

# RESEARCH HIGHLIGHTS

## HIGHLIGHT ADVISORS

### MICHAEL AKAM

UNIVERSITY OF CAMBRIDGE,  
UK

### SEAN B. CARROLL

UNIVERSITY OF WISCONSIN,  
USA

### NANCY J. COX

UNIVERSITY OF CHICAGO, USA

### SUSAN FORSBURG

UNIVERSITY OF SOUTHERN  
CALIFORNIA, USA

### RALPH J. GREENSPAN

THE NEUROSCIENCES  
INSTITUTE, CALIFORNIA, USA

### YOSHIHIDE HAYASHIZAKI

RIKEN GENOMIC SCIENCES  
CENTER, JAPAN

### MARK JOBLING

UNIVERSITY OF LEICESTER, UK

### PETER KOOPMAN

UNIVERSITY OF QUEENSLAND,  
AUSTRALIA

### LEONID KRUGLYAK

FRED HUTCHINSON CANCER  
RESEARCH CENTER, USA

### BARBARA MEYER

UNIVERSITY OF CALIFORNIA,  
BERKELEY, USA

### JOHN QUAKENBUSH

THE INSTITUTE FOR GENOMIC  
RESEARCH, USA

### JANET ROSSANT

MOUNT SINAI HOSPITAL,  
TORONTO, CANADA

### MARC VIDAL

DANA-FARBER CANCER  
INSTITUTE, BOSTON, USA

### VIRGINIA WALBOT

STANFORD UNIVERSITY, USA

### DETLEF WEIGEL

MAX PLANCK INSTITUTE FOR  
DEVELOPMENTAL BIOLOGY,  
GERMANY

### PHIL ZAMORE

UNIVERSITY OF  
MASSACHUSETTS, USA

### LEONARD I. ZON

CHILDREN'S HOSPITAL,  
BOSTON, USA

## STEM CELLS

# Small RNAs cross the divide

One of the properties that make stem cells special is their ability to ignore signals that tell surrounding cells to stop dividing. Previously, how they do this has been something of a mystery, but two new studies now reveal that small RNAs hold the key.

Zamore and colleagues uncovered this role for small RNAs after identifying a new component of the miRNA processing machinery in *Drosophila melanogaster*. They showed that the dsRNA-binding protein Loquacious (LOQS) is essential for the processing of miRNA precursors by the Dicer 1 (DCR1) endonuclease and for the function of small interfering RNAs that silence repetitive regions. Intriguingly, *loqs* mutant female flies are sterile and have small ovaries.

Mutations that block the division or maintenance of germline stem cells (GSCs) are known to give rise to similar phenotypes, as they block the formation of egg chambers (which produce oocytes) by GSCs. The authors found that although GSCs were absent from *loqs* mutant females at 3–4 days of age, some oocytes were produced, so GSCs must have been present initially. Zamore and colleagues concluded that lack of LOQS function, and therefore small RNA production, leads to loss of GSCs due to either death or a failure to divide and produce daughter cells.

In the second study, Ruohola-Baker and colleagues showed that small RNAs have a role specifically in GSC division. They generated

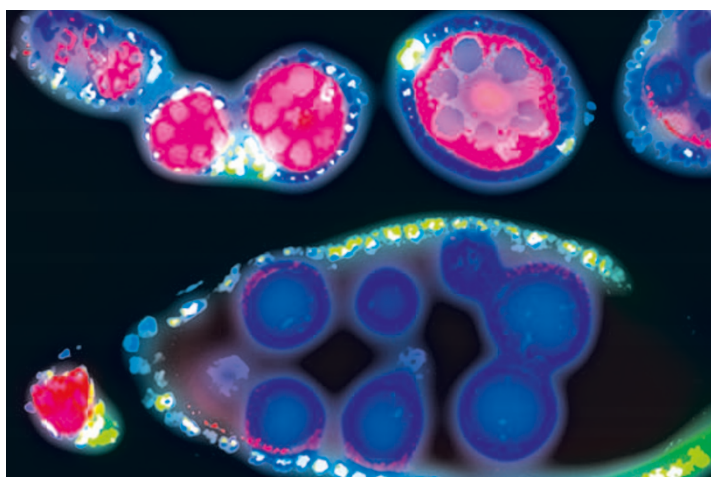


Image courtesy of Hannele Ruohola-Baker, University of Washington, Seattle

flies with ovaries containing GSC clones that were mutant for *dcr1*, and therefore completely lacked miRNAs. The number of GSCs was not altered, indicating that GSC maintenance is not impaired. However, the ovaries contained fewer developing egg chambers, which again indicated a defect in the ability of GSCs to give rise to these structures. In particular, the numbers of GSCs in S, G2 and M phase were reduced, indicating that these cells are blocked in G1 phase.

This study also showed that miRNAs normally allow GSCs to escape cell-cycle arrest by blocking the expression of Dacapo (DAP), a cell-cycle inhibitor. A *dcr1* mutation increased the number of DAP-positive GSCs, and *Dap* overexpression produced a *dcr1*-like phenotype. Furthermore, reducing DAP levels rescued the defects in *dcr1* mutants.

These studies show an essential role of small RNAs in *Drosophila* GSCs, enabling these cells to escape the controls on division that other cells obey. An important aim now will be to determine whether this function of small RNAs is conserved in mammalian stem cells.

Louisa Flintoft

## References and links

### ORIGINAL RESEARCH PAPERS

Förstemann, K. *et al.* Normal microRNA maturation and germ-line stem cell maintenance requires Loquacious, a double-stranded RNA-binding domain protein. *PLoS Biol.* **3**, e236 (2005) | Hatfield, D. S. *et al.* Stem cell division is regulated by the microRNA pathway. *Nature* **435**, 974–978 (2005)

**FURTHER READING** He, L. & Hannon, G. J. MicroRNAs: small RNAs with a big role in gene regulation. *Nature Rev. Genet.* **5**, 522–531 (2004)

### WEB SITES

Hannele Ruohola-Baker's laboratory: <http://depts.washington.edu/taneli>

Phillip Zamore's laboratory: <http://www.umassmed.edu/bmp/faculty/zamore.cfm?start=Research&>