

Taxonomy needs evolution, not revolution

Some changes are clearly necessary, but science cannot be replaced by informatics.

Sir—H. C. J. Godfray in his Commentary¹ suggests that we throw out the past mechanisms of doing systematics and begin anew in a revolutionary ‘brave new world’ of unitary, web-based taxonomy, each group under the administration of an authoritarian body. We agree with Godfray that problems of synonymy can be frustrating and that the web is important in the dissemination of taxonomic information, but do we need a new mechanism to do taxonomy? Working within the current enabling conventions is more positive and practical than throwing them out and beginning again.

The international codes of zoological, botanical and bacteriological nomenclature are the rulebooks that have long governed how organisms are named, providing clear instructions on how to go about the process — a facility either lacking or in the process of being invented in other disciplines concerned with naming things.

At the core of the zoological and botanical codes is the type specimen. Types bring order and stability to taxonomy because they are the specimens upon which the original author based his or her descriptions, and which ultimately fix the name. Even DNA taxonomy needs archived voucher specimens to ensure that future generations can check and replicate findings. The codes operate for taxonomists as conventions, which, like UN conventions, are international in scope and have evolved during decades of intellectual debate.

Taxonomy provides a vocabulary to discuss the world: specifically, the names of organisms. We taxonomists therefore have a special role in communicating to the widest possible set of audiences. The Internet, being a distributed system of linked information, is ideal for this purpose — the various approaches under way^{2,3} will revolutionize taxonomical informatics in a positive, community-driven way.

Taxonomists have not yet made as much use of the web as they could, but first we need to identify with confidence core components of essential information, such as species lists, identification keys and illustrations. From our privileged position in the information-rich developed world, we run the risk of providing merely what we ourselves need and forgetting those in whose countries most of the diversity on Earth resides. Information is critical for global conservation, and much of it, particularly original descriptions of species

and the specimens on which these are based, remains inaccessible to those who need it most.

Building a ‘biodiversity commons’ (ref. 4), where access to original taxonomic descriptions is part of the distributed web system, is critical. Much taxonomic information is already available online: FishBase (www.fishbase.org) and the Cycad pages (<http://plantnet.rbgsyd.gov.au/PlantNet/cycad/index.html>), to name just a couple, are excellent examples. At present, we need meta-databases to link dispersed information, which is where the Global Biodiversity Information Facility (GBIF) is concentrating its efforts.

Web-provided taxonomy is clearly the way for the future, but the technologies needed for this to operate successfully on the scale required are only starting to be available, and quality control is something that must also be addressed⁵. The Natural History Museum is putting on its website (www.nhm.ac.uk), as a priority, information about its type specimens, which will provide the kind of focus for scientifically rigorous and accessible

taxonomy that Godfray advocates.

Informatics, however, is not a substitute for science. To ensure worldwide consistency and accuracy we also need open access to the foundations of our taxonomy, by making high-quality illustrations and descriptions of the type specimens available on the web. For an institution such as ours, housing nearly a million type specimens, this is a huge task. It will be achieved, but not soon, unless the world is ready to support more taxonomists doing taxonomy. This in turn requires widespread acceptance of taxonomy as a mature and stimulating science.

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Metastasis: the role of chance in malignancy

Sir—The Concepts essay “A progression puzzle” by René Bernards and Robert A. Weinberg (*Nature* **418**, 823; 2002), demolishing a popular view of cancer metastasis, is welcome. To take their argument even further, the concept that tumours evolve by sequential selection of gene changes suggests that both malignancy and metastasis are mechanistically rather simple processes, and follow from a complete abolition of the signals that normally prevent cells from surviving and growing in the wrong place.

Bernards and Weinberg argue that the gene changes that make cancer metastasis possible cannot be fundamentally distinct from the preceding gene changes that occur as the cell evolves to form a primary tumour, and conclude that “genes and genetic changes specifically and exclusively involved in orchestrating the process of metastasis do not exist”. If there is little difference between a primary malignant tumour and its metastases, the crucial issue becomes: what makes a tumour malignant (capable of metastasis)?

Applying the Bernards–Weinberg argument leads to the idea that malignancy

must also be a short step from earlier stages in tumour development. It can be separated by at most one unique gene event from overproliferation, and hence there is probably no more than one gene and genetic change per tumour that is specifically and exclusively involved in malignancy.

Malignancy can be defined either as the ability of a tumour to spread into the surrounding normal tissue and grow there to form a primary malignant tumour, or as the potential to form metastases. The two definitions are almost interchangeable because the one almost invariably implies the other. Pathologists observed this over a century ago and it is a cornerstone of clinical histopathology — and strong support for Bernards’ and Weinberg’s view.

Applying the Bernards–Weinberg selectability argument to malignancy itself, the transition from non-malignant to malignant can involve at most one gene change that is unique to the malignant transition, because cells cannot accumulate mutations that provide malignancy-specific properties (the ability to spread) during their evolution before they begin to spread. At most, one critical gene change could occur at the point at which malignancy begins.

This leads to a very simple view of malignant tumours and metastasis: malignant cells are cells that can grow in alien environments, and by a process that is not subtle, but largely random accident, they spread, first locally and then eventually through the body to form life-threatening secondary tumours. Metastasis is merely a rare, stochastic event: the chance escape of a cell into the vasculature, its arrival at a suitable site and its growth there.

Much has been made of the need for cells to cross basement membranes, but damage by trauma, inflammation or necrosis can breach basement membranes, and even normal somatic cells can cross vessel walls (S. Koop *et al. Proc. Natl Acad. Sci. USA* **93**, 11080–11084; 1996). Perhaps what is crucial is that when malignant cells are exposed to surrounding connective tissue they simply establish growth in the connective tissue space, instead of helping to repair the tissue organization by closing gaps or going into apoptosis (programmed cell suicide) when in the wrong place.

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Metastasis: objections to the same-gene model

Sir—The model of cancer metastasis suggested by René Bernards and Robert A. Weinberg in their Concepts essay (*Nature* **418**, 823; 2002) is, in my view, a tautology. The suggestion that the same genes are exclusively responsible both for cancer-cell metastasis and for the emergence and proliferation of cancer cells is tantamount to saying “cancer cells that can proliferate do proliferate”. It would be a great loss if this type of idea caused a decline in research to investigate the existence of new genes involved in metastasis, a major factor in cancer mortality.

There is a finite probability that any cancer cell that can proliferate at one body site can also proliferate at other sites, if it can get there and stay there. How these two requirements are met is the real crux of the metastasis question. Bernards and Weinberg wish to dismiss the possibility that specific genetic changes, beyond those that govern proliferation, are required for successful cancer-cell relocation.

However, the argument Bernards and Weinberg used to arrive at this idea is, in my opinion, flawed. They argue that cells that acquire both proliferative and metastatic changes will be rare in primary tumours, thereby making it “difficult to

imagine how metastasis can ever proceed”. This is a remarkable proposition in the context of a discussion of the initiation of cancer cells, which is itself an extremely rare occurrence. The authors’ new concept — that metastasis is not due to a selected cell phenotype — would be better supported by a stochastic mechanism formulation.

Clinically, metastases range from presentation with large primary tumours to presentation without any identifiable primary tumour at all. It may be that the factors responsible for metastasis are cancer-cell proliferation plus myriad other small, unknowable variables that combine to create the conditions for relocation. This is a restatement of the tautology of Bernards’ and Weinberg’s argument.

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Bernards and Weinberg reply — We appreciate the interest that our Concepts essay (*Nature* **418**, 823; 2002) has evoked. But Edwards misrepresents our thinking when he writes: “If there is little difference between a primary malignant tumour and its metastases, the crucial issue becomes: what makes a tumour malignant (capable of metastasis)?”. In fact, we argued that there are various types of primary tumour, some of which are preordained to become metastatic, others not. Hence, the differences lie between various distinct types of primary tumour. We suppose that in some tumours, the particular combination of alterations/mutations that enables cells to create a robustly growing primary tumour cell population also incidentally empowers them to become metastatic. Also, we do not imply that a single genetic change per tumour is involved in malignancy, as Edwards concludes.

We did not say, as Sherley asserts, that “the same genes are exclusively responsible both for cancer-cell metastasis and for the emergence and proliferation of cancer cells”. Instead, we argued that there are multiple alternative genetic pathways that lead to the creation of a primary tumour, each path being defined by the identities of the particular genes that are altered during tumorigenesis. According to our thinking, some combinations of genes that lead to primary tumour formation create growths that are unlikely to metastasize. Other combinations yield tumours that have a high proclivity for metastasizing. In the latter case, the combination of genes that yielded the primary tumour happens to be able to confer invasive/metastatic ability even though these phenotypes were not selected during the clonal expansions that

created the primary tumour mass.

We did not say, as Sherley asserts, that cells that acquire both proliferative and metastatic changes will be rare in primary tumours. Instead, we said that certain combinations of genetic alterations that are selected for the proliferative advantage they confer will, incidentally, also confer invasive/metastatic phenotypes. This is in no sense tautological. It is simply the statement of the possibly pleiotropic actions of certain cancer-associated genes.

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Chilean decree will save nights for star-gazers

Sir—Your editorial “Save starry nights” (*Nature* **418**, 709; 2002) states that Czechoslovakia is the only country with a national policy aimed at limiting light pollution. In fact, Chile, which now contains the largest concentration of optical telescope apparatus in the world, has taken a similar step.

The Association of Universities for Research in Astronomy, the European Southern Observatory and the Carnegie Institution worked for several years with the major Chilean universities and local and national government authorities to implement a strategy for controlling light pollution.

In December 1998, then-President Eduardo Frei signed a decree to establish an environmental norm regulating all outdoor lighting, not only in the areas surrounding the existing observatories, but in all of the II, III, and IV Regions of northern Chile, one-third of the total area of the country. The decree states in part: “The astronomical quality of the skies of the II, III and IV regions of our country constitute a valuable environmental and cultural patrimony recognized internationally as the best existing in the Southern Hemisphere for astronomical observations.”

The projected savings in energy costs from replacing polluting lights with well-shielded, energy-efficient ones should more than pay for the initial investment required for the changeover.

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