

Discovering mutations that cause phenotype in real time

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For nearly 100 years, classical geneticists have gained insight into biological systems through the creation of phenotype. This is accomplished by administering mutagens: agents that change the sequence of DNA in germ cells, damaging or destroying genes. When a phenotype is observed, it is possible to find the mutation responsible for it, and thereby understand the essential function of a particular gene. But this was a difficult process, sometimes requiring years of effort. Recently, we have developed methods that allow us to track down the mutational cause of phenotypes in mice almost instantaneously. By solving hundreds of mutationally induced immunological abnormalities we have been able to find many new parts of the biological machine that gives us resistance to infections. We have also been able to study many other biological phenomena (neurobehavioral, metabolic, and developmental abnormalities). At present, the pace of gene discovery is limited only by the speed at which mutations can be created and screened for their biological effects.