nature genetics

Delivering essential function

Two months ago I was a research geneticist in Oxford dissecting the gene networks for the cell cycle transitions which mark the life cycle transitions in transgenic *Drosophila*. I'd had the joy of publishing—concisely—in *Nature*, and the disappointment of rejection, by *Nature Genetics*, of some of my best work. *Nature Genetics* is in the envied position of publishing a constellation of authors who have combined molecular biology with genetic analysis to yield deep insights into the functioning of the genome. The competition is intense and the journal's extraordinary peer reviewers are justly proud of your exacting standards.

The challenge of integrating in this journal all the fields of genetic experimentation appealed to me, as did identifying coherent strategies, encouraging communication and crossover between disciplines. I joined a superb group of dedicated editors: the interests and experience of Alan Packer, David Gresham and Michael Stebbins together encompass human medical and population genetics, neurogenetics, cancer, development, epigenetics, functional genomics and proteomics. We recruited Kyle Vogan, an experienced and widely published researcher in vertebrate development from Harvard, and we had our complete editorial team.

The genetics research community's most stringent criteria are ably interpreted and explained by my new colleagues, reinforced by their individual interests, contacts and expertise. The team structure is important too, because research practice evolves. Consequently, we research for, study and check one another's work, effectively peer reviewing and rationally refining our own judgments. This means you have the care of your primary editor to guide you through the review process, and you have the attention of the whole crew on my watch. We're holding the line, expecting your very best research, complete stories, comprehensive studies and, perhaps once in the career of prepared minds that chance did favor, a new paradigm.

Genetic methods, namely heredity and phenotypic analysis of gene networks perturbed by mutation, have an unparalleled record of delivering biological function, of providing the link between genome and phenotype. Now the genomes, most of which are published in *Nature*, can be seen as communities of interlinked individual genes rather than 'genetic background'. Even the deepest divide in genetic thinking, the rift between population and single-gene genetics, is rapidly being filled by powerful strategies for association studies and their application to the unconquered territory of complex traits.

For example, in this issue, two genes associated with autoimmune diseases are described in different ways: as residing in chromosomal region identified by its level of linkage disequilibrium, or as a candidate locus inherited within nuclear families. But because these mutations both interfere with regulation by the RUNX1 transcription factor, these studies deliver a result stronger than association of a locus with a disease. These genes have found their context as participants in a shared molecular mechanism that amounts to a cause of many diseases with an autoimmune component. Cynthia Helms and her collaborators (p. 349) show this genetic mechanism operates in psoriasis and Shinya Tokuhiro and his coauthors (p. 341) in rheumatoid arthritis. Marta Alarcón-Riquelme and her colleagues (*Nat. Genet.* **32**, 666–669; 2002) found the same mechanism in lupus. As she points out in her accompanying News and Views article (p. 299), RUNX1 is also translocated in leukemia and has a family resemblance to the *Drosophila* patterning gene, *runt*, that is not misleading: RUNX1 too has a developmental role, in vertebrate hematopoesis. For epigenetics epicures, its parental origin is probably important too, as its mutations are haploinsufficient. I think this multilayered complexity is typical and that geneticists must be prepared to move flexibly between fields to develop a framework where each gene fits into its module of phenotypic influence.

Nature Genetics provides the core resources for the research geneticist, such as our User's Guide to the Human Genome II (http://www.nature.com/naturegenetics/web_specials/). Geneticists provide a web of functional information, powered by the human race's 6 billion–member, self-reporting screen for medically relevant alleles. Add to this our natural curiosity about ourselves and how we have evolved, combine it with the desire of clinicians and pharmaceutical researchers to alleviate genetic disease and with the public concerns about the ethical obstacles suddenly erected or whisked away by technological progress, and the genetics endeavor reaches daily into the lives of us all. ■

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