Pinning Down Cell Division?

With regard to the Research News article by Gretchen Vogel (12 Dec., p. 1883) about the purportedly essential human Pin1 protein analyzed by Yaffe *et al.* (*1*), we would like to make two points about priority of publication and functional genomics.

First, contrary to the statement that "Lu and Hunter first discovered Pin1 2 years ago," a member of this family was discovered in yeast nearly 10 years ago by Hanes *et al.* (*2*), who recognized its essential role in cell division and named it ESS1. Its protein-protein binding WW domain was documented by Bork and Sudol (*3*), and its peptidyl-prolyl *cis/trans* isomerase activity was inferred by Hani *et al.* (*4*). The existence of conserved metazoan homologs, named *Drosophila* and human *dodo*, was published by Maleszka *et al.* (*5*).

Second, the functional genomics issue was addressed by these authors (*5*), who showed the functional interchangeability of the yeast *ESS1* gene with the fly *dodo* gene in vivo, and who also unequivocally demonstrated that, in contrast to yeast, fly *dodo* is not essential to the organism under laboratory conditions. In the wake of these publications, Lu *et al.* (*6*) isolated and further characterized human dodo (Pin1) by virtue of its interaction with the NIMA cell-cycle kinase and described an essential function for it on the basis of antisense experiments in HeLa cells. However, HeLa cells are not a substitute for knockout, deletion, or misexpression experiments in developing organisms, and whether Pin1 is essential to vertebrates remains unresolved.

The challenging future issues revolve around the roles that different members of this gene family play in global cell division processes in many phyla. These require understanding of the different phenotypic end points that occur in different organisms, rather than the importance attached to the supposed essentiality of any single one of them.

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Clinical Applications for Neural Noise?

The article "Mastering the nonlinear brain" by James Glanz (Research News, 19 Sept., p. 1758) makes an excellent contribution to general understanding of how scientists are extending nonlinear methods to study brain dynamics, particularly in epilepsy. While Glanz focuses on research done in the United States, several groups in Europe (Germany, Holland, and France) have also made important contributions.

Le Van Quyen *et al.* have shown that human epileptic data contains unstable periodicities (*1*). Our group has also shown how the temporal dynamics of an epileptic focus can be affected by simple cognitive

tasks, providing another window to prevention through psychomotor training (*2*). Finally, with the use of methods that build on those of Manuca and Savit and the team at the University of Michigan, we have found that more than half of epileptic crises can be anticipated by a brief window and are amenable to electrical intervention of the kind described in Glanz's article (*3*).

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Glanz quotes one investigator to the effect that neural noise does not have clinical application as yet. But three decades ago, it was discovered that the pupil motor response has a neural noise component (*1*). We uncovered a signal processing method to isolate this noise from the rest of the pupil response and found that the noise variance had a significant clinical application in that it could accurately (90% confidence) distinguish individuals with attention deficit disorder (narcoleptics) from normal (control) individuals (*2*). In memory experiments, we also observed that neural noise has a dramatic impact on cognitive performance. We believe that the reticular activating system controls the noise we measure and, if so, there should be more clinical applications for attention deficit disorders in the future.

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Haeckel's Embryos

A recent paper that we authored with several colleagues challenges the idea that there is a single, highly conserved embryonic stage in the vertebrates (*1*). Principally because of our conclusions regarding the inaccuracies of drawings made by the 19th-century naturalist-philosopher Ernst Haeckel, our paper received considerable coverage in the popular and scientific press (*2*), including an article by Elizabeth Pennisi ("Haeckel's embryos: Fraud rediscovered," Research News, 5 Sept., p. 1435). Regrettably, in the resulting debate over Haeckel and the reality of the vertebrate "phylotypic" stage, what we regard as one of the main implications of our results for contemporary studies of the developmental basis of evolutionary change has been largely overlooked.

The idea that there is an identical embryonic stage (the phylotypic stage) common to all vertebrates implies that changes in development that underlie the considerable variation in adult morphology of these animals appear only later in ontogeny. In this sense, the concept of the phylotypic stage is an explicit statement, or hypothesis, about the temporal deployment of evolutionary changes in development. Yet we show that at least some significant differences in adult morphology, involving characters as fundamental to the vertebrate body plan as limbs and somites, begin to appear before, and are apparent at, the putative phylotypic stage. These and similar observations (*3*) seriously diminish the validity and applicability of the phylotypic stage concept for the vertebrates. More important, they remind us of the potential significance of earlier developmental events to the determination of animal form, and that these too are frequent targets of evolutionary perturbation.

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Secretion of Thiols and Disulfide Bond Formation: Retraction

In our report "Cysteine and glutathione secretion in response to protein disulfide bond