALL INSTITUTE, NY, USA

MARY KENNEDY

CALIFORNIA INSTITUTE OF
TECHNOLOGY, CA, USA

LYNN NADEL

UNIVERSITY OF ARIZONA,
AZ, USA

DENNIS O'LEARY

THE SALK INSTITUTE, CA, USA

TERRY SEJNOWSKI

THE SALK INSTITUTE, CA, USA

WOLF SINGER

MAX-PLANCK-INSTITUT FÜR
HIRNFORSCHUNG, GERMANY

CLAUDIO STERN

UNIVERSITY COLLEGE LONDON,
UK

PATRICK TAM

CHILDREN'S MEDICAL
RESEARCH INSTITUTE, SYDNEY,
AUSTRALIA

RICHARD W. TSJEN

STANFORD UNIVERSITY
SCHOOL OF MEDICINE,
CA, USA

RAFAEL YUSTE

COLUMBIA UNIVERSITY,
NY, USA

DEVELOPMENT

Odd SOX

Many of the molecular mechanisms that promote neuronal differentiation are poorly understood. Now, Sandberg and colleagues report the surprising discovery that the transcription factor SOX21 is involved in promoting neuronal differentiation — a finding that is at odds with the action of other members of a subset of the SOX gene family, which block neurogenesis.

Proneural proteins are crucial for neurogenesis. They trigger the exit of precursors from the cell cycle and initiate events that promote neuronal differentiation. However, until now, the mechanisms by which they achieve this have not been clear.

SOX1–3, which are found in most progenitor cells in the developing CNS, block neuronal differentiation by obstructing the action of proneural proteins. Suppression of SOX1–3 activity is therefore essential to enable proneural genes to influence neurogenesis. Sandberg and colleagues were interested in the role of SOX21 in neurogenesis because it inhibits gene expression that is activated by SOX1–3 and because it is expressed in the ventricular zones, where self-renewing precursor cells originate.

These researchers found that, in the chick neural tube, SOX21 is expressed primarily in progenitor cells that are positive for SOX1–3. Forced expression of SOX21 caused cells to leave the cell cycle with subsequent downregulation of progenitor markers and upregulation of

many neuronal markers, indicating that SOX21 promotes a neuronal fate.

Sandberg and colleagues went on to show that variations in the balance of expression of SOX21 relative to SOX1–3 determine whether neural cells remain as progenitor cells or progress to neuronal differentiation. SOX21 must be upregulated to tip this balance so that SOX1–3 activity is suppressed and neuronal differentiation can take place.

Importantly, overexpression of the proneural transcription factor neurogenin 2 (NGN2) led to higher expression of SOX21 before the expression of neuronal markers was initiated, an effect that was lost when ID2, which blocks the activity of NGN2, was co-expressed with NGN2. These data indicate that proneural protein activity upregulates SOX21

levels and point to an important link between the action of these two types of protein. The requirement for SOX21 in neurogenesis was confirmed using RNA interference to reduce SOX21 expression, which led to a marked reduction in the upregulation of neuronal markers.

This elegant study highlights a synergistic relationship between proneural proteins and SOX21 in their regulation of neuronal formation, thereby providing an important advance in our understanding of the molecular mechanisms involved in neurogenesis.

Alison Rowan

References and links

ORIGINAL RESEARCH PAPER Sandberg, M., Källström, M. & Muhr, J. Sox21 promotes the progression of vertebrate neurogenesis. *Nature Neurosci.* **8**, 995–1001 (2005)

FURTHER READING Diez del Corral, R. & Storey, K. G. Markers in vertebrate neurogenesis. *Nature Rev. Neurosci.* **2**, 835–839 (2001)