Obituary

Rosa Beddington (1956–2001)

Rosa Beddington's death on 18 May cut short her career at the untimely age of 45, but not before she had rewritten the textbooks. Generations of biologists had been taught about the classical studies that had identified the Spemann organizer, a region in amphibian embryos that emits signals responsible for inducing adjacent tissues to form the body axis, complete with head and tail. Working in the mouse, Beddington made the greatest contribution to understanding axis formation since those original 1920s observations. Her experiments revealed that the anterior–posterior axis of the vertebrate embryo forms as the result of a cooperative interaction between two sources of inducing activities that we now term the 'head' and 'trunk' organizers. Perhaps more notably, her studies helped to uncover the importance of the mammalian extra-embryonic tissues for induction of the future head; these tissues had previously been viewed as mere evolutionary add-ons required for viviparity.

As a D.Phil. student at the University of Oxford in the late 1970s, Beddington took on the challenge of understanding events in the early-stage mouse embryo. Mouse embryos grow outside the protective environment of the uterus only for short periods of time. Moreover, early axis formation is accompanied by extraordinary growth and cell movements. Undaunted by these complexities, Beddington painstakingly grafted pieces of tritium-labelled tissue from different regions of donor embryos to various sites in a host embryo. She then scrutinized histological sections to see whether donor tissues could adopt new fates or whether the graft's developmental potential was restricted by its site of origin. Together with work by Kirstie Lawson and Patrick Tam, her papers provided the all-important fate map of post-implantation lineages in the mammalian embryo. Without this basic information, all the subsequent work on how, when and what a cell is instructed to become in the embryo would have been impossible.

At the Imperial Cancer Research Fund laboratories in Oxford, Beddington harnessed the new transgenic technology to generate strains of mice expressing β -galactosidase. She fondly dubbed her most famous animal Levi — a mouse with 'blue genes' that simplified analysis of tissue grafts and embryo manipulation. She also started working on embryonic stem cells, made from mutant mice, that provided

Exceptional talent and influence in developmental biology

insights into the cellular defects underlying the truncated body axis of the classical T (brachyury) mutation.

On moving in 1991 to the Centre for Genome Research in Edinburgh, she decided that the future of mouse embryology lay in understanding the embryo's own molecular mechanisms. Together with Bill Skarnes, she developed gene-trap vectors to identify the molecules expressed in different regions of the embryo. She also made complementary DNA libraries from tissue she herself dissected, to obtain cells corresponding to the germ layers (endoderm, mesoderm and ectoderm) of the early embryo. These libraries were widely distributed and proved a rich source of new genes.

In 1993, during a period of great progress in understanding the signals responsible for mesoderm formation in frog embryos, Beddington moved to the National Institute for Medical Research at Mill Hill in north London, to set up a new division of mammalian embryology. Convinced that all vertebrate embryos had developmental pathways in common, she performed grafting experiments with a mouse node, the 'classical organizer'. These were a technical *tour de force* but, contrary to findings in the frog, the result was only partial axis duplication. She worried about this and ultimately discovered the basis for the discrepancy. Analysis of gene-expression patterns led her to observe that a handful of genes were expressed asymmetrically in the extra-embryonic tissue of the visceral endoderm, long before any visible signs of the axis became apparent. In particular, she showed

that certain transcription factors are expressed on the prospective anterior side of the embryo many hours before the onset of gastrulation, several days before the node forms. She discovered that the initial proximal–distal polarity of the embryo is converted to the anterior–posterior axis by a coordinated movement of the visceral endoderm to the prospective anterior side. Thus she identified the anterior visceral endoderm as the signalling centre responsible for anterior patterning during early mammalian development. She was elected a fellow of the Royal Society in recognition of this seminal work. With her Mill Hill colleagues, she showed that similar processes occur in frog development.

For many years Beddington helped to teach the Cold Spring Harbor course on mouse molecular embryology. In teaching, too, she was exceptional. With her exquisite hand-drawn illustrations, she effortlessly conveyed the complexity of the mouse embryo, and often improvised using a felt pen and polystyrene coffee cup to explain gastrulation. Like all great biologists, she had a breadth of vision and a true understanding of all vertebrates, allowing her insights denied to others. A fierce critic, as tough on herself as on others, she did not tolerate fools gladly and liked arrogance even less.

Rosa was refreshingly modest for someone of her prodigious talents and intellectual range, often expressing doubts as to the significance and quality of her own work. She was always critical of her contemporaries — and certainly didn't cut us any slack — yet was exceptionally warm and generous with junior colleagues, in turn engendering fierce loyalty from them. In dying, as in living, she defied expectations, extending predictions of a few weeks' life expectancy into almost three years.

She will be remembered in good times as we learn more about the embryo and miss knowing what she would think about our experiments, and perhaps even more in the difficult periods when she would inevitably insist we should rise to the occasion and battle on, no matter what the obstacles. Rosa had a profound influence on her chosen field of study, an achievement she allowed herself. She was perhaps less aware of the lasting impression she made on all of us who shared her life.

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