1.5: The Function of Genes

1.5.1 Beadle and Tatum: one gene, one enzyme hypothesis

Life depends on (bio)chemistry to supply energy and to produce the molecules to construct and regulate cells. In 1908, A. Garrod described “in born errors of metabolism” in humans using the congenital disorder, alkaptonuria (black urine disease), as an example of how “genetic defects” led to the lack of an enzyme in a biochemical pathway and caused a disease (phenotype). Over 40 years later, in 1941, Beadle and Tatum built on this connection between genes and metabolic pathways. Their research led to the “one gene, one enzyme (or protein)” hypothesis, which states that each of the enzymes that act in a biochemical pathway is encoded by a different gene. Although we now know of many exceptions to the “one gene, one enzyme (or protein)” principle, it is generally true that each different gene produces a protein that has a distinct catalytic, regulatory, or structural function.

Beadle and Tatum used the fungus Neurospora crassa (a mold) for their studies because it had practical advantages as a laboratory organism. They knew that Neurospora was prototrophic, meaning that it could synthesize its own amino acids when grown on minimal medium, which lacked most nutrients except for a few minerals, simple sugars, and one vitamin (biotin). They also knew that by exposing Neurospora spores to X-rays, they could randomly damage its DNA to create mutations in genes. Each different spore exposed to X-rays potentially contained a mutation in a different gene. After genetically screening many, many spores for growth, most appeared to still be prototrophic and still able to grow on minimal medium. However, some spores had mutations that changed them into auxotrophic strains that could no longer grow on minimal medium, but did grow on complete medium supplemented with nutrients (Figure 1.12). In fact, some auxotrophic mutations could grow on minimal medium with only one, single nutrient supplied, such as arginine.
**Figure 1.12:** A single mutagenized spore is used to establish a colony of genetically identical fungi, from which spores are tested for their ability to grow on different types of media. Because spores of this particular colony are able to grow only on complete medium (CM), or on minimal medium supplemented with arginine (MM+Arg), they are considered Arg auxotrophs and we infer that they have a mutation in a gene in the Arg biosynthetic pathway. This type of screen is repeated many times to identify other mutants in the Arg pathway and in other pathways. (Original-Deyholos-CC:AN)

### 1.5.2 B&T’s 1 gene: 1 enzyme hypothesis led to Biochemical Pathway dissection using genetic screens and mutations

Beadle and Tatum’s experiments are important not only for its conceptual advances in understanding genes, but also because they demonstrate the utility of **screening for genetic mutants** to investigate a biological process – **genetic analysis**. Beadle and Tatum’s results were useful to investigate biological processes, specifically the metabolic pathways that produce amino acids. For example, Srb and Horowitz in 1944 tested the ability of the amino acids to **rescue** auxotrophic strains. They added one of each of the amino acids to minimal medium and recorded which of these restored growth to independent mutants. For example, if the progeny of a mutagenized spore could grow on minimal medium only when it was supplemented with arginine (Arg), then the auxotroph must bear a mutation in the Arg biosynthetic pathway and was called an “arginineless” strain (arg-).
Figure 1.13: A simplified version of the Arg biosynthetic pathway, showing citrulline (Cit) and ornithine (Orn) as intermediates in Arg metabolism. These chemical reactions depend on enzymes represented here as the products of three different genes. (Original-Deyholos-CC:AN)

Synthesis of even a relatively simple molecule such as arginine requires many steps, each with a different enzyme. Each enzyme works sequentially on a different intermediate in the pathway (Figure 1.13). For arginine (Arg), two of the intermediates are ornithine (Orn) and citrulline (Cit). Thus, mutation of any one of the enzymes in this pathway could turn Neurospora into an Arg auxotroph (arg-). Srb and Horowitz extended their analysis of Arg auxotrophs by testing the intermediates of amino acid biosynthesis for the ability to restore growth of the mutants (Figure 1.14).

![Figure 1.14: Testing different Arg auxotrophs for their ability to grow on media supplemented with intermediates in the Arg biosynthetic pathway. (Original-Deyholos-CC:AN)](image)

They found that some of the Arg auxotrophs could be rescued only by Arg, while others could be rescued by either Arg or Cit, and still other mutants could be rescued by Arg, Cit, or Orn (Table 1.1). Based on these results, they deduced the location of each mutation in the Arg biochemical pathway, (i.e. which gene was responsible for the metabolism of which intermediate).

**Table 1.1:** Ability of auxotrophic mutants of each of the three enzymes of the Arg biosynthetic pathways to grow on minimal medium (MM) supplemented with Arg or either of its precursors, Orn and Cit. Gene names refer to the labels used in Figure 1.11

<table>
<thead>
<tr>
<th>Gene A Mutants</th>
<th>MM + Orn</th>
<th>MM + Cit</th>
<th>MM + Arg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Gene B Mutants</td>
<td>MM + Arg</td>
<td>MM + Cit</td>
<td>MM + Orn</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Gene C Mutants</td>
<td>MM + Arg</td>
<td>MM + Orn</td>
<td>MM + Orn</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>
1.5.3 Genetic screens for mutations help characterize biological pathways

Using many other mutations and the “one gene: one enzyme model” permitted the genetic dissection of many other biochemical and developmental pathways.

The general strategy for a genetic screen for mutations is to expose a population to a mutagen, then look for individuals among the progeny that have defects in the biological process of interest. There are many details that must be considered when designing a genetic screen (e.g. how can recessive alleles be made homozygous). Nevertheless, mutational analysis has been an extremely powerful and efficient tool in identifying and characterizing the genes involved in a wide variety of biological processes, including many genetic diseases in humans.

1.5.4 The Central Dogma

How does the structure of DNA and genes relate to inheritance of biological traits such as the flower color of Mendel’s peas? The answer lies in what has become known as molecular biology’s Central Dogma (Fig 1.15), which has come to be described as the genetic information of each gene is encoded in DNA, and then, as needed, this information is transcribed into an RNA sequence, and then translated into a polypeptide (protein) sequence. The core of the Central Dogma is that genetic information is NEVER transferred from protein back to nucleic acids. In certain circumstances, the information in RNA may also be converted back to DNA through a process called reverse transcription. As well, DNA, and its information, can also be replicated (DNA→DNA). The sequence of bases in DNA directly dictates the sequence of bases in the RNA, which in turn dictates the sequence of amino acids that make up a polypeptide. Proteins do most of the work in a cell. They (1) catalyze the formation and breakdown of most molecules within an organism as well as (2) form their structural components and (3) regulate the expression of genes. By dictating the structure of each protein, DNA affects the function of that protein, which can thereby affect the entire organism. Thus the genetic information, or genotype, defines the potential form, or phenotype, of the organism.

![Figure 1.15: Central Dogma of molecular biology. (Original-Deyholos-CC:AN)](https://bio.libretexts.org/Bookshelves/Genetics/Book%3A_Online_Open_Genetics_(Nickle_and_Barrette-Ng)/01%3A_Overvie...)

In the case of Mendel’s peas, purple-flowered plants have a gene that encodes an enzyme that produces a purple pigment molecule. In the white-flowered plants (a purple-less mutant), the DNA for this gene has been changed, or mutated, so that it no longer encodes a functional protein. This is an example of a spontaneous, natural mutation in a biochemical pathway.
Contributors

- Dr. Todd Nickle and Isabelle Barrette-Ng (Mount Royal University) The content on this page is licensed under CC SA 3.0 licensing guidelines.