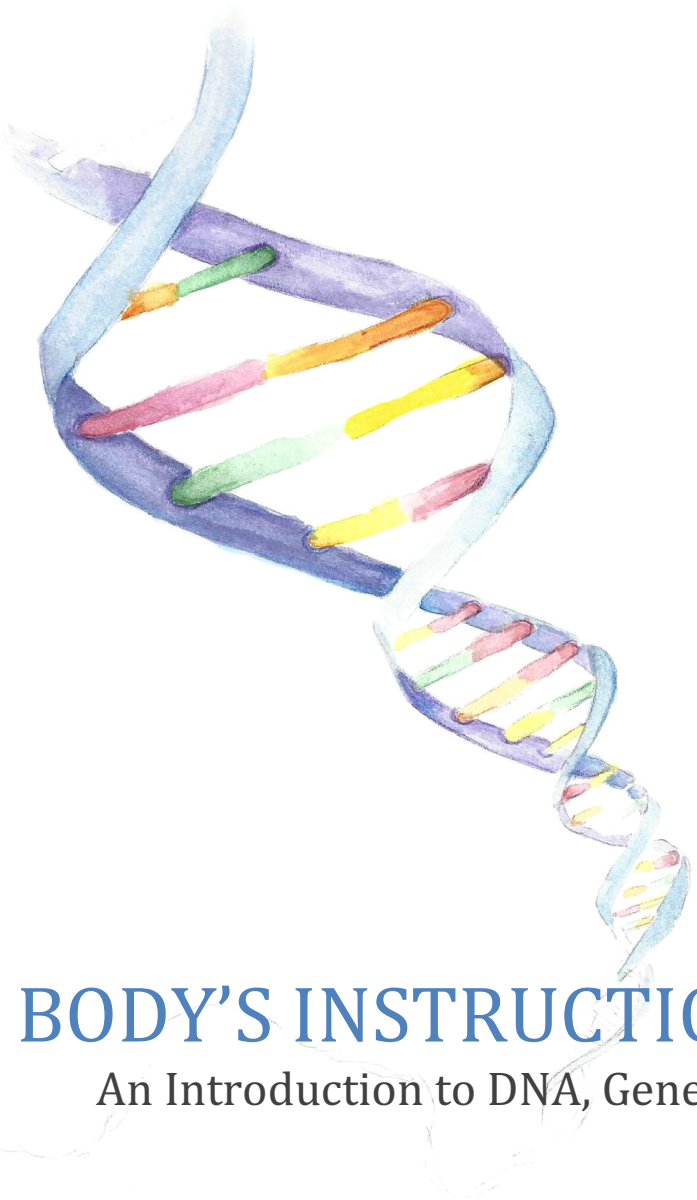


YOUR BODY'S INSTRUCTION MANUAL

An Introduction to DNA, Genes and Chromosomes

This booklet explains the basics of genetics and conditions related to genetics. This knowledge can help you understand your risks for inherited or genetic conditions, equip you to make decisions about medical care, and enable you to share this knowledge with loved ones or friends.

Some things your provider may discuss with you:

Do you know why you are seeing a clinical geneticist?

Are you familiar with these terms?

- DNA
- Genes
- Heredity

If you don't know these answers or have other questions, don't worry. Your provider wants to help you to understand these terms and more.

What is DNA?

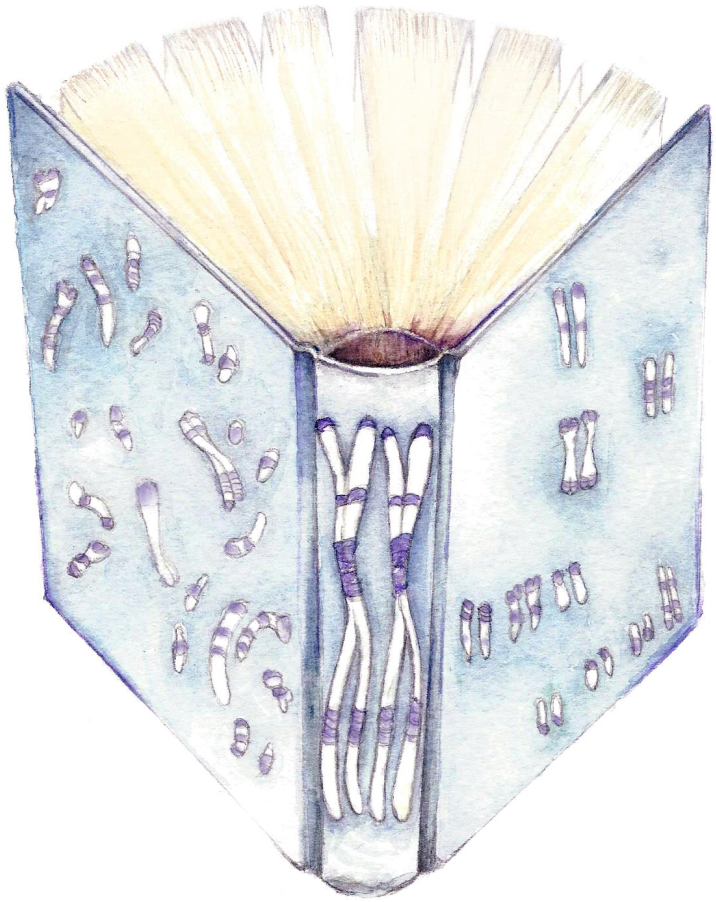
DNA is present in the cells of all living organisms. It is the basic building block of all of your genetic material. A person's genetic material determines physical traits like eye and hair color and height. It is passed from parents to children—this is called **heredity**. Another way to say this is that a person's genetic material is **inherited** from their parents.

What are chromosomes and genes?

Genes are made up of DNA. A person inherits genes from both parents. Each **chromosome** contains many genes.

DNA➔GENES➔CHROMOSOMES

Your Body's Instruction Manual



In each one of your cells, your chromosomes act as your body's instruction manual for how to form and how to function. This instruction manual is so detailed that it must be written in a set of 46 different books (chromosomes). Those individual books (or 46 chromosomes) work together to give directions for how your body is made and how your body knows what it's supposed to do. Every person in the world has genetic material that gives similar instructions, but at the same time, each person's instruction manual is unique (just like no two people have the same fingerprint).

It starts with the sperm and the egg…

When the egg from a mother and the sperm from a father combine to make a baby, they carry genetic potential from each parent. When the egg and sperm merge, the parents' instruction manuals have been copied and half of the manual from each parent is combined (the "genetic potential" of the parents is combined) to make a new, unique instruction manual. In the end, each cell in the baby will get 46 books, but they exist in 23 pairs: two copies of book number one, two copies of book number two, and two copies of the number three, and so on.

THINK ABOUT IT:

- **How is DNA passed from one living thing to another?**
- **In your body, where is the DNA?**
- **DNA helps your body form and function. TRUE or FALSE**
- **Is there anyone else in the world that shares your exact DNA?**
- **Which of these carries your body's complete instruction manual?**
  - **Egg**
  - **Sperm**
  - **Chromosomes**
- **Name some physical traits you have inherited from your parents or grandparents:**

When there's a problem with the body's instruction manual…

Remember, in each one of your cells, your chromosomes act as your body's instruction manual for how to form and how to function.

Inside your multi-volume instruction manual are hundreds of thousands of instructions on how to make things. What we know is that *everybody*, everybody in the whole world, including everybody you've ever met, has about one hundred thousand spelling errors in their instruction manual.

Most of the time your body just reads right through the spelling errors—kind of like when you wrote an assignment for school and you thought it looked good until you handed it to your mom (who started circling your errors) and she said, "Did you even read this?" What happened is your brain knew what you wanted to say, so you overlooked the errors, but your mom (who didn't know what each word was supposed to be) found the errors.

Your body reads your instructions in much the same way as you did when you write that paper. As it gets to most spelling errors in your instruction manual, it decides, "Oh! I know what this is supposed to be." And it goes right through and does the right job. Occasionally, there is a spelling error that changes the meaning of a word, or a whole paragraph altogether. When that happens your body can be confused as to interpret your instruction manual. Errors in your chromosomes can confuse the body as to how to form or how to function, and that's when genetic disorders happen.

When you need to see the geneticist:

If you or your family member has been diagnosed with a genetic condition, or is suspected of having one (due to medical signs or symptoms, learning difficulties, and/or a family history of a genetic disorder), you may be referred to a geneticist. This is doctor who specializes in the study and diagnosis of inherited or genetic conditions. Also, some pregnant women are referred to the geneticist because of their family history or the findings on a scan or test during pregnancy. For others, there might be a known risk in their families for a particular medical condition such as heart disease or cancer, and the geneticist is asked to assess that risk.

For some kinds of genetic conditions, there are specialized tests to determine the problem. This can help doctors find a diagnosis or plan medical care.

If the doctor says you need genetic testing…

When a problem is suspected, the clinical geneticist's job is to look for a needle in a needle stack, to use all of the patient's information (the medical history, the family history and the physical exam) to identify the medical cause for the problem. Sometimes, the geneticist orders specific blood tests to help with the diagnosis. Genetic tests comb through the hundred thousand different spelling errors in a person's instruction manual to find the one that is causing the medical trouble. It is important to remember that most spelling errors are overlooked by the body and do not result in a problem.

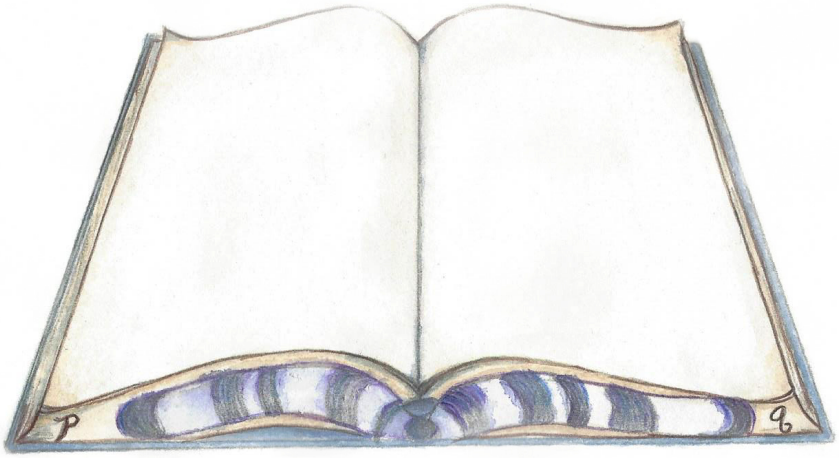
What is a Karyotype?

Remember: In each cell of a person, chromosomes act as an instruction manual, like 46 books containing instructions for how to form and how to function (these books exist as 23 pairs, so there are two copies of book number one and two copies of book number two, etc.).

When a problem with your chromosomes is suspected, the doctor may suggest a test called a **karyotype**, or a **chromosome study**. For this test, it's as if the instruction manual (all 46 books) has been laid out, onto a slide, to examine all the details. In the lab, they straighten all the chromosomes and line them up in perfect little rows, from the longest one to the shortest one.

The karyotype test looks to see if all of the books of your instruction manual are present, if any have been deleted, if any have been duplicated, if all of the chapters are there, and if any books are stuck to any of the other books.

What is a Microarray?



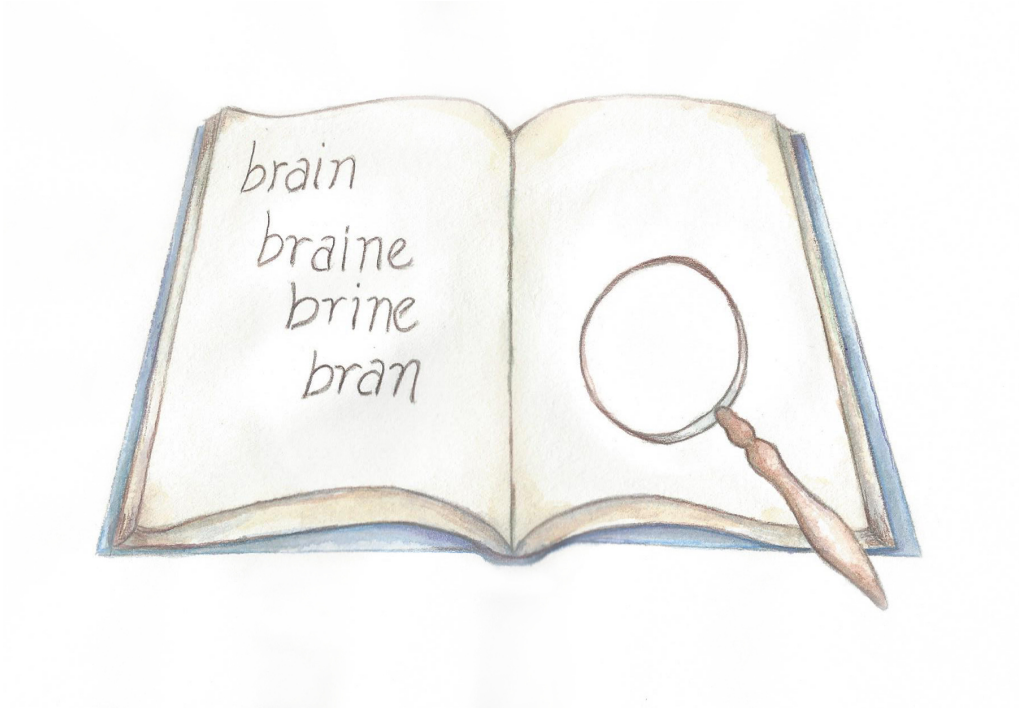
Remember, how each one of your chromosomes like a book?

Each chromosome has a **centromere**, which acts like the binding of the book; it's what holds the entire chromosome together. Each one of the chapters for the book is numbered as they go out from the centromere.

A **microarray** examines each chromosome. These are like the books in your instruction manual. This test asks, "Is each page of each book there? Is each page there once, twice, three times? Are any pages missing? Have any page been deleted?" It can't tell about the organization of the book, it just looks at the pages.

Between the Karyotype and the Microarray tests, you can find out how your set of instruction books is arranged and if any of the pages are missing.

What are single gene and multiple gene panel testing



Single gene tests and multiple gene panel tests are looking for genetic variants. We can think of these as spelling errors (substitutions, deletions and insertions) in words, or in the specific instructions about how your body should form or function. A single gene test looks for errors in one gene (for example: sickle cell disease is caused by an error in one gene). The multiple gene panel usually tests groups of genes that, together, are related to a particular genetic disorder (for example: testing all of the genes that are associated with the development of short stature).

What do my results mean?

Whenever tests are performed on your genetic material, like chromosomes or genes, it is as if someone is proofreading your instruction manual. With each test, there are a few possible results:

- **Positive result** Genetic variant is detected. It is known that this genetic variant, or spelling error, confuses the body (it doesn't know how to interpret the error), which can cause a particular set of symptoms.

- **Negative result** No genetic variant is detected, or none of the words being spell-checked are misspelled.

- **Variant of uncertain clinical significance** Genetic variant is detected, but there's not enough scientific evidence to say how your body will interpret the error that has been found. If there's no record of someone else having the variant your have—if you are the only one known to have this spelling error in your instruction manual—there is no evidence for how your body will interpret that information. (Sometimes somebody with a disease and somebody without that disease both have the same error, which can be confusing). When this happens, the geneticist will explain about what that variant means and will attempt to interpret it, to explain how this may or may not affect your health.

THINK ABOUT IT:

- **Errors in the genetic material can cause problems with how the body forms or functions. TRUE or FALSE**

- **What are genetic tests looking for?**

- **Which of these are true about spelling errors in your body's instruction manual:**
  - **They are very uncommon and rare**
  - **They occur in everyone**
  - **They always cause a problem**
  - **They do not always cause a problem**

- **Which of these is a genetic test:**
  - **Microarray**
  - **Multiple Gene Panel Test**
  - **Karyotype**
  - **Single Gene Test**
  - **ALL of these are genetic tests**

Match each of the following terms with the correct description:

a. Positive Test Result
b. Negative Test Result
c. Variant of uncertain clinical significance

_____ No genetic variant is detected.

_____ A spelling error is detected in your instruction manual (a genetic variant is found) and *IS* known to be related to certain symptoms or medical problems.

_____ A spelling error is detected in your instruction manual (a genetic variant is found) and *IS NOT* known to be related to certain symptoms or medical problems.

When you go home, who will need to hear the story about your visit today?

What will you tell them to help them understand what you learned today about heredity, the basics of genetics, and conditions related to genetic disorders?
(Hint: tell how each cell carries an instruction manual for how to form and function, and that there are always some spelling errors in the instruction manual, but some errors cause medical problems that can be inherited).