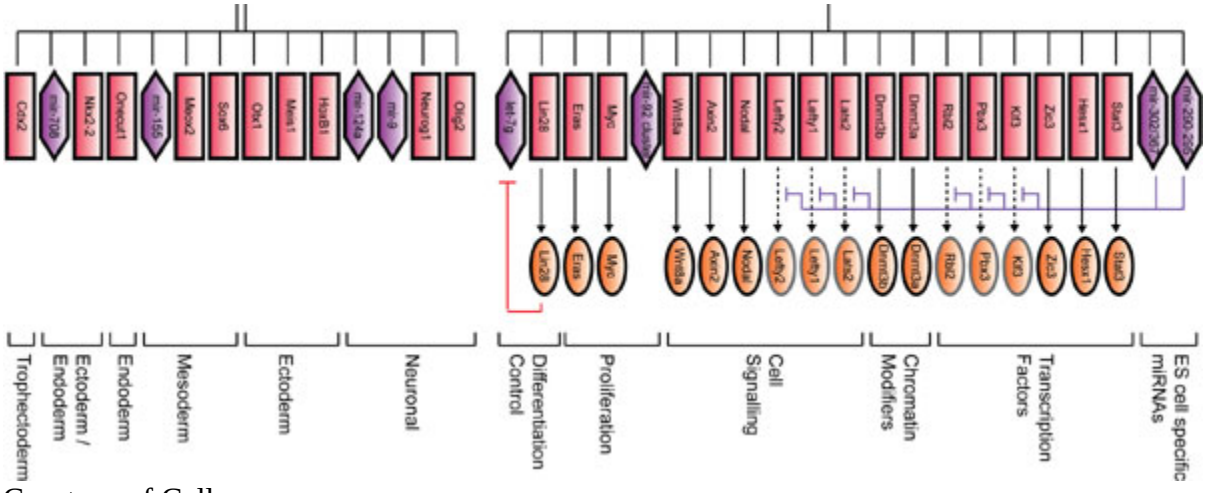
Visual Science

The Gang of Four at the Gateway of Life



Courtesy of Cell
By NICHOLAS WADE
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How does an egg cell divide and direct its progeny to turn into each of the many types of cell needed by the adult? Researchers led by Richard A. Young of the Whitehead Institute in Cambridge have been chipping away at this central question in biology. This graphic, from an article by Alexander Marson, Stuart S. Levine and others in the Aug. 7 issue of the journal Cell, presents the Young lab's latest version of the genetic circuitry that controls embryonic cells.

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Visual Science

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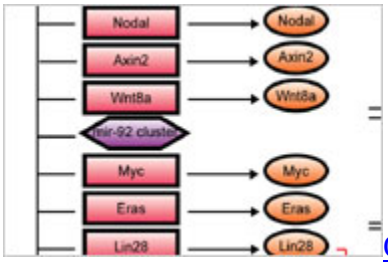

Graphic

The Gateway of Life

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The principal players in a cell's governance are proteins called transcription factors, which control the activity of genes. The transcription factors bind to short stretches of DNA called promoters and set in motion the process of translating the gene's information into protein. The promoters sit just upstream on the DNA strand of the gene they control. One transcription factor can control many genes — all that have the kind of promoter it binds to.

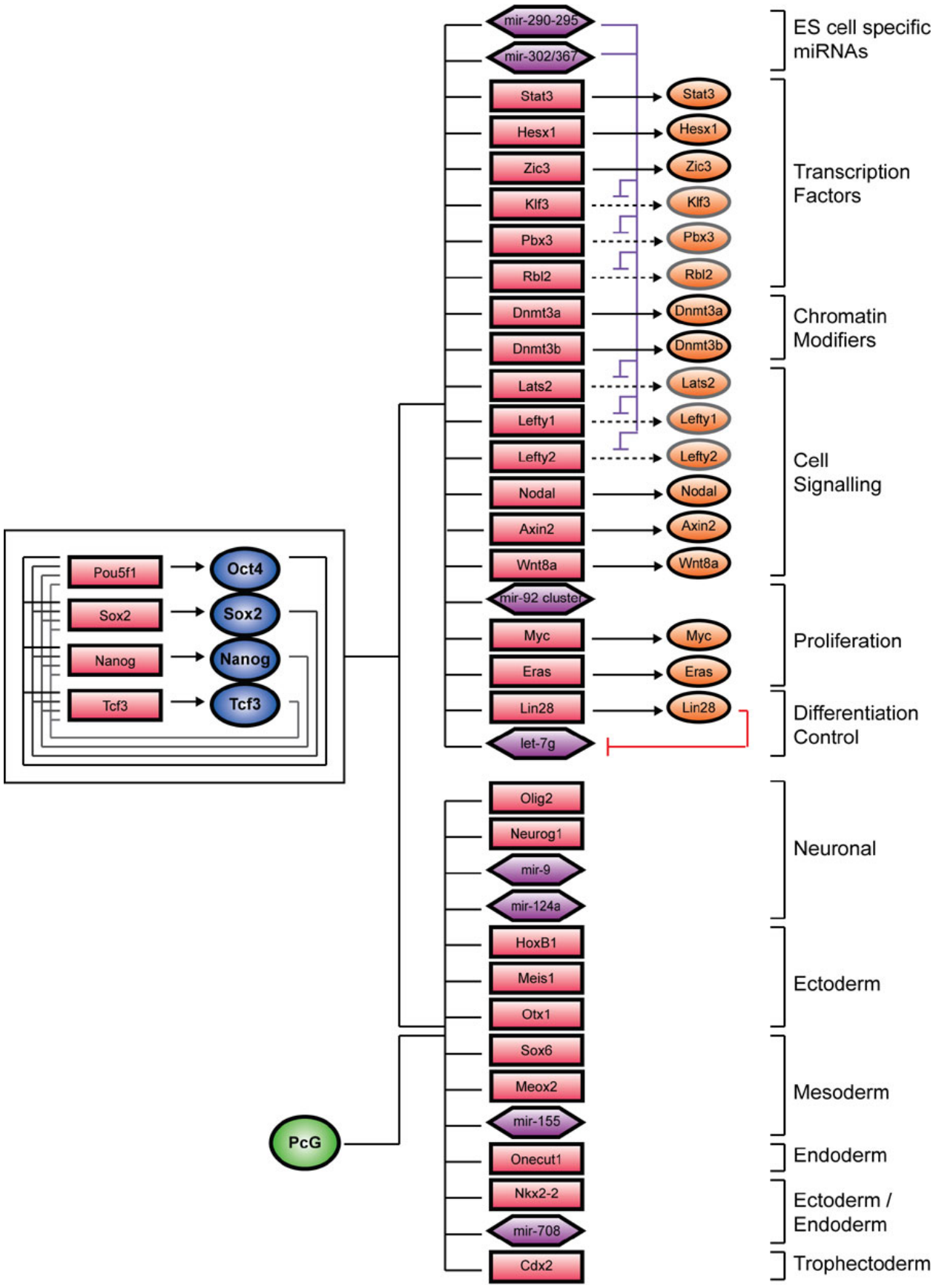
Four transcription factors control the embryonic cell. They are Oct4, Sox2, Nanog and Tcf3 (shown as blue circles on left). This gang of four binds to the promoters (red rectangles next to the circles) of their own genes, keep the genes constantly active, and thus perpetuate their own rule.

The four factors also bind to promoters (red rectangles to right) that control lower-level transcription factors and to promoters (purple hexagons) for another kind of control factors called micro-RNAs. The lower-level transcription factors each control major cell functions (black type at right).

Embryonic cells must do two things: divide like crazy, and then direct groups of cells to morph into different cell types. The promoters in the top half of the central column control transcription factors (orange circles) that govern all functions that the cell must invoke to divide and multiply.

The promoters in the lower half govern cell fate; they tell each cell which of the major tissue types it is destined to become. But as long as the cell remains in the embryonic state, the action of all these promoters is held in arrest by a protein called a polycomb (green circle). Only when polycomb's hold is lifted can the embryonic cells differentiate.

One of the gang of four, Tcf3, is influenced by signals from the cell's environment. It may be a change in Tcf3 that upsets the gang of four's rule and sends the mass of embryonic cells cascading down the cell lineages that lead to adulthood.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Stat3
Hesx1
Zic3
Klf3
Pbx3
Rbl2
Dnmt3a
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Lats2
Lefty1
Lefty2
Nodal
Axin2
Wnt8a
mir-92 cluster
Myc
Eras
Lin28
let-7g
Pou5f1
Sox2
Nanog
Tcf3
Oct4
Sox2
Nanog
Tcf3
PcG
Olig2
Neurog1
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mir-124a
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