behave as two-dimensional metals and conduct electric current. In ordinary insulators, such surface states are typically fragile and can be destroyed by coarsening the surface. In topological insulators, however, the surface states are robust, and according to theory they should essentially persist—despite damaging the surface by chemical or mechanical means, altering its shape or orientation with respect to the crystal lattice, or even disordering the bulk—as long as such changes are applied in moderation. The conducting surface states can be destroyed only by changes that also destroy the insulating character of the bulk.

The above statements are subject to an important caveat: They apply exclusively to systems that respect time reversal symmetry (TRS)—that is, nonmagnetic topological insulators in zero external magnetic field. When TRS is broken, all bets are off, and even a weak magnetic perturbation can open up a gap in the spectrum of the topologically protected surface states. Chen *et al*. exploit this point to show that the gapless surface states of the pristine topological insulator Bi_2Se_3 become gapped upon introducing magnetic impurities (Mg and Fe) into the crystal.

Although this finding confirms one of the basic predictions of the theory underlying the physics of topological insulators, it also raises several new questions. Perhaps the most interesting concerns the nature of magnetism in Mg/Fe-doped Bi_2Se_3. It might be expected that gapping of the surface state would require a "uniform" breaking of TRS, whereby the magnetic moments of the dopant atoms all point in the same direction, with a component perpendicular to the surface. Whether such ordering occurs in the bulk (or on the surface only) is currently unknown, as is the mechanism behind this ordering.

Where does the exact quantization fit into this picture described above? According to theory (*4*–*6*), when the gap opens as the result of a magnetic perturbation, the resulting surface is no ordinary insulator; instead, it is a quantum Hall insulator, with properties similar to those of the familiar quantum Hall systems realized in 2DEGs. Its Hall conductance is predicted to be $(2n + 1)e^2/2h$, where n is an integer and $2n + 1$ corresponds to the (odd) number of gapless surface states in the underlying pristine topological insulator. In Bi_2Se_3 there is a single surface state ($n = 0$), and one thus expects $\sigma_{Hall} = e^2/2h$. The appearance of such a "fractional" value of quantized conductance (due to the factor of 2 in the denominator) in a weakly interacting system of electrons is itself very interesting, as is the fact that it should appear in the absence of an externally applied magnetic field. These two features set this effect apart from the conventional quantum Hall effects in 2DEGs and make it a likely new candidate for the list of solid-state systems exhibiting the phenomenon of exact quantization.

As yet, direct experimental measurement of the quantized surface Hall conductance in a topological insulator remains elusive. But once observed, aside from testing a fundamental physical paradigm, it will offer possibilities for future practical applications, such as the proposed dissipationless switching of magnetic moments that can be of use in the magnetic recording industry (*7*, *8*).

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DEVELOPMENTAL BIOLOGY

Versatile Germline Genes

When do germ cells establish their separate, independent identity during animal development?

Celina Juliano[1] and Gary Wessel[2]

Animal germline cells ultimately produce eggs and sperm, providing an immortal link to the next generation. Establishing and maintaining the germline requires a conserved gene set (*1*), but traditionally classified "germline genes" may have a broader role in development than originally anticipated. Recent findings from less well-studied animal models suggest that in some taxa, germline genes appear to specify a multipotent cell lineage during embryogenesis, the fates of which include both somatic cells and the germ line.

During animal embryogenesis, the germ line is segregated from somatic cells (*2*), but this lineage dichotomy is not universal in animals. Studies exploring this segregation have primarily focused on organisms from two major animal groups, the vertebrates and the ecdysozoans, including the model organisms *Drosophila melanogaster* (fruit fly), *Caenorhabditis elegans* (roundworm), *Mus musculus* (mouse), *Danio rario* (zebrafish), *Xenopus laevis* (frog), and *Ambystoma mexicanum* (axolotl). In these animals, the germ line separates from the rest of the embryo prior to gastrulation, an early developmental stage in which cells organize into specific layers that will establish the animal's body plan. Thus, the development of these segregated cells in vivo is absolute and limited to a germ cell fate. In the fly, worm, zebrafish, and frog, the germ line is established autonomously by the inheritance of cytoplasm during cell division that contains specification factors, such as the RNA-binding proteins encoded by the genes *vasa*, *nanos*, and *piwi*. Alternatively, the mouse and axolotl segregate their germ line during embryogenesis through inductive cell-to-cell interactions, yet a highly similar gene set is involved.

However, in other animal taxa, germline segregation occurs after gastrulation. In these animals, long-term multipotent precursor cells are established during embryogenesis, from which the germ line separates after embryonic development is completed. For example, in the marine annelid *Platynereis dumerilii* (a lophotrochozoan), one of the embryonic cells (the 4d lineage) gives rise to proliferating cells that express *vasa*, *nanos*, and *piwi*. However, after embryogenesis is complete, these cells contribute both to the somatic mesodermal tissues of the developing adult segments and to the germ line (*3*). Similarly, in the snail *Ilyanassa* (a lophotrochozoan), the 4d lineage, which expresses *vasa* and *nanos*, gives rise to multipotent cells during embryogenesis that later contribute to the germ line and to mesoderm and endoderm of the adult (*4*, *5*). Furthermore, *nanos* is required to maintain

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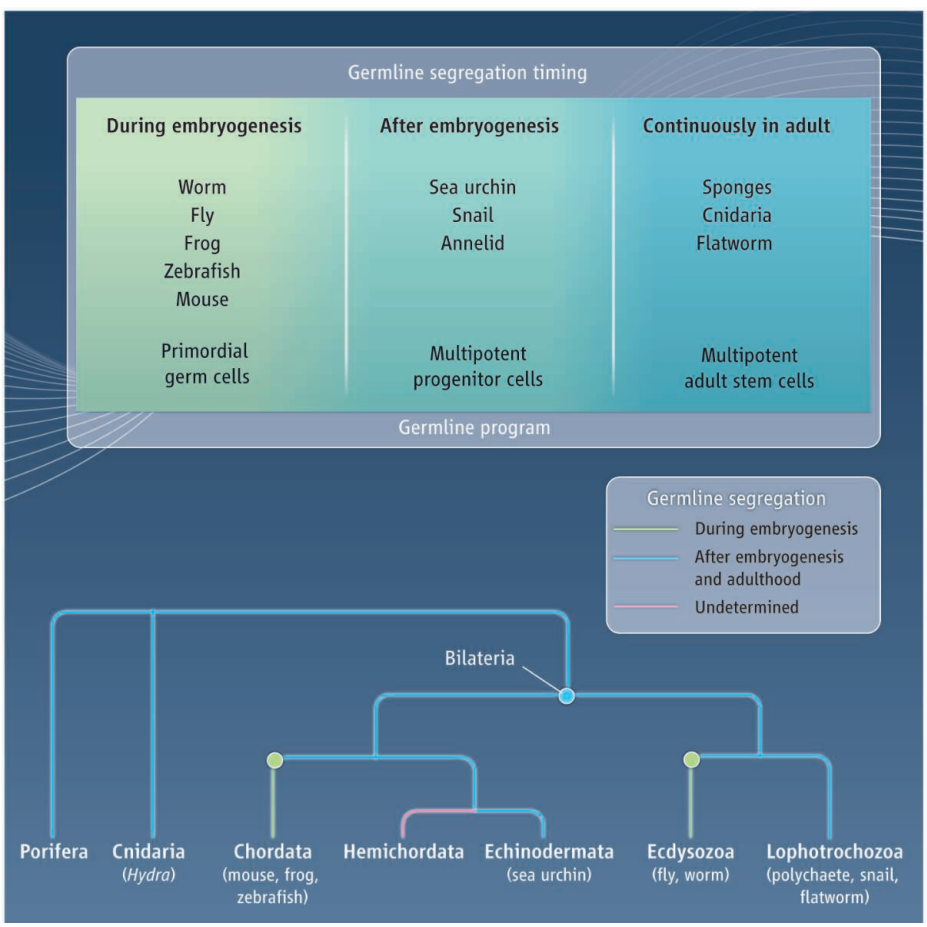
the fate of the snail 4d lineage; loss of *nanos* function results in a loss of all 4d-derived adult structures (*4*). Thus, similar to the marine annelid germ line, the snail germ line segregates from multipotent descendants after embryogenesis, and these multipotent cells likely depend on conserved "germline" genes such as *vasa*, *nanos*, and *piwi* for their establishment and maintenance.

The germ line of the echinoderm *Strongylocentrotus purpuratus* (sea urchin) also segregates from the soma well after embryogenesis. Sea urchin embryogenesis culminates in the formation of a swimming larva. At metamorphosis, a juvenile sea urchin emerges and larval tissues are destroyed. Cells of the small micromere lineage, which are specified at the 32-cell embryo stage, are multipotent but contribute only to adult tissues and not to the larva (*6*, *7*). This small micromere lineage expresses *vasa*, *nanos*, and *piwi*; loss of *nanos* function disrupts formation of the juvenile, and metamorphosis does not occur (*6*, *8*, *9*). Thus, similar to the snail and the marine annelid germ lines, the sea urchin germ line segregates after embryogenesis and arises from a long-term multipotent precursor cell that is established during embryogenesis through the functions of genes originally ascribed only to the germ line.

Many adult flatworms, cnidarians, and sponges contain multipotent or totipotent stem cells that give rise to various adult cell types, including the germ line. These animals continually segregate germ line from stem cells throughout adulthood. The lophotrochozoan flatworms, such as planarians, contain totipotent cells (neoblasts) that express *piwi*, *vasa*, *tudor*, and *pumilio*, and give rise to all tissue types. These genes are required for neoblast function, but were first identified as germline genes in *Drosophila* (*10*). Several members of the phylum Cnidaria, the sister group to the Bilateria, contain adult multipotent stem cells (I-cells) that give rise to both somatic cells and germ cells. In adult *Hydra*, for example, I-cells selectively express *vasa* and *nanos*, but their functions are not yet known (*11*, *12*). Similar to the cnidarians, members of the phylum Porifera (sponges) are non-Bilateria and segregate their germ line continuously from adult stem cells. Adult sponges contain a totipotent stem cell (the archeocyte) that gives rise to somatic cells and to germ cells. *Piwi* is selectively expressed in the archeocytes of the sponge *Ephydatia fluviatilis*, suggesting the presence of a conserved gene program in the cnidarian, echinoderm, and lophotrochozoan multipotent germline precursors (*13*).

The timing of germline segregation in animals appears to occur along a continuum, with onset at embryogenesis and continuously throughout adulthood at the extremes (see the figure). In all cases, germline segregation requires that a population of cells, either multipotent or germline limited, be established in the embryo. Given that germline segregation from a multipotent precursor occurs after embryogenesis in the lophotrochozoans, echinoderms, cnidarians, and sponges, it is parsimonious to conclude that it is the ancestral mechanism of establishing a germline. This would predict that embryonic germline segregation evolved independently in vertebrates and ecdysozoans. It may be that the germline molecular program, which includes genes such as *vasa*, *nanos*, and *piwi*, originated in multipotent cells, and was subsequently coopted by more specialized, embryonic germ cells. However, it will be necessary to collect more functional data from animals spanning diverse taxa to reveal the most ancient and essential portions of such a multipotency molecular program.



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Germline segregation in animals. (**Top**) The timing of germline segregation from somatic cells varies, from early embryogenesis to continuously in the adult. The same underlying molecular program may operate in all cases. In segregation during embryogenesis, primordial germ cells migrate to the somatic gonad to give rise to germ cells. In segregation after embryogenesis, a long-term multipotent precursor is established in the embryo from which the germline segregates during larval development or adulthood. (**Bottom**) If germline segregation that occurs after embryogenesis (blue line) is the ancestral mechanism, then embryonic germline segregation (green line) must have evolved independently in vertebrates and ecdysozoans.

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