

## Bright Ideas: Highlights of Innovative Journal Articles

### Stem Cell Division Is Regulated by the MicroRNA Pathway

S.D. Hatfield, H.R. Shcherbata, K.A. Fischer, K. Nakahara, R.W. Carthew, and H. Ruohola-Baker, *Nature* 435, 974 (2005).

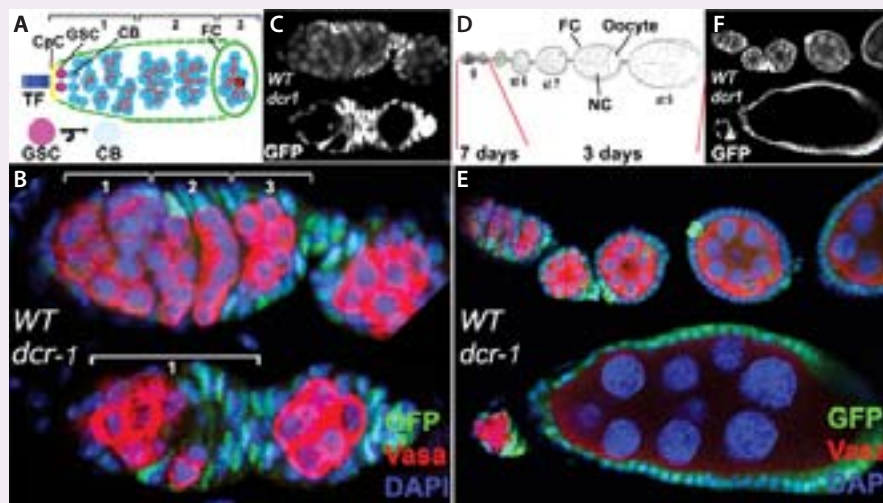
What controls stem cell division? A recent study employed fluorescence immunostaining and confocal microscopy, coupled with a variety of Molecular Probes immunofluorescence reagents, to investigate the mechanism by which stem cells elude the cellular controls that keep normal cells from dividing. This study examined *Drosophila* germline stem cells (GSCs) deficient in the RNase Dicer-1, which is involved in the processing of microRNAs (miRNAs). miRNAs are believed to repress gene expression by binding to and preventing translation of certain messenger RNAs. The group used an array of primary and fluorescently labeled secondary antibodies to assess the rate of egg chamber production, to evaluate changes in protein markers of GSCs, and to analyze levels of proteins associated with cell cycle control.

Oogenesis in *Drosophila* involves self-renewing GSCs in the ovary. The group found that Dicer-1 mutants produced fewer egg chambers than did wild-type *Drosophila* GSCs, indicating a role for Dicer-1 in germline production. However, Dicer-1 mutant GSCs retained stem cell identity, as shown by immunofluorescence analysis of the

expression of three markers of GSCs (the presence of p-mad and adducin and the absence of BamC). An increase in Cyclin E (CycE) expression was also observed, suggesting that Dicer-1-deficient GSCs are arrested in the G<sub>1</sub> to S transition. This arrest was further shown to be mediated by the protein Dacapo (Dap), a cyclin-dependent kinase inhibitor known to be involved in negatively regulating the G<sub>1</sub> to S transition; levels of Dap protein were significantly elevated in Dicer-1 mutants as compared to wild-type GSCs.

The results of this study suggest that miRNAs allow stem cells to bypass controls over the G<sub>1</sub> to S transition by repressing Dap protein. These findings could have important implications in the study of tumorigenesis, a process in which miRNAs may also be involved.

For a complete list of our extensive line of fluorescently labeled secondary antibodies, please visit us at [probes.invitrogen.com/signalamp](http://probes.invitrogen.com/signalamp). Other products across Invitrogen have proven to be valuable tools for various aspects of stem cell research—the table on the facing page highlights many of these reagents.



Loss of Dicer-1 (Dcr-1) function in GSCs reduces the rate of egg chamber production. A) Schematic of a germarium divided into three regions. Region one contains GSCs and dividing cysts. B, C) All three regions are observed in a wild-type heterozygous *dcr-1<sup>Q1147X</sup>/+* germarium (WT, top), but not in a mosaic *dcr-1<sup>Q1147X</sup>* germarium 12 days after clone induction (no GFP, *dcr-1*, bottom). D) Oocyte development is divided into 14 stages. E, F) Many of the developmental stages are missing in ovarioles that are complete *dcr-1<sup>Q1147X</sup>* germline clones (no GFP, 12 days after clone induction; bottom of panels E and F). CpC, cap cells; CB, cystoblast; DAPI, 4,6-diamidino-2-phenylindole; FC, follicle cells; NC, nurse cells; TF, terminal filaments. Vasa marks the germ line. Absence of GFP marks *dcr-1* mutant cells. Image contributed by Halyna Shcherbata, University of Washington, and reproduced with permission from *Nature* 435, 974 (2005).

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*Stem Cells* details the use of our high-quality reagents and kits at all stages of stem cell research.

Reference	Invitrogen Products Used				
	Molecular Biology	Labeling and Detection (Molecular Probes)	Cell Culture (GIBCO)	Antibodies (Zymed)	Magnetic Beads (Dyna)
Segev, H. <i>et al.</i> Differentiation of human embryonic stem cells into insulin-producing clusters. <i>Stem Cells</i> 22, 265 (2004)		<ul style="list-style-type: none"> <li>TO-PRO<sup>®</sup>-3 iodide (T3605)</li> </ul>	<ul style="list-style-type: none"> <li>Knockout Dulbecco's modified Eagle's medium (D-MEM)</li> <li>Knockout Serum Replacement</li> <li>L-glutamine</li> <li>MEM Nonessential Amino Acids Solution</li> <li>2-mercaptoethanol</li> <li>Basic Fibroblast Growth Factor (bFGF), Human, Recombinant</li> <li>Collagenase</li> <li>D-MEM/F-12</li> <li>insulin-Transferrin-Selenium-A Supplement</li> <li>N-2 supplement</li> <li>B-27 Serum-Free Supplement</li> <li>Digest-All 3 (Pepsin)</li> </ul>	<ul style="list-style-type: none"> <li>BrdU Streptavidin-Biotin Labeling Kit</li> </ul>	
Harraz, M. <i>et al.</i> CD34+ blood-derived human endothelial cell progenitors. <i>Stem Cells</i> 19, 304 (2001)		<ul style="list-style-type: none"> <li>CellTracker<sup>™</sup> CM-Dil (C7000)</li> <li>SP-DiOC<sub>18</sub>(3) (D7778)</li> </ul>	<ul style="list-style-type: none"> <li>Medium 199</li> <li>Antibiotic/Antimycotic, liquid</li> <li>TRizol<sup>®</sup> reagent</li> <li>M-MLV (Moloney Murine Leukemia Virus) reverse transcriptase (RT)</li> </ul>		<ul style="list-style-type: none"> <li>CD34 antibody-coated magnetic beads</li> <li>CD14 antibody-coated magnetic beads</li> </ul>
Szczypka, M.S. <i>et al.</i> Rare incorporation of bone marrow-derived cells into kidney after folic acid-induced injury. <i>Stem Cells</i> 23, 44 (2005)		<ul style="list-style-type: none"> <li>Fluorescein di-β-D-galactopyranoside (FDG) (F1179)</li> <li>Propidium iodide (P1304MP)</li> <li>Alexa Fluor<sup>®</sup> 488 goat anti-rabbit IgG (H+L) (A11008)</li> <li>Alexa Fluor<sup>®</sup> 594 goat anti-mouse IgG (H+L) (A11005)</li> <li>Streptavidin, Alexa Fluor<sup>®</sup> 488 conjugate (S11223)</li> <li>DAPI (D1306)</li> </ul>	<ul style="list-style-type: none"> <li>Leibovitz's L-15 Medium</li> </ul>	<ul style="list-style-type: none"> <li>Anti-α-acetylated tubulin-1 (AT1) (32-2700)</li> <li>Anti-zona occludens-1 (ZO1) (61-7300)</li> </ul>	
Fink, T. <i>et al.</i> Induction of adipocyte-like phenotype in human mesenchymal stem cells by hypoxia. <i>Stem Cells</i> 22, 1346 (2004)	<ul style="list-style-type: none"> <li>Random decamer primers</li> </ul>	<ul style="list-style-type: none"> <li>Hoechst 33342 (H1399)</li> <li>SYPRO<sup>®</sup> Ruby protein blot stain (S11791)</li> </ul>	<ul style="list-style-type: none"> <li>Minimal Essential Medium (MEM)</li> <li>Penicillin-Streptomycin</li> <li>D-MEM</li> </ul>		
Schulz, T.C. <i>et al.</i> Differentiation of human embryonic stem cells to dopaminergic neurons in serum-free suspension culture. <i>Stem Cells</i> 22, 1218 (2004)	<ul style="list-style-type: none"> <li>Goat serum</li> <li>SuperScript<sup>™</sup> First-Strand Synthesis System</li> </ul>	<ul style="list-style-type: none"> <li>Alexa Fluor<sup>®</sup> 488 conjugated goat anti-mouse IgG</li> <li>Goat anti-rabbit, anti-sheep, anti-rat, or anti-mouse antibodies conjugated to Alexa Fluor<sup>®</sup> 350, Alexa Fluor<sup>®</sup> 488, Alexa Fluor<sup>®</sup> 568, or Alexa Fluor<sup>®</sup> 647</li> <li>Anti-HuC/HuD neuronal protein (human), mouse IgG<sub>2b</sub> monoclonal 16A11 (A21271)</li> </ul>	<ul style="list-style-type: none"> <li>D-MEM/F-12</li> <li>Knockout Serum Replacement 1X</li> <li>MEM Nonessential Amino Acids</li> <li>L-glutamine</li> <li>Penicillin-Streptomycin</li> <li>Collagenase</li> <li>Trypsin/EDTA</li> <li>EDTA-Free Trypsin</li> <li>D-MEM</li> <li>N-2 Supplement</li> <li>Neurobasal<sup>™</sup> Medium</li> <li>B-27 Serum-Free Supplement 1X</li> <li>TRizol<sup>®</sup> Reagent</li> </ul>		

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