

tumultuous time under communism, and links to famed thirteenth-century ruler Genghis Khan.

### Rising from ruins

When Schaller first visited Mongolia in 1989, government and people were on the edge of financial ruin, with the collapse of the Soviet Union, essentially their sole trading partner. Fuel, when available, was tightly rationed. Trying to provision expeditions to the farthest corners of the vast country, Schaller faced shop shelves empty apart from the occasional box of matches or packet of cigarettes (and vodka, of course).

He rejoiced when he found a few cans of peanuts – hardly adequate to keep a research team alive for weeks in the Gobi Desert. Thrifty and field-hardened, Schaller and his team followed the customs of Mongolia's nomadic herders, who required little beyond mutton, flour, tea and a bit of rice. They benefited, too, from the nomads' traditional hospitality towards travellers, relishing the soup, tea and rock-hard dried cheese curds insistently offered.

The team did not experience such generosity from its local scientific counterparts, whose apparent lack of enthusiasm irritated Schaller and slowed research progress. Disbelief best describes his feelings when the Mongolian snow-leopard biologist does not get out of his sleeping bag on the morning they capture and radio-collar one of the rare cats. He is no less indignant when the national bear biologist passes up an opportunity to track the rare Gobi bears they had fitted with collars. He laments what he sees as a *laissez-faire* attitude in many biologists, rangers and managers of protected areas he meets, fearing that Mongolia cannot save its unique treasures unless things change.

Schaller's more engaged companions in the field often included his wife, Kay, who contributed practically and scientifically. His adult son, Eric, joined one trip, spending part of it huddled in a tent in sub-freezing temperatures listening to the pings of a distant snow leopard's radio-collar to decipher its pattern of activity. At least he caught a rare glimpse of the enigmatic beast.

Schaller was also joined by biologists from the United States, Russia and Europe, and eventually by several young, bright and enthusiastic Mongolian scientists through whom he saw a positive future for conservation in the country. His relief was compounded when strong leaders started to emerge for new national conservation organizations and government agencies.

Schaller – with whom I have worked at various times over the past three decades – is driven by his vision of what must be done if wild spaces and rare species are to persist. The vast, fragile eastern steppe is the part of Mongolia that he holds most dear, along with its seemingly endless herds of gazelles. He is eloquent in his condemnation of what he deems gross mismanagement by the nation's current political leaders, who allow oil drilling, mining

and road-building in crucial protected areas.

Ultimately, he enjoins Mongolians to heed the rallying cry of their ancient rulers – that if the natural world is taken care of, it will take care of them.

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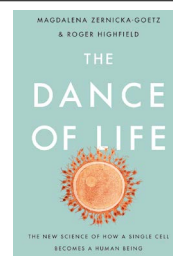
## From egg to animal: an embryo's first steps

A pioneering developmental biologist reflects on an epic journey. **By Sarah Franklin**

**S**tudying the early development of humans and other mammals takes colossal dexterity and stamina. Unlike, say, sea-urchin embryos – which are transparent – mammalian embryos are hidden from view. Investigating their development is also tricky because of the delicate timing and sequence of events that produce highly complex organisms. As a result, the story of how scientists have ingeniously deciphered many of the basic mechanisms of development over the past century is often as gripping as what they've discovered.

Magdalena Zernicka-Goetz has been a key player in that story. A pathbreaking figure in developmental biology and stem-cell science for several decades, her work has reset the clock for the determination of cell fate in the early mammalian embryo. Among other discoveries, her lab perfected a culture system that can extend human embryonic development *in vitro* (M. N. Shahbazi *et al. Nature Cell Biol.* **18**, 700–708; 2016), providing a powerful model for basic research with implications for improving understanding of pregnancy loss. Her book *The Dance of Life* – written with science journalist Roger Highfield – is a vivid first-hand account of epic technological changes and revelations in her field. It is also a personal tale of an ongoing scientific odyssey, replete with failure, exhaustion and tenacity as much as thrilling new vistas.

Drafted over 15 years, the book's main narrative is the remarkable transformation,

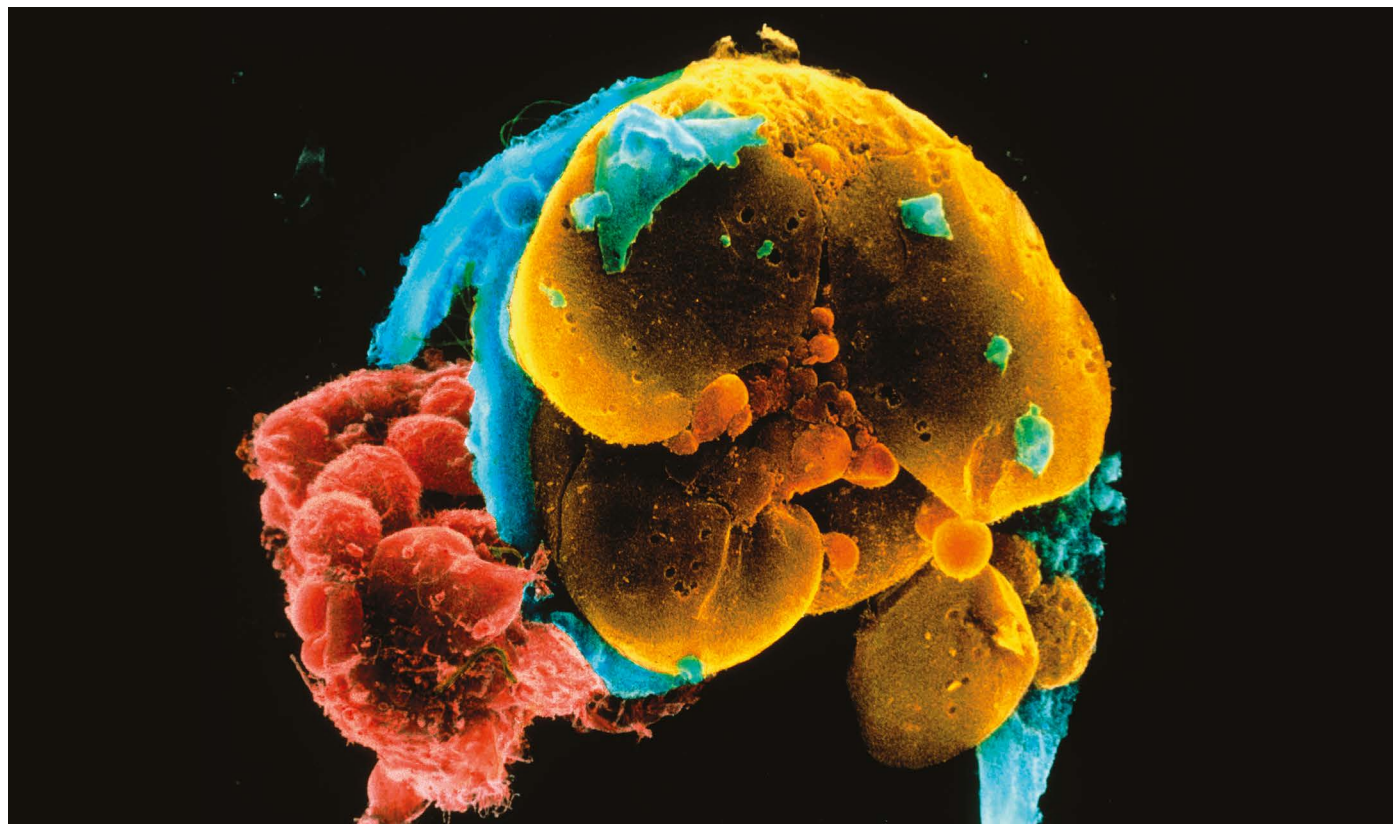


**The Dance of Life: The New Science of How a Single Cell Becomes a Human Being**  
Magdalena Zernicka-Goetz & Roger Highfield  
Basic (2020)

in just a few days, of a single spherical mammalian egg cell to a tube containing all the types of stem cell needed for a full body plan (see [go.nature.com/2vgrjpw](http://go.nature.com/2vgrjpw)). Until the early 2000s, it was thought that this diversity arose from cells that were initially identical. For example, at the four-cell stage, all cells were presumed to be equally capable of giving rise to all cell types – a state known as symmetrical totipotency. It turns out that they are not.

Embryologist Martin Johnson's group, working at the University of Cambridge, UK, in the late 1970s and 1980s, had developed the 'polarization hypothesis'. This suggested that differences that developed in each individual cell of the early embryo could become the basis of distinct cell populations, or lineages. Zernicka-Goetz subsequently strove to understand the importance of asymmetry in establishing which cells become what, where, why and how. She confirmed that the early embryo's famous plasticity derives not from uniformity, but from divergence.

Several tools enabled Zernicka-Goetz



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Scanning electron microscope image of a human embryo in the early stages of cell division.

to track pattern formation at the start of development. One was green fluorescent protein, a jellyfish molecule that glows under ultraviolet light and can be used to tag individual cells so that their movements can be mapped. This tool enabled her team to follow the different fates of embryonic cells during the first few stages of cell division. The refinement of this laborious yet powerful methodology forms a major strand of the book.

The other crucial instrument was the theoretical model of asymmetry as the origin of form, provided by mathematician Alan Turing. In his 1952 paper ‘The Chemical Basis of Morphogenesis’, written two years before his death, Turing described how two interacting chemicals with different diffusion rates can create a stable pattern – a process later known as reaction–diffusion theory (A. M. Turing *Phil. Trans. R. Soc. B* 237, 37–72; 1952).

Could it be that minor differences between the earliest embryonic cells might be enough to give rise to separate lineages of brain cells, blood cells and so on? To find out, Zernicka-Goetz needed to compare cells that divided in different ways, to test their inherited biases towards specific developmental pathways.

At the start of the millennium, in what she calls a “grueling” set of experiments, the author and her team manually assembled, disassembled and reassembled colour-coded chimaeras made up of first-division mouse cells with particular polarization taken from different embryos. They used these handmade models

to track and compare subsequent patterns of cell division, again with fluorescent labels. By 2005, they had followed the fates of hundreds of cells in chimaeras and several thousand in embryos. Results indicated that distinct cellular identities influenced cell fate, from the splitting of the first cell into two, and two into four. Paper after paper was rejected by scepti-

**“This bespoke biology has not yet been translated into treatments. Social and ethical challenges remain acute.”**

cal reviewers, but consensus finally began to shift as the evidence became irrefutable.

To explore the dance of life further, better tracking methods were needed, including live imagery. These have materialized over the past decade, thanks to the ability to film the very earliest stages of embryo development *in vitro* and to extend the period under study beyond day 11 or 12, right up to the 14-day legal limit enforced in many countries for human embryos in culture. Here, researchers can peer into “the black box of implantation in culture”, as Zernicka-Goetz puts it.

These techniques are complemented by rapidly expanding knowledge of the key molecular-signalling pathways involved, and the use of increasingly sophisticated organoids. These embryo-like structures, grown in culture, are

now so complex that they can be induced to undergo gastrulation, the process by which cells develop layers that in life give rise to the internal structure of the organism. With gene-editing tools such as CRISPR, the ability to model, redirect and control embryogenesis has ushered in a new age of creative biology.

The power of this bespoke biology has not yet been translated into clinical treatments. And the social and ethical challenges of the field remain acute. Zernicka-Goetz writes compellingly about her own experiences of a pregnancy in which the fetus was diagnosed through chorionic villus sampling with a risk of severe chromosomal abnormality. (Her son was born healthy.) A key theme is the powerful influence of this experience on her desire to understand how early embryos sort and order their cells. She also reflects on the challenges of being a female scientist and balancing work and family life, as well as the opposition she faced from her peers over her results.

Zernicka-Goetz’s honest and passionate depiction of the complexity of science as a vocation will have wide appeal. It is a chronicle of the intellectual excitement of basic science, the thrill of the chase, and the intensity of the emotional ups and downs along the way to transformational discoveries.

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