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IS CLIMATE CHANGE TO BLAME?

See page 182.
~~Pravin~~
(Srinivasan & Ruina)
SAVE

cell, bone cell, brain cell, or any other kind of cell.

Stem cells' unique capacity to develop into any type of cell—a property known as pluripotency—underlies their medical promise. Researchers argue that this trait could someday lead, for example, to lab-grown tissue and organs that would be useful for transplants.

The scientists set out to determine what genes define a stem cell. “We thought if we could uncover this network of genes, then we could see how pluripotency is established,” says Laurie A. Boyer of the Whitehead Institute in Cambridge, Mass. And with knowledge of the mechanics behind pluripotency, she says, scientists might learn to reprogram a mature cell so that it, too, could have the pluripotency of a stem cell.

Boyer and her collaborators investigated three proteins known to play defining roles in keeping stem cells from developing into a specific cell type. The proteins, dubbed Oct4, Sox2, and Nanog, are classified as transcription factors. As such, they bind to specific genes and regulate the genes' activities. Scientists didn't know how these three transcription factors maintain stem cell pluripotency.

To fill that information gap, the researchers identified the genes to which Oct4, Sox2, and Nanog bind. In the Sept. 23 *Cell*, the researchers report that these three transcription factors attach to a region of the genome that contains genes that other researchers have shown to control cell development. At least one factor bound to each of 2,260 genes.

The researchers also found that 1,303 of these genes were active in the stem cell and that the protein products of some of these genes, in turn, activated more genes.

At the same time, the three factors repressed many genes essential for stem cells to differentiate into specific cell types during embryonic development.

The findings suggest that Oct4, Sox2, and Nanog are “master regulators,” Boyer says. “These three shut off differentiation and allow for a pluripotent state.”

Besides discovering that pivotal role for these regulators, the researchers mapped out the molecular biology behind pluripotency. Because all three regulators bind to 353 of the genes, the researchers concluded that the regulator proteins work together in keeping a stem cell undifferentiated.

The research also suggests that Oct4, Sox2, and Nanog interact in a complex way

that controls how much of each of the three proteins is present in the cell.

The work by Boyer's group “identifies a cohort of genes” that are targets of these master regulators, comments Ian Chambers of the University of Edinburgh. This is a starting point to test more aspects of the stem cell regulatory network, he says.

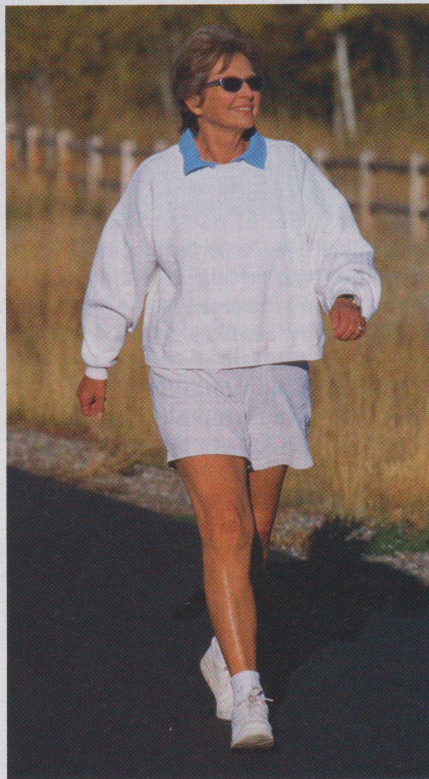
To tease out additional molecular details, Boyer's group plans to perturb the proteins and genes underlying stem cell behavior and to observe how the cells respond. This work, Boyer predicts, will provide more insights both about pluripotency in stem cells and about the remarkable process by which a single fertilized cell becomes an entire organism. —K. GREENE

Stepping Lightly

New view of how human gaits conserve energy

For 200,000 or more years, the fine-tuned mechanics of human motion have enabled our species to traverse enormous distances on foot with remarkably little energy expenditure. Scientists have long pondered which specific qualities of walking and running render those means of getting around so efficient.

Now, a pair of biomechanics theorists say



EASY WALKER A mathematical model of human locomotion suggests why the most-used gaits consume the least energy.

that they've captured the essence of what makes human locomotion as thrifty as it is. Their model explains why any number of silly-looking gaits, such as the crouching strut of Groucho Marx, tire us out more than routine styles of perambulation do, says Manoj Srinivasan of Cornell University.

The analysis by Srinivasan and Andy Ruina, also of Cornell, offers a new “conceptual framework” for human locomotion, says Arthur D. Kuo of the University of Michigan in Ann Arbor. As such, it could prove useful in various biomechanics-associated fields, including treating disabled people and building better two-legged robots (*SN*: 8/6/05, p. 88).

Srinivasan and Ruina used a computer to create an exceptionally simple model of bipedal motion in which pistonlike legs propel the upper body, represented as a pointlike mass, through space along perfect arcs.

The model, to be unveiled in an upcoming issue of *Nature*, assumes that a moving bipedal creature uses metabolic energy only when pushing against the ground at the start and finish of each of stride, Ruina explains.

In between, a walker's foot becomes a fixed point around which the leg swings like an upside-down pendulum. Just as a regular pendulum traces a circular arc with extraordinary energy efficiency, so, too, does this leg motion, the researchers propose. In running, the model shows that the energy efficiency derives mostly from the fact that the runner spends considerable time flying through the air, at no energy cost, along parabolic arcs.

When Ruina and Srinivasan simulated a wide range of possible gaits based on these fundamentals, they found that ordinary walking and running were two of the three most-efficient gaits.

The third efficient stride was a peculiar lope halfway between walking and running that resembles no gait known to biomechanics specialists. People with certain disabilities might use it without the gait having been previously recognized, the Cornell scientists suggest. On the other hand, the hybrid gait might be an artifact of the model's extreme simplicity, Srinivasan admits.

The researchers have practiced the newfound gait. “It's like the way I would run if I was really tired,” say Ruina. Videos of Ruina and others demonstrating all three gaits are at http://ruina.tam.cornell.edu/research/topics/locomotion_and_robotics/papers/WhyWalkandRun/index.htm.

Antonie J. van den Bogert of the Cleveland Clinic Foundation faults the new model as too simple to be realistic. Yet he also notes that more-complex models haven't achieved such an “elegant proof” that our natural modes of motion are also the most efficient ones. —P. WEISS

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