The New York Times
nytimes.com

August 27, 2001

What Only the Embryo Knows

By STEPHEN JAY GOULD

Thomas Henry Huxley designated three men as the finest intellects of 19th century natural history: his dear friend Charles Darwin; his most worthy opponent Georges Cuvier; and Karl Ernst von Baer, who discovered the mammalian egg cell in 1827 and wrote the founding treatise of modern embryology in 1828. Of these three, posterity has largely forgotten von Baer, who suffered a severe mental breakdown in the 1830's, but then recovered and moved to Russia (not uncommon for a German-speaking Estonian national), where he enjoyed a distinguished second university career, largely in anthropology and lasting well into the 1870's.

In 1828, von Baer enunciated the central principle of embryological development, later known as "von Baer's law" and now regarded as the correct interpretation of Ernst Haeckel's famous (and erroneous) claim that "ontogeny recapitulates phylogeny," or that the successive forms of embryology repeat the adult stages of a lineage's evolution -- with the gill slits of an early human embryo representing an ancestral fish and the later tail an ancestral reptile, for example.

By contrast, von Baer proposed a principle of progressive specification and differentiation: One can first tell that an embryo will become a vertebrate and not some sort of invertebrate, then a mammal and not another kind of vertebrate, then a carnivore and not a rodent or ruminant, then a dog and not a cat, and finally Buster the Beagle and not another breed.

Von Baer summarized his principle in an epigram: "The development of the organism is the history of growing individuality in every respect." In other words, successive narrowing and determination of parts as complexity coagulates. No turning back after the blueprint becomes finalized from a broad mass of initial potential. For an appropriate literary metaphor, think of Lot's wife or Omar Khayyam's lines: "The moving finger writes; and having writ, moves on."

Von Baer's law epitomizes the central issue, unfortunately rarely discussed and little understood, in our current debate over embryonic stem cells. The very structure of material reality imposes a principle of trade-offs in both nature and human affairs: One always gives something in order to gain. In particular, we usually pay for complexity by surrendering flexibility -- and von Baer's law encapsulates the embryological version of this structural generality.

In genetic terms that von Baer could not know, each cell of our body contains a full set of genes. But embryological differentiation into a specialized adult role -- as a brain cell, liver cell or heart cell, for example -- leads to a "freezing" or "turning off" of most of this potential apparatus, leaving active only those few components regulating the specialized adult form and function. The cells of the earliest, undifferentiated embryo (little more than a clump of identical units in appearance) maintain full capacity to develop in any direction; that is, all their genes remain potentially active and recruitable.

The irony of the trade-off, explicitly recognized by von Baer nearly 200 years ago, inheres in the evolved surrender of this embryonic flexibility as development proceeds toward our maximal complexity. Cut a planarian flatworm in two, and the tail end regenerates a head while the head end regrows a tail. For in this simplest of bilaterally symmetrical invertebrates, with minimal differentiation of internal organs, all cells retain the embryonic potential to build any part of the body. This capacity for regeneration -- the ability of

cells at a wound site to "dedifferentiate," or return to a state of early embryonic flexibility -- becomes progressively lost in animals that evolve greater adult complexity by von Baer's universal process of "locking in," with increasing specialization of parts. We have, in short, traded regenerative capacity for the undeniable evolutionary advantages of maximal complexity.

For this reason, we must use embryonic stem cells if we wish to pursue a large body of enormously important, highly promising and deeply humane research in how specific tissues and organs grow from the broad potential of early cells derived from the fertilized ovum. Speaking personally, I do not grant the status of a human life to a clump of cells in a dish, produced by fertilization in vitro and explicitly destined for discard by the free decision of the man and woman who contributed the components. But I also have no desire to offend the sensibilities of those who disagree. Thus, if I could derive cells of similar flexibility in a different way, I would gladly do so, even at considerable extra time and expense. (By analogy, I did not mean to mock or flout our laws in using marijuana to stave off severe and continuous nausea during some particularly nasty and lengthy chemotherapy 20 years ago. But I tried all the available anti-emetics, and they just didn't work. I continue to regard my decision as fair, humane and, believe me, importantly sustaining and life-affirming.)

Unfortunately, von Baer's law, and nature's broader structural rules of trade-off between complexity and flexibility, give us no alternative to embryonic stem cells for now -- and the research is important and far more than merely theoretically lifesaving. (Moreover, if we hope to find ways to dedifferentiate adult cells -- and therefore learn to recover the requisite flexibility from cells derived without offense to anyone -- then we must experiment with embryonic cells in order to understand and control the mechanism of their broad potentiality).

As an old man, from his Russian periphery, von Baer made the famous and rueful remark that all new and truly important ideas must pass through three stages: first dismissed as nonsense, then rejected as against religion, and finally acknowledged as true, with the proviso from initial opponents that they knew it all along. Genetic technology has brought us through the first stage. Our current debate on stem cells resides in von Baer's second stage, with the religious views of a clear, if powerful, minority setting an unfortunate opposition to one of the most vital avenues of beneficial research in our time. The third stage will arrive, and we will marvel that we ever rejected a pathway toward knowledge so imbued with life-saving capacity. May this third stage come soon, as our understanding differentiates further into a true and humane grasp of the virtues of flexibility.

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