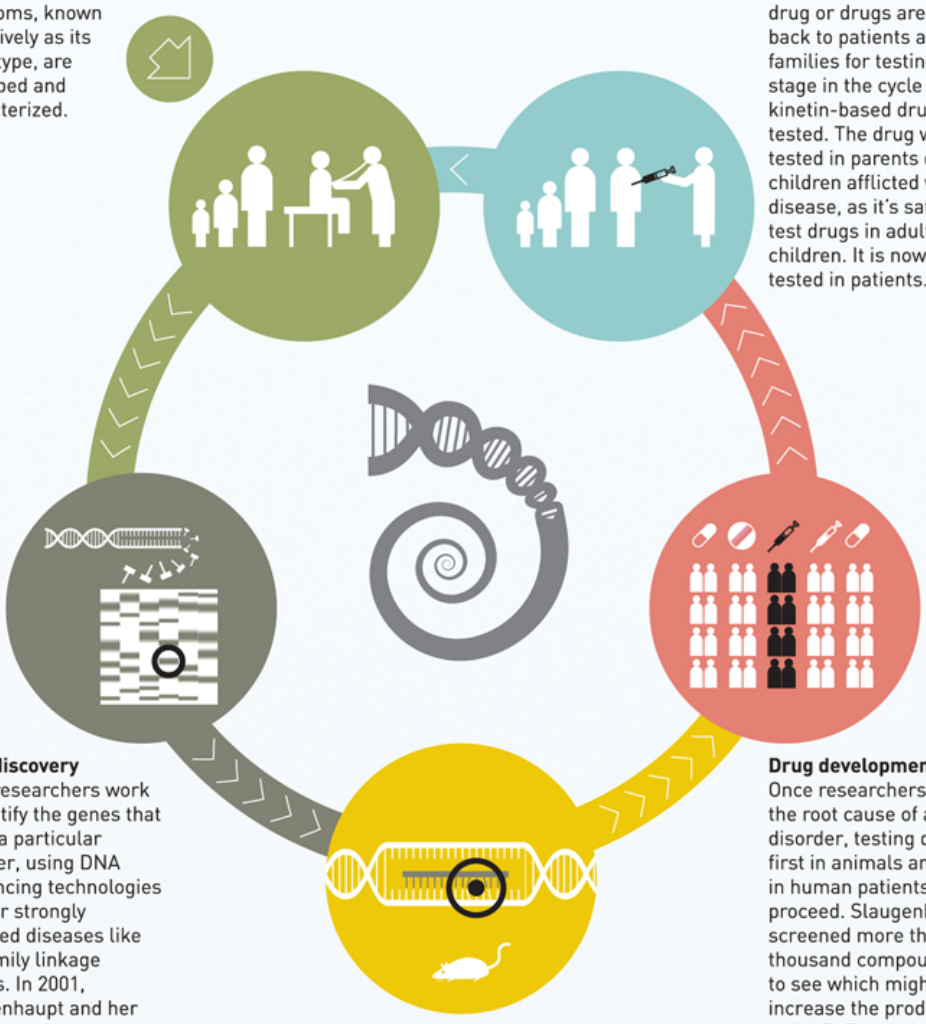
INFOGRAPHIC //

The Cycle of Gene Discovery

Whether researchers are studying a single-gene disorder or a complex one, their work follows the same basic cycle: They start by studying patients' symptoms and, ideally, end by testing a treatment in those patients. Thanks to work by Susan Slaugenhaupt, a principal investigator at Massachusetts General Hospital's Center for Human Genetic Research, the cycle is nearing completion for familial dysautonomia (FD), an inherited disease that is carried by one in 27 Ashkenazi Jews, causing neural problems that result in stunted growth, respiratory difficulties and severe eye problems. Here was her process.

Patients and families
In the beginning of the cycle, a disease's symptoms, known collectively as its phenotype, are described and characterized.

Patients and families II
Once potential treatments have been identified, the drug or drugs are brought back to patients and families for testing. At this stage in the cycle for FD, a kinetin-based drug is tested. The drug was first tested in parents of the children afflicted with the disease, as it's safer to test drugs in adults than in children. It is now being tested in patients.



Gene discovery
Next, researchers work to identify the genes that cause a particular disorder, using DNA sequencing technologies and, for strongly inherited diseases like FD, family linkage studies. In 2001, Slaugenhaupt and her colleagues found the gene that causes FD and showed that the mutation results in a reduced amount of a protein called IKAP.

Understanding the mechanism
By inserting the aberrant gene or genes into mice and looking at the effects on the mice's cellular processes compared with "normal" mice, researchers pinpoint how the gene causes the disorder. At the root of the FD mutation is faulty mRNA splicing, the process by which DNA orders the production of proteins by creating a complementary strand of messenger RNA.

Drug development
Once researchers know the root cause of a disorder, testing drugs, first in animals and then in human patients, can proceed. Slaugenhaupt screened more than a thousand compounds to see which might increase the production of IKAP. This led to the discovery of a plant compound, kinetin, that modifies mRNA splicing and boosts the level of the protein.