CRISPR

A POWERFUL WAY TO CHANGE DNA

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INTRODUCTION

Imagine a world where no one ever gets sick—not even your pet. Imagine there's enough food to feed everyone without destroying the environment. A world where cloned versions of extinct animals are free to roam the earth once again.

Sound too good to be true?

You might be surprised to learn that all of this—and more—could be our new reality thanks to CRISPR, a biotechnology that gives humans the power to edit genes in a way that's never been possible before.

In this book, we'll discuss how gene editing could be used to wipe out disease-carrying mosquitoes and bring back a version of the woolly mammoth. How it could help cure cancer and prevent future pandemics. And how we may be able to create food that can adapt to climate change and be allergy-free and packed full of nutrition. (Chocolate that's even more nutritious than kale? Yes, please!)

Since CRISPR technology is new and constantly evolving, it's hard to predict what life will be like in a gene-edited future. The possilibites are endless and amazing—but they're also a bit scary. Humans haven't done a great job of caring for our planet so far, so what happens when we start messing with the entire web of life? Or altering the natural course of evolution? At what point do we change the definition of what it means to be human?

As we dig into the science behind CRISPR, we'll also explore the pros and cons of gene editing (check out the Stop, Go, and Yield sections at the end of each chapter) and ask some questions to get you thinking about how it might affect your life (see Cutting Questions). In the not-so-distant future, it will be up to each and every one of us to decide whether society should proceed, not proceed, or proceed with caution as we move forward with this powerful technology.

1

Jumping into GENETICS

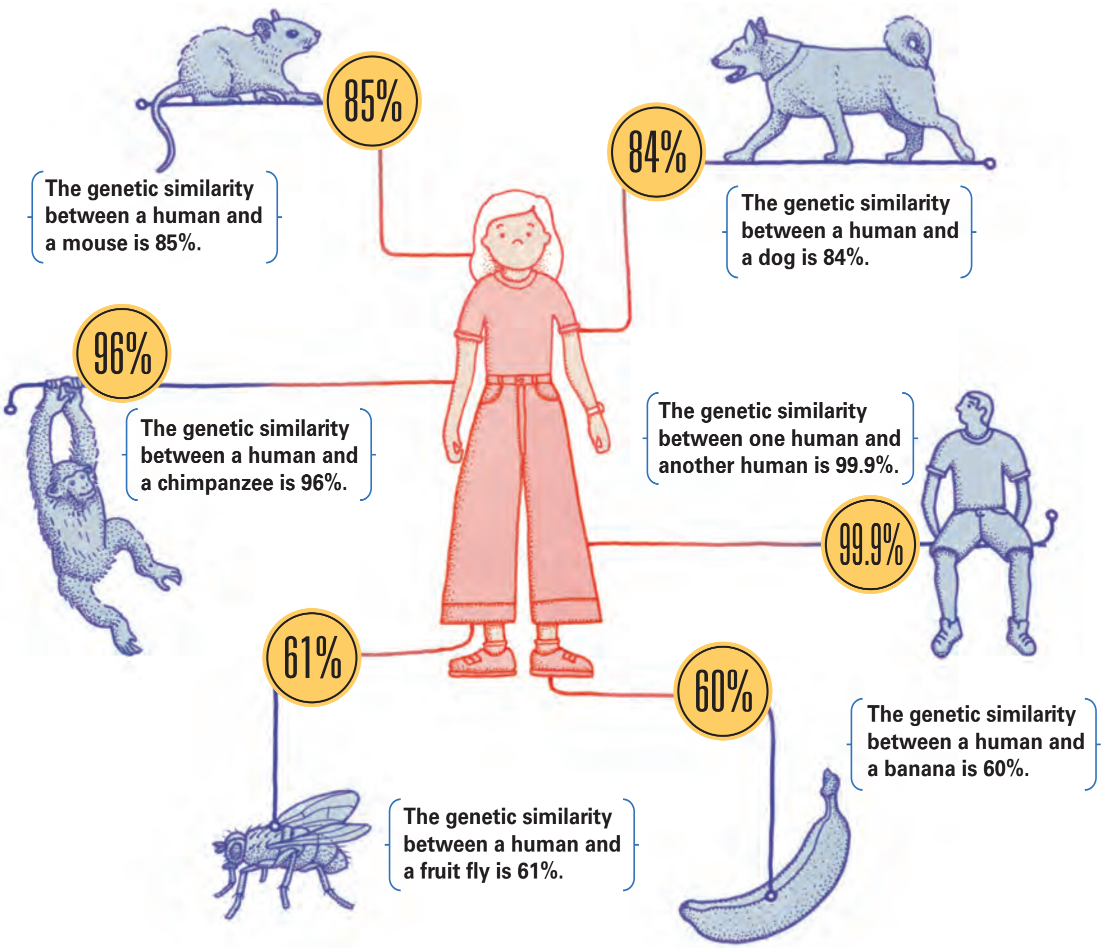
Knowing it's possible to gene-edit our way to better health, better nutrition, and a world without extinctions is one thing, but understanding how is something else altogether. How can we "edit out" a person's chance of inheriting a certain disease, for example, or "edit in" a particular crop's resistance to a certain pest? In order to understand how gene editing works, we first need to understand how genes themselves go about their business.

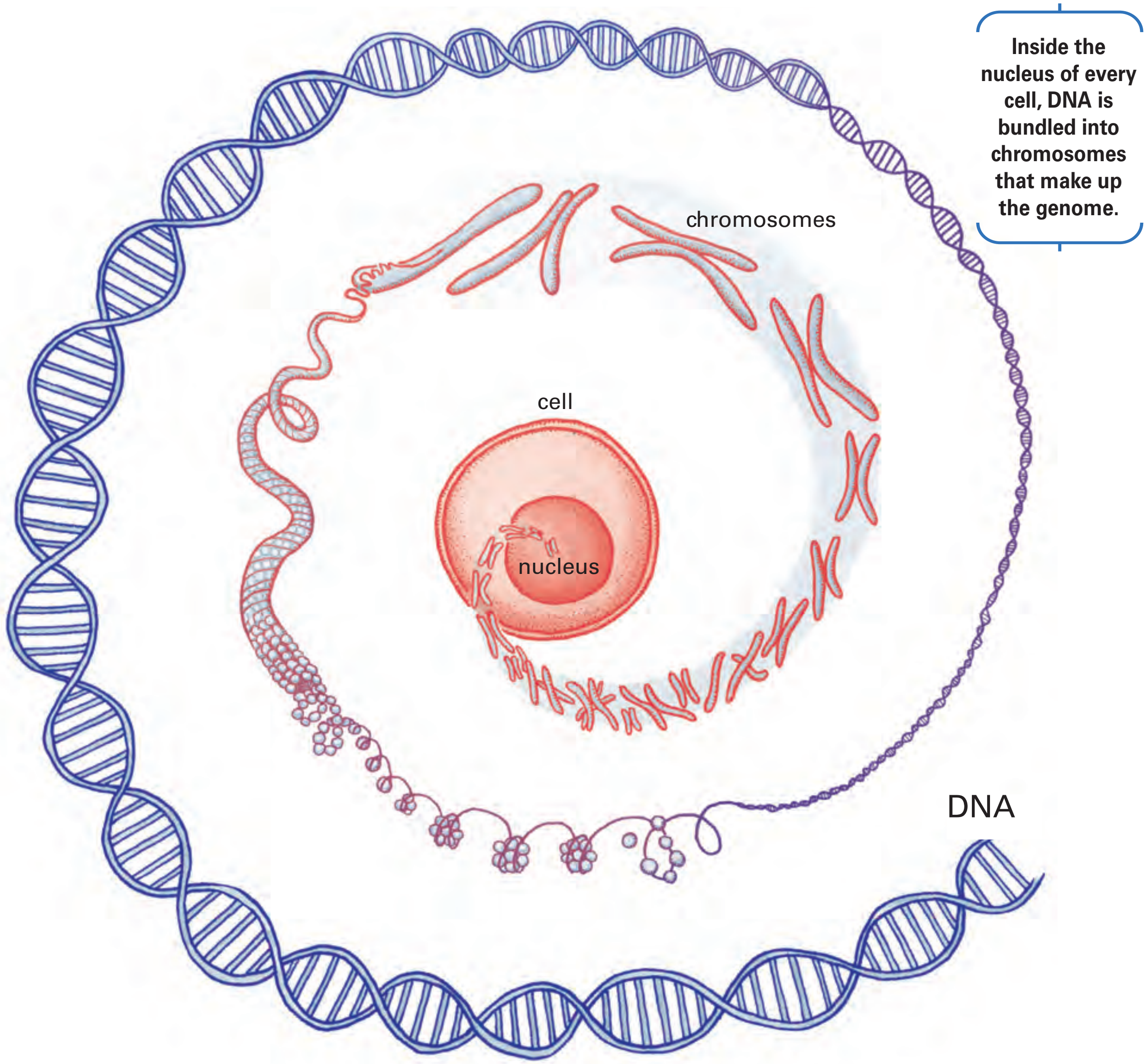
The Genome: Your Personal Instruction Manual

Let's start with the big picture. Every living being—from a bacteria to a monkey—has a genome. The genome is like a really detailed instruction manual. Not only does it tell the body how to function, but it also makes sure this information gets passed down from generation to generation. It's the instructions in your genome that told your body how to do everything from growing a toe to building a brain (with added information about how to keep it running). The genome gave your parents a similar set of instructions, and it will make sure that any kids you have will know how to do this stuff too.

Since every species is different, the genome of every species is different (although the genome of a mosquito and the genome of an elephant are more similar than you might expect). For now, let's focus on the being that matters to us most—the human being.

Most cells in the human body keep a copy of the entire instruction manual in their command center—otherwise known as the nucleus. It's estimated that the average human body is made up of 37.2 trillion cells—yes, you read that right: 37,200,000,000,000. That's a lot of instruction manuals!





DNA

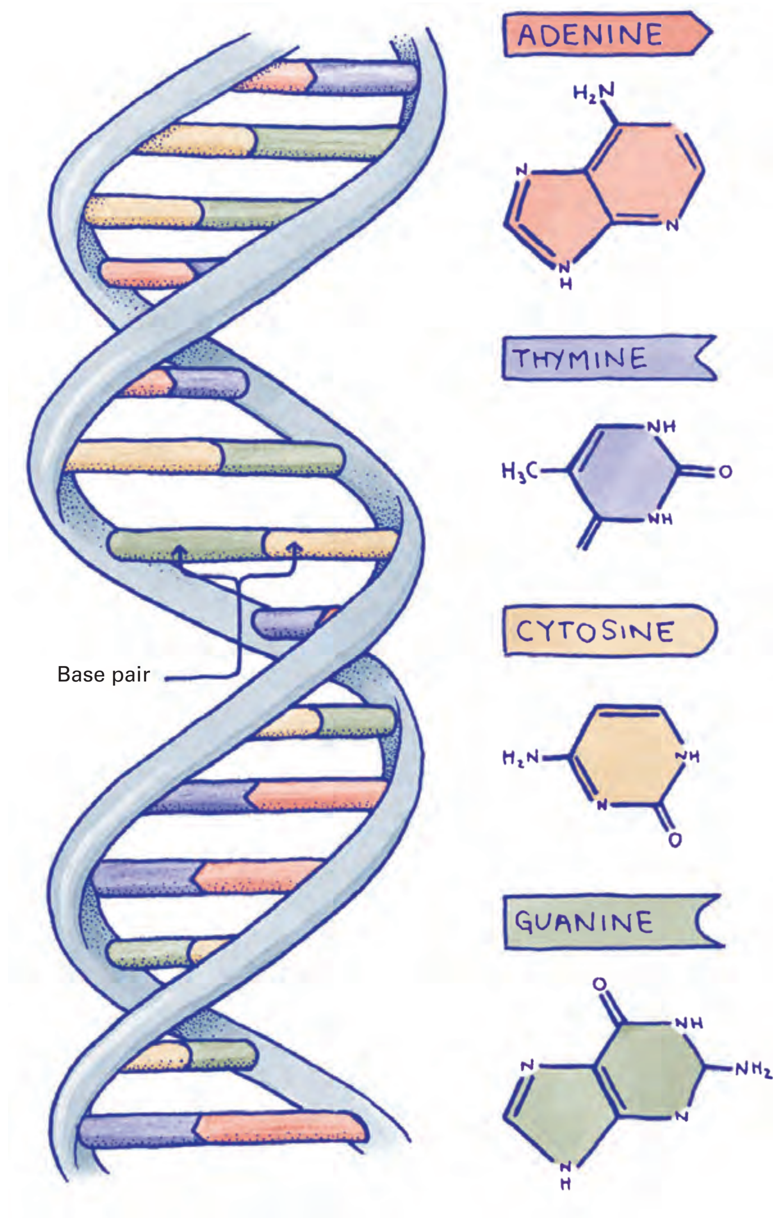
Instead of being written in words, like the instruction manuals we're used to, the genome is written with DNA. If you were to unravel the genome and zoom in with a *really* powerful microscope, you'd eventually see that DNA is the core of it all.

So, what is DNA? The letters stand for "deoxyribonucleic acid," which is a long way of saying that DNA is made up of two long strings of molecules called nucleotides. These strings—or strands—spiral together to create what's known as a double helix. If you think of DNA as a twisted ladder, each strand of nucleotides is one side of the ladder. The rungs that attach the sides together are formed by the nitrogen base of each nucleotide binding with its mate on the other side. This is why nucleotide pairs are often referred to as "base pairs."

Our alphabet has 26 letters; DNA has 4—A, G, T, and C—which stand for the nucleotides adenine, guanine, thymine, and cytosine. In DNA, adenine pairs with thymine, and cytosine pairs with guanine.

The workers inside the cell read sequences of three nucleotides as three-letter words, or codons. These three-letter words then string together to form a sentence. And these sentences make up the instruction manual.

A nucleotide (or base) is a molecule with a nitrogen base that binds (or pairs) with the nitrogen base of the nucleotide on the opposite strand.



To get a sense of how this works, let's imagine that our genome is an instruction manual on how to build things out of toy bricks.

Of course, the human genome isn't instructing the body on how to build a rainbow. Instead, it's telling our 37 trillion cells how to do everything from thinking to digesting food—all of the essential "instructions" we need to function.

1 We look through the instruction manual to find what we want to build—say, a rainbow.

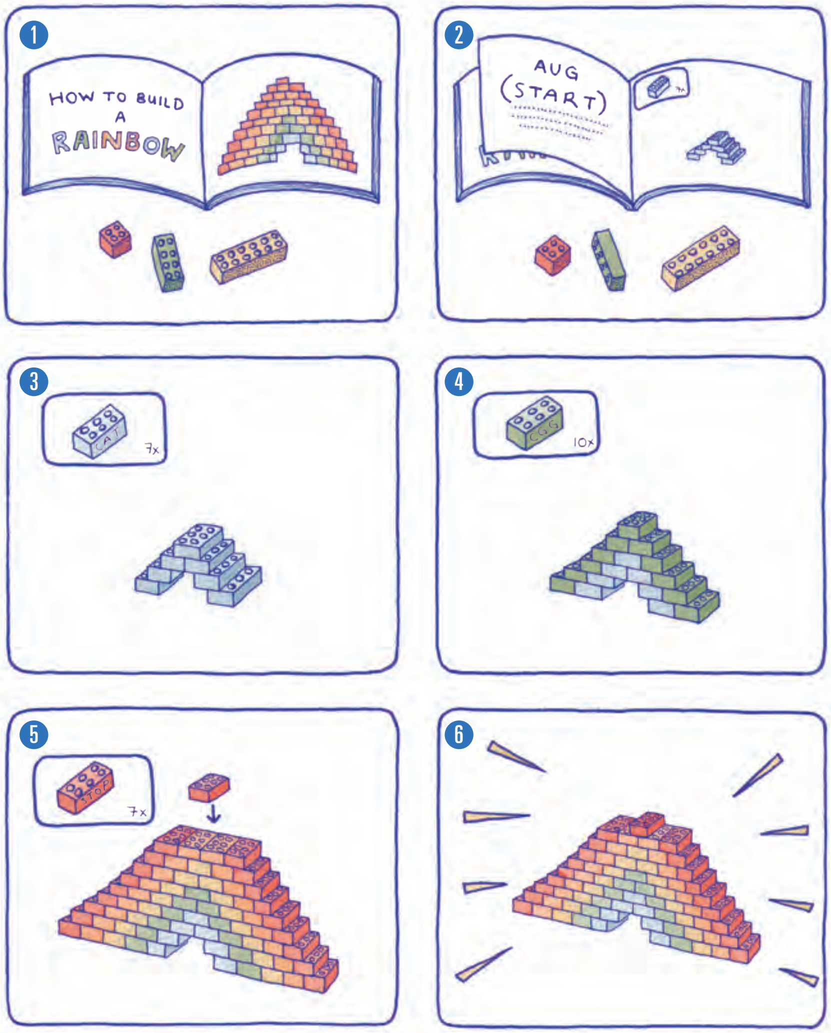
2 At the beginning of the step-by-step instructions on how to build a rainbow, there will be a three-letter word (or codon) that means START.

3 Right after that will be a three-letter word that tells us which brick to get first.

4 The three-letter word that comes next is the code for the next size and shape of brick you need to add.

5 And so on . . . until you get to a three-letter word that means STOP.

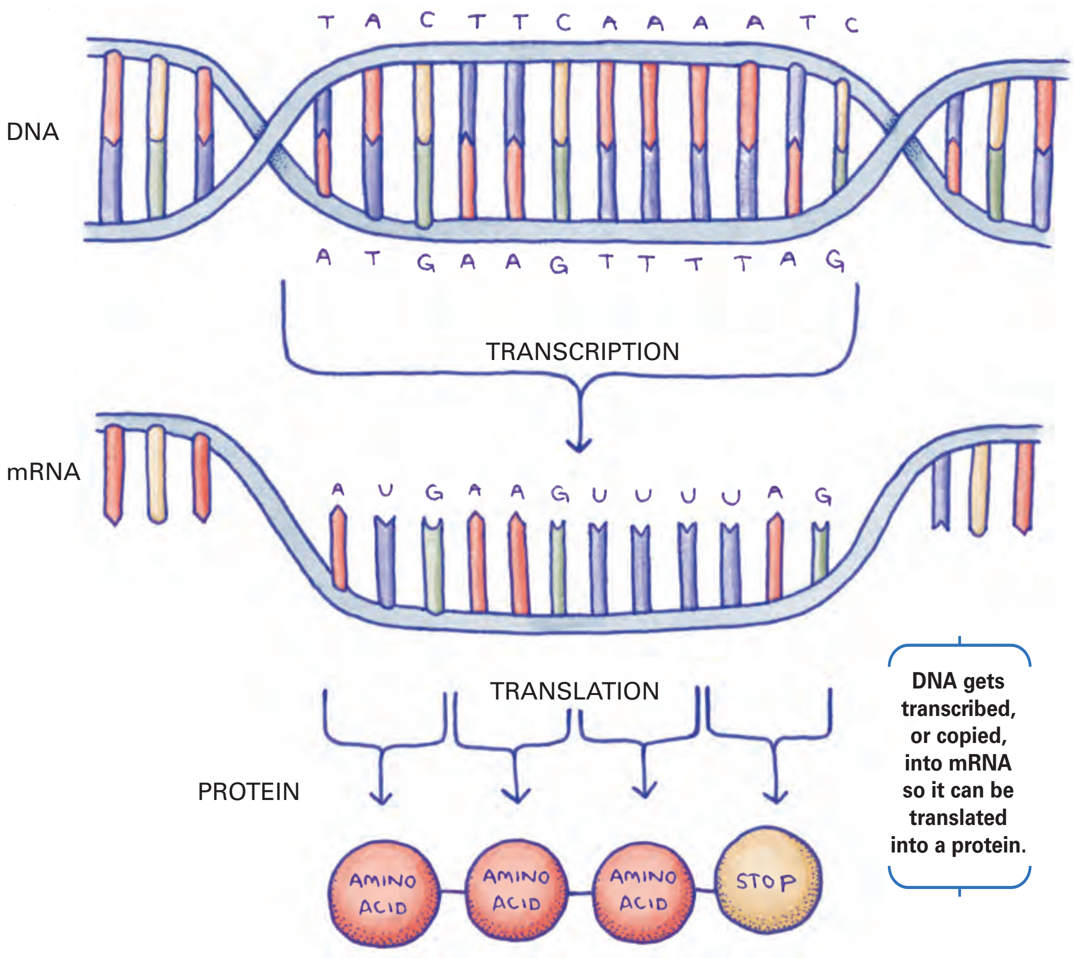
6 Your rainbow is complete!



Genes

So, where do genes fit in? If the genome is the cell's entire instruction manual, the gene is like a specific sentence. It tells the cell how to make one specific thing—a protein. When making a protein, the two strands of DNA split apart so they can be copied by something called messenger RNA, or mRNA. (RNA, which stands for "ribonucleic acid," is just a single-stranded version of DNA with U standing in for T.) The three-letter words in the mRNA are then used to build a protein using amino acids. Like the toy bricks used to make our rainbow, amino acids are building blocks made of elements from the periodic table that come together in different combinations to form a protein.

Now, a rainbow's not particularly useful (unless you're into photography or hunting for pots of gold), but proteins are necessary for every single thing our bodies do, from digesting food (using enzymes) to determining traits like eye color (with different pigment proteins) or height (through hormones).

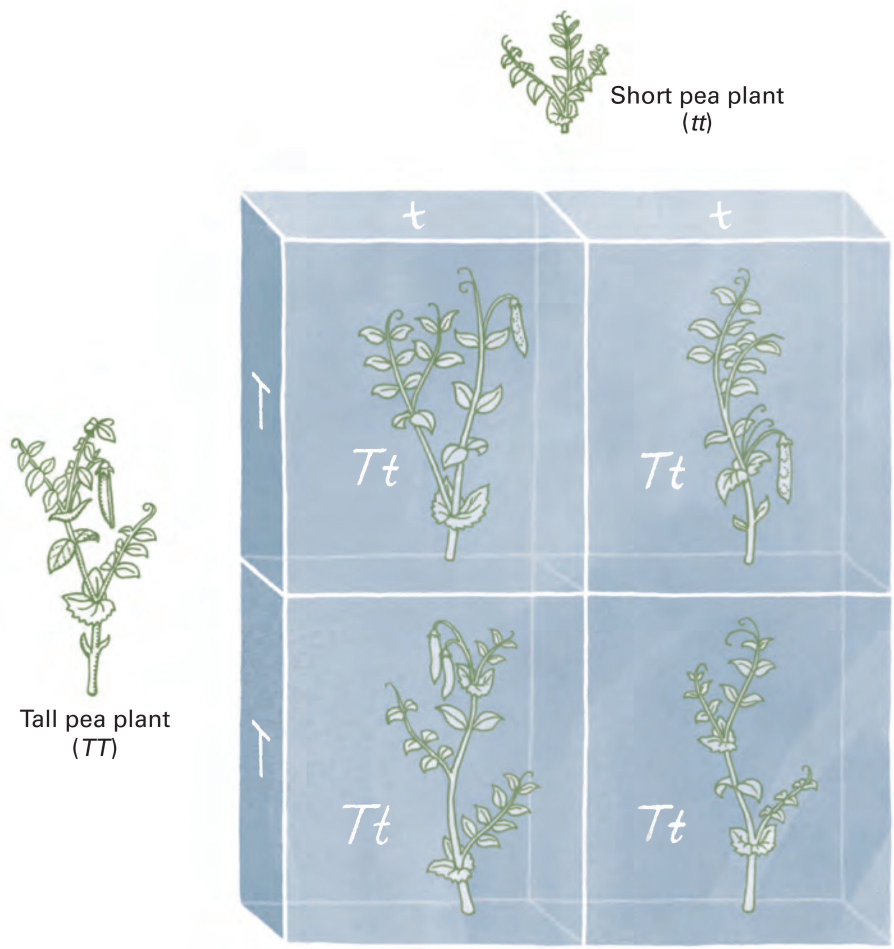


DNA gets transcribed, or copied, into mRNA so it can be translated into a protein.

The Father of Genetics

Gregor Mendel—the "father of genetics"—was an Austrian monk who liked to grow peas. Also a budding scientist, he was curious as to why plants had different traits. To test how things like height, shape, and color were inherited, Mendel made plant "moms" and plant "dads" produce plant "babies" by controlling pollination.

When a tall mama plant crossed with a small papa plant, it did not produce a medium-sized baby plant, as Mendel had predicted. Instead, the baby plant was tall. Over the course of his experiments, Mendel learned that the tall trait was "dominant" over the small trait. What Mendel discovered from these experiments done in the 1850s formed the basis of what we now know about dominant and recessive traits.



If a tall pea plant has two tall genes (labeled *T*), it can only pass on a *T* to the next generation. If a small pea plant has two small genes (labeled *t*), it can only pass on a *t* to the next generation. Every pea plant in the next generation will be tall since the *T* version of the gene is dominant over *t*.

All baby pea plants are tall

Chromosomes

All of this DNA—the letters that code for genes and the non-coding regions in between them—are bundled into chromosomes. The human genome has 46 chromosomes that are grouped into pairs.

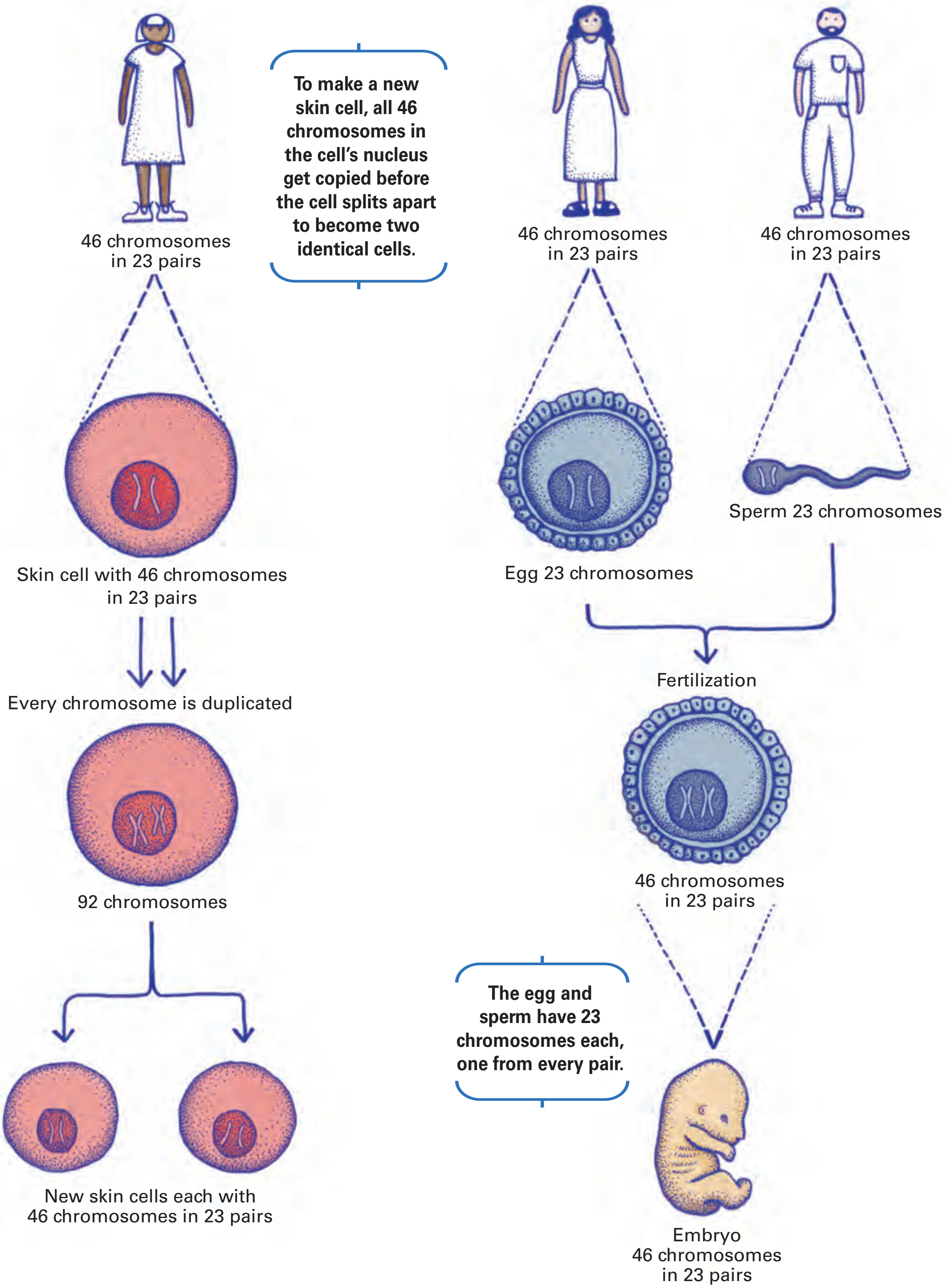
Chromosomes 1 through 22 (the autosomes, conveniently numbered according to size) all have a partner that's similar but not identical. Both copies of chromosome 15, for example, contain a gene for eye color. But one copy of that gene might code for brown eyes and the other for blue eyes—similar but not identical (see "Look Into My Eyes," page 12).

The 23rd pair—the sex chromosomes—do not necessarily pair up. Females have two X chromosomes, which are as similar to each other as a pair of autosomes. Males have one X chromosome and one Y chromosome, which are quite different in both size and content. In fact, the Y chromosome only contains genes that code for proteins needed to make male reproductive parts. So, if you get a Y—biologically, you're a boy.

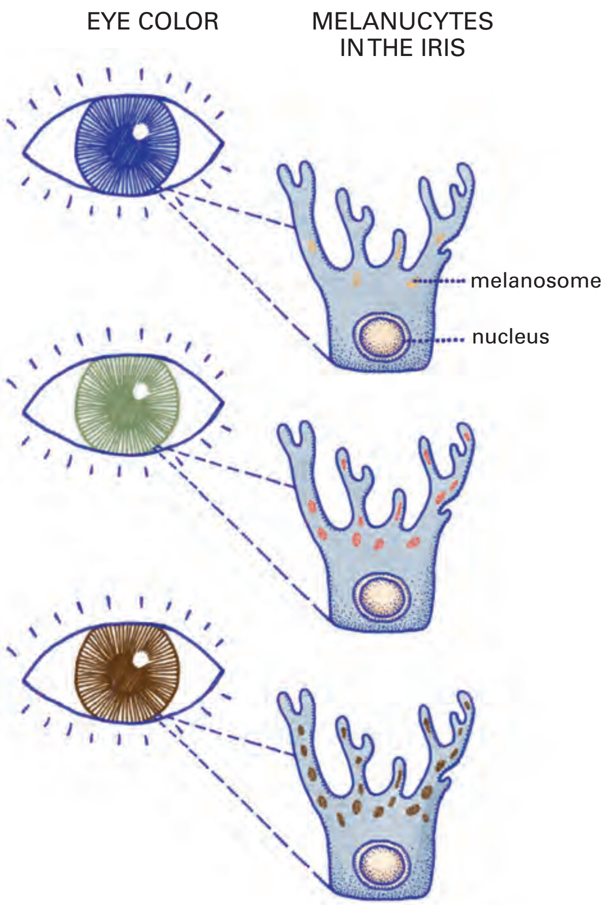
A complete set of human chromosomes after they've been isolated in the nucleus, stained, and magnified

Why do we need two copies of every chromosome? Mainly because of inheritance. Each pair contains one chromosome from our mom and one from our dad.

When a skin cell or a brain cell, for example, divides to make a new cell, it copies every page of the instruction manual—or every chromosome—to produce a clone of itself. But when a reproductive cell divides to make an egg or sperm, it reduces its chromosomes by half. This is why human children are not clones of their parents but rather a combination of the two.


46 chromosomes in 23 pairs
To make a new skin cell, all 46 chromosomes in the cell's nucleus get copied before the cell splits apart to become two identical cells.
Skin cell with 46 chromosomes in 23 pairs
Every chromosome is duplicated
92 chromosomes
New skin cells each with 46 chromosomes in 23 pairs
46 chromosomes in 23 pairs
46 chromosomes in 23 pairs
Egg 23 chromosomes
Sperm 23 chromosomes
Fertilization
46 chromosomes in 23 pairs
The egg and sperm have 23 chromosomes each, one from every pair.
Embryo 46 chromosomes in 23 pairs

So now we understand why we're half like our mom and half like our dad (although some of us may prefer to think of ourselves as more like one than the other!). We also understand how DNA makes up genes, and genes make up chromosomes, and chromosomes make up our entire genome, which acts like an instruction manual for producing the proteins we need to develop, grow, and function. Now that we've got that figured out, we're ready to explore the amazing technology that is gene editing.



Eye color is determined by the amount of pigment produced and stored in the cells within the iris.

Look into My Eyes

When scientists first figured out that genes were responsible for the traits passed on from parents to children, they assumed that simple characteristics like eye color were controlled by a single gene. Just like Gregor Mendel described the "tall" pea plant trait as dominant over the "small" trait (see "The Father of Genetics," page 9), brown eyes were thought to be dominant over blue eyes and green eyes.

Turns out that was too simple an explanation. We now know there are many different genes involved in determining eye color. Some of these genes provide a set of instructions on how much pigment specific cells within the iris should make. In addition to other factors such as the structure of your eye, color is determined by the amount of pigment made and stored in the iris.

Chromosome 15 has two genes that play a big role in this. Since those two genes are close together on the same autosome, they usually get passed on as a pair, which is why two blue-eyed parents are very likely to have blue-eyed children. But if you happen to have brown eyes, even though your parents both have blue eyes, don't assume you were switched at birth. It's just the result of those other genes doing their thing.