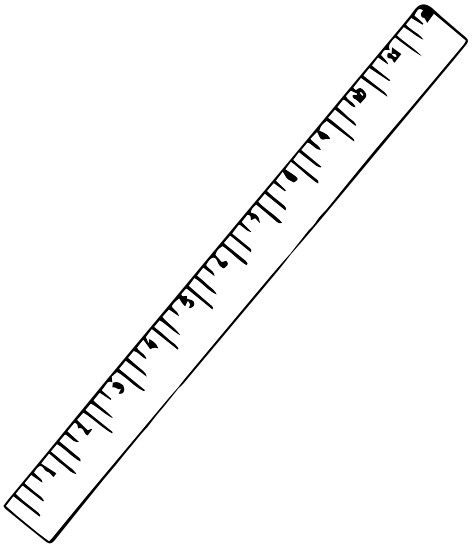
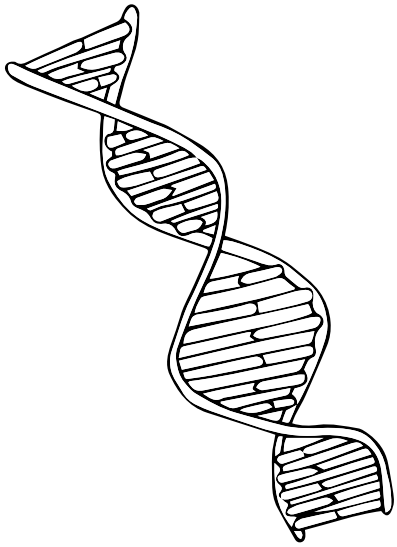
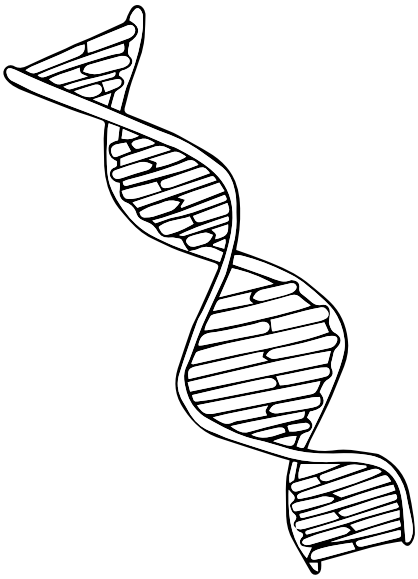
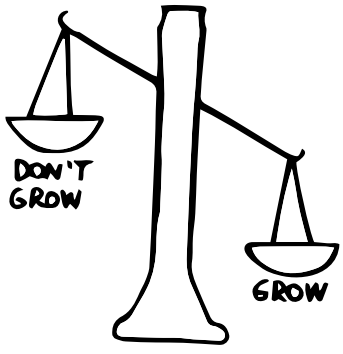




BWS AND YOU





An Educational Coloring Book

THIS BOOK BELONGS TO:

_____

Dear BWS family,

This book was developed through our conversations with families of children with Beckwith-Wiedemann Syndrome/Spectrum (BWS). We understand that receiving a diagnosis of BWS can be overwhelming. The genetic and epigenetic causes of BWS are some of the most complex to understand and explain. Our descriptions are based on how we explain BWS to patients and families in clinic. We hope that this book helps you on your BWS journey and can be used as a resource to share information with family, friends, and other caregivers.

Through continued conversations and working together, we can further guide and enlighten our knowledge of BWS and continue to answer the many unanswered questions.

We welcome you into our BWS community and hope that through the partnership between our team and BWS families, we can further improve understanding and care for children with BWS.

Warm regards,

Jenn Kalish, MD, PhD

Assistant Professor of Pediatrics
Division of Human Genetics
Center for Childhood Cancer Research
Beckwith-Wiedemann Syndrome Registry
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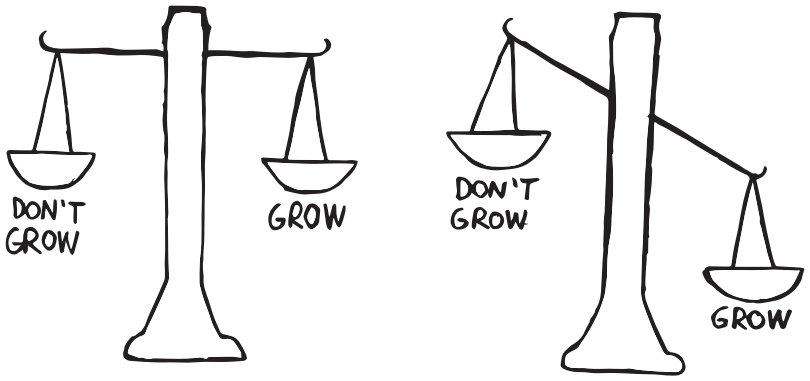

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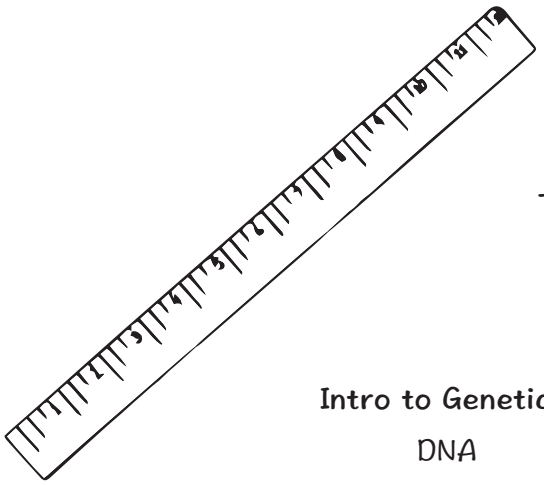

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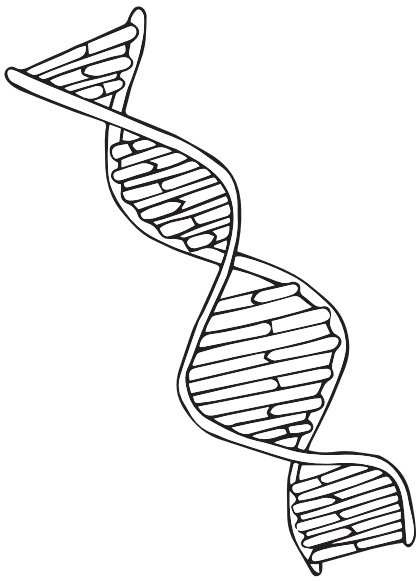
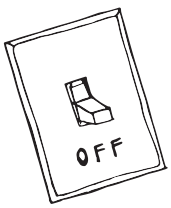
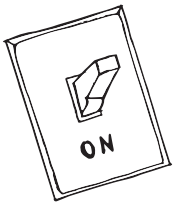
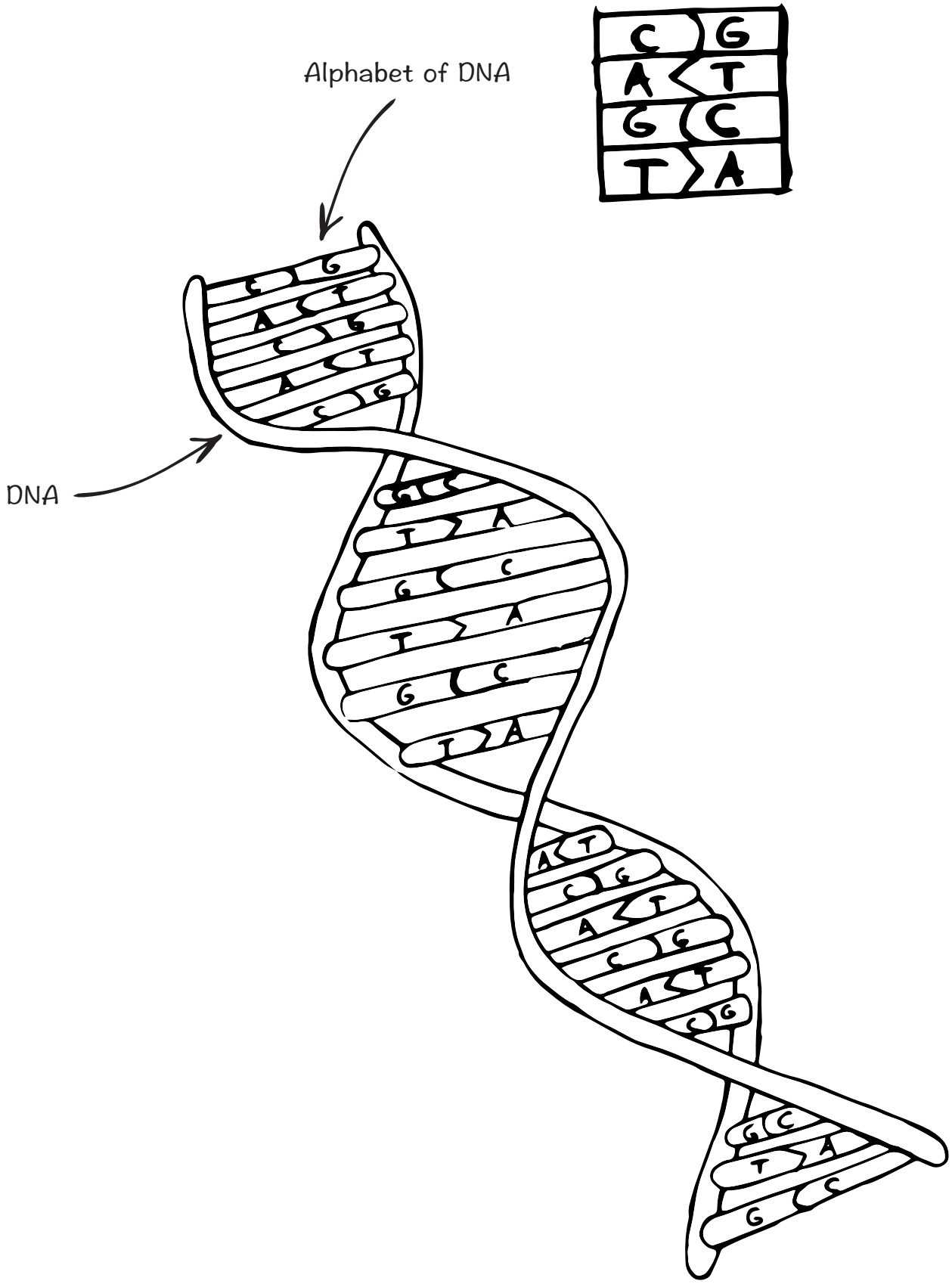




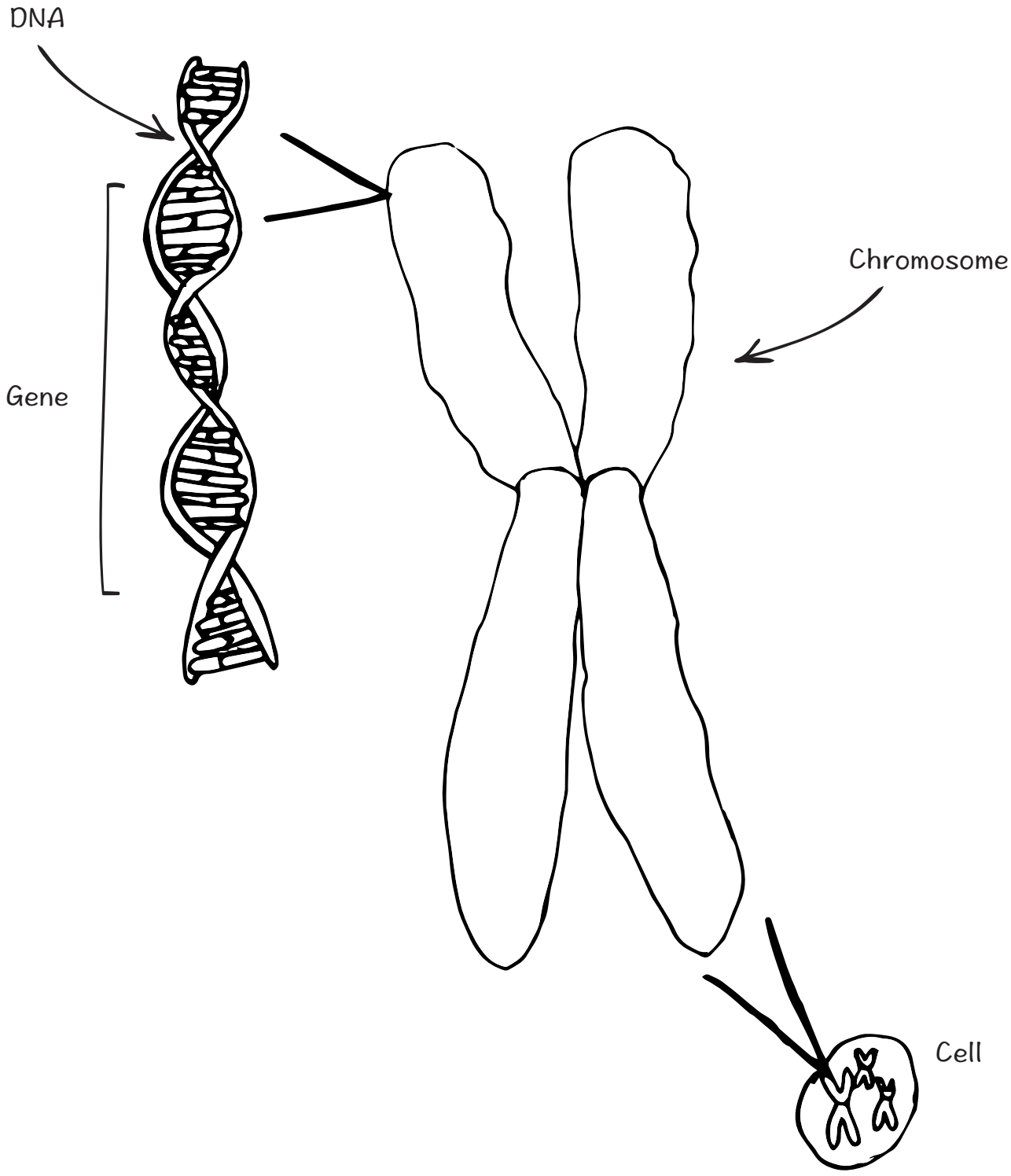


DNA, or deoxyribonucleic acid, is a substance that carries genes from biological parents to their children.

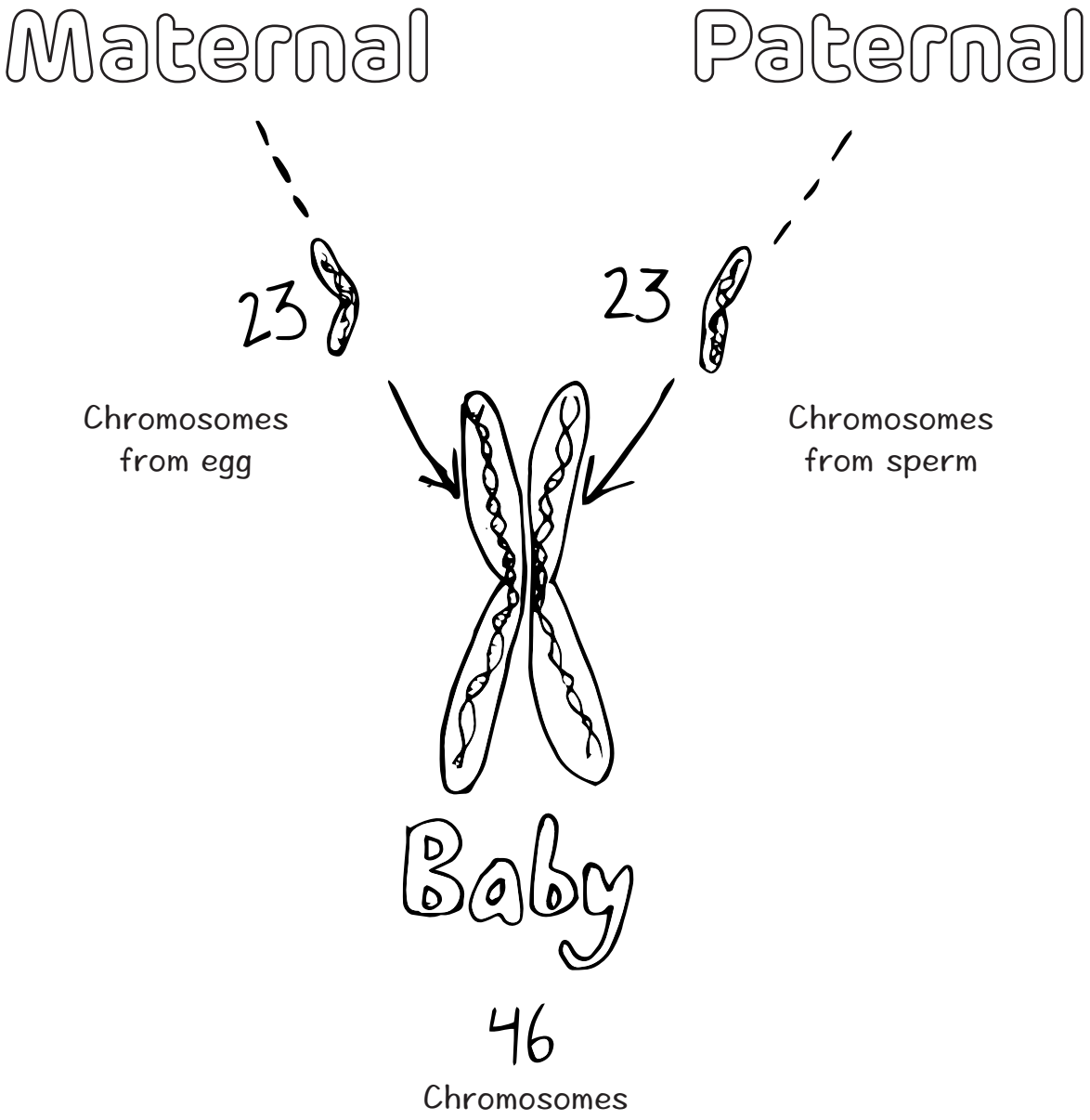


Genes are pieces of DNA that are passed down from parents to their children and represent traits or characteristics, such as hair color or growth.

Chromosomes are the parts of cells that contain genes. Cells are the building blocks of all living things.



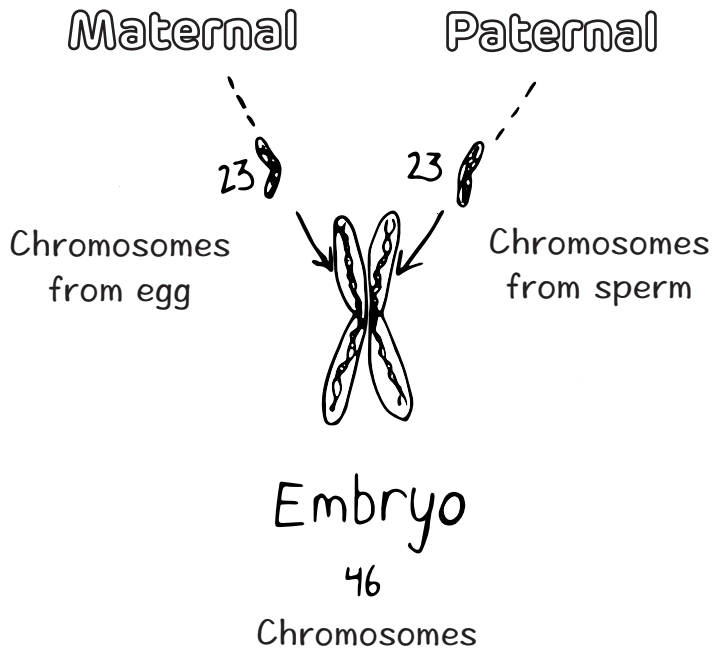
A child will inherit one set of chromosomes from the egg and one set of chromosomes from the sperm. Usually, a child receives 23 chromosomes from each biological parent, making a total of 46 chromosomes.



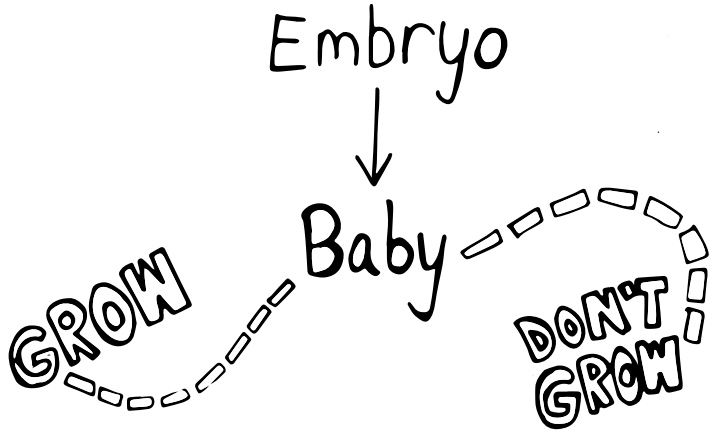
Intro to Genetics

Genetics is the study of the process when children inherit genes from their biological parents. Epigenetics is the study of how the function of a person's genes change. Some genes may or may not express certain traits. Epigenetic changes occur after conception as the embryo turns into a baby.

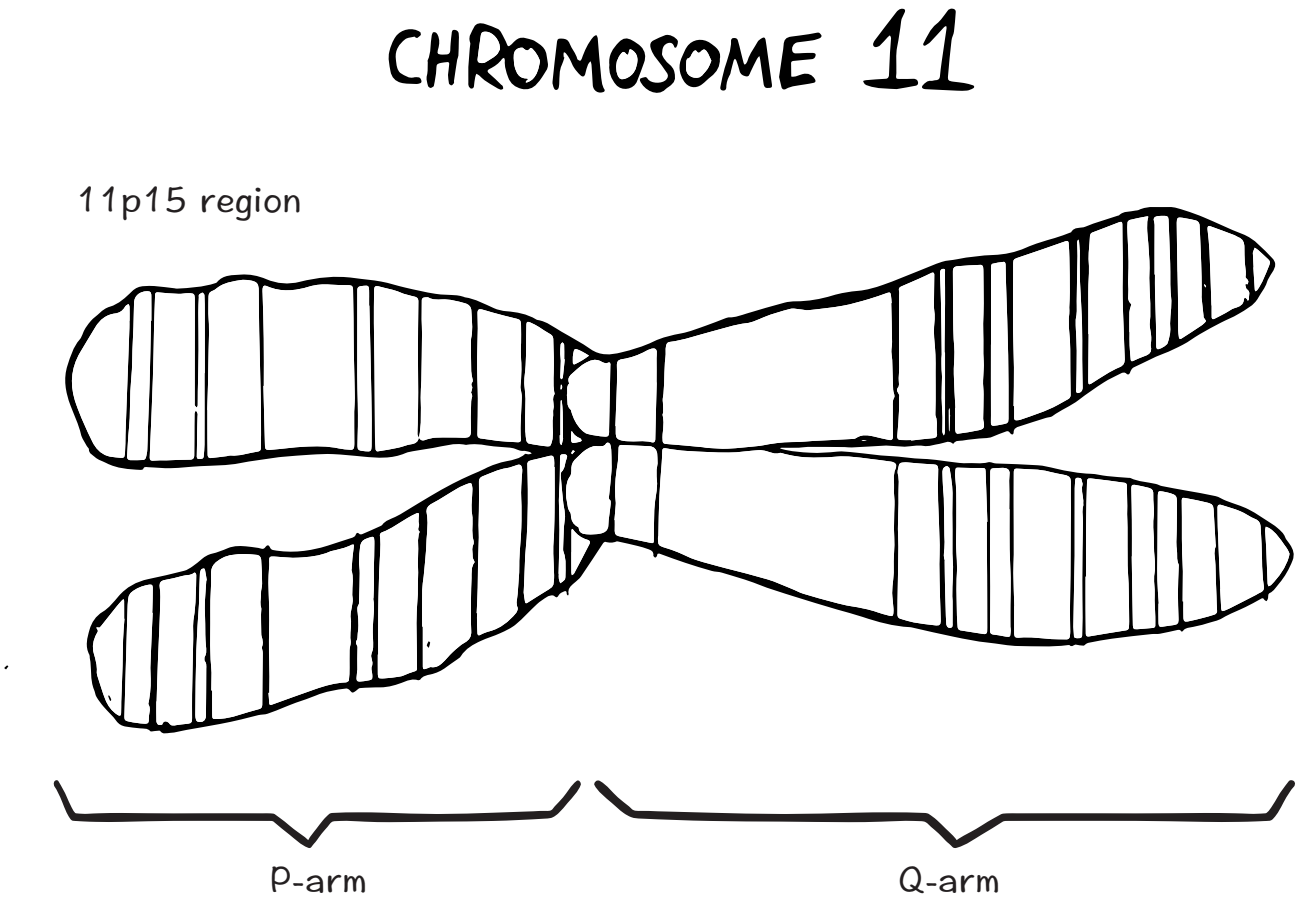
Genetics



Epigenetics

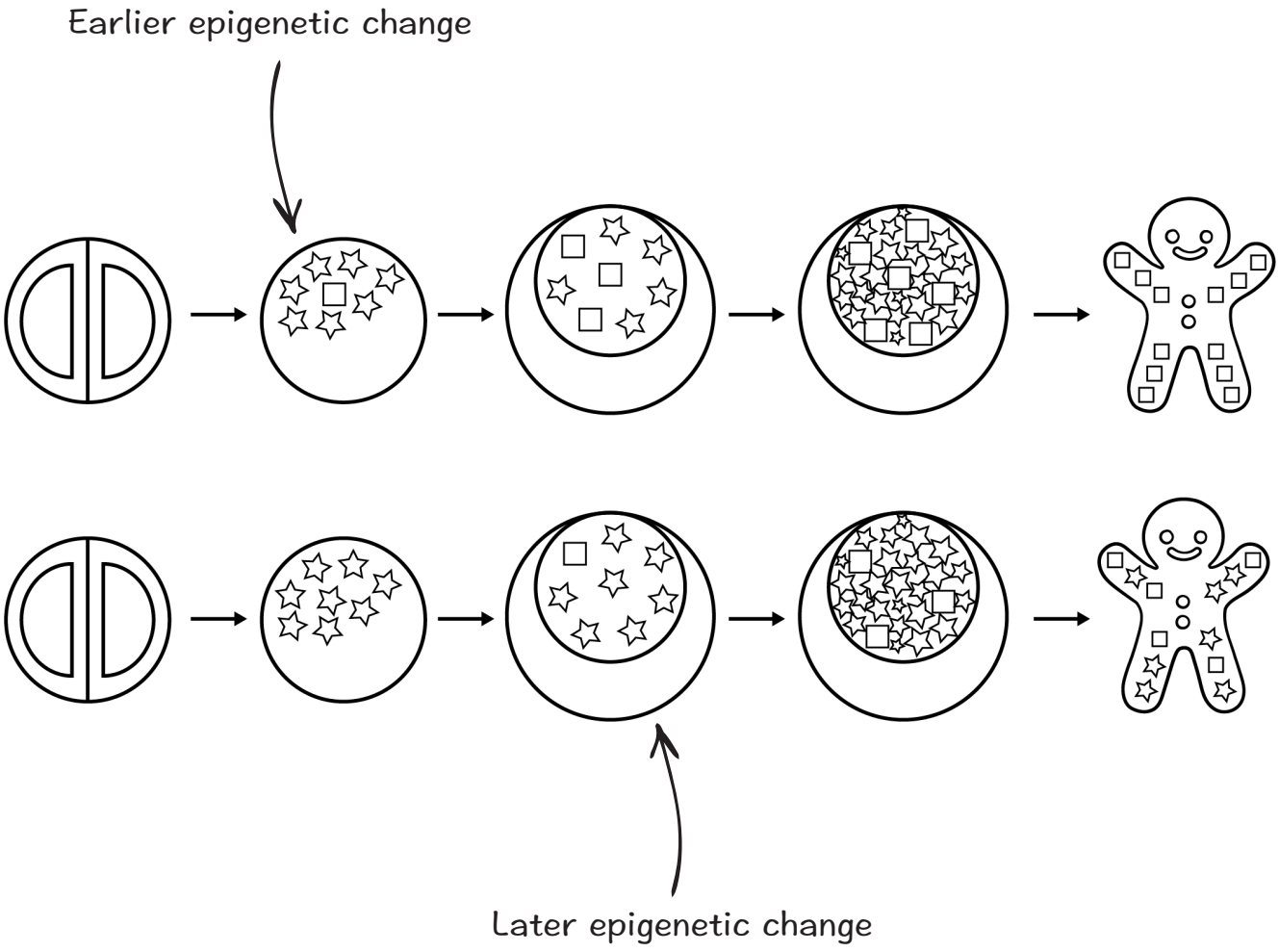


Beckwith-Wiedemann Syndrome is a disorder that is caused by a change in one or more of the genes at a region of chromosome 11, called 11p15. This specific chromosome region regulates growth, which is why Beckwith-Wiedemann Syndrome is referred to as an overgrowth disorder. Most times, this change happens in some cells, but not every cell.



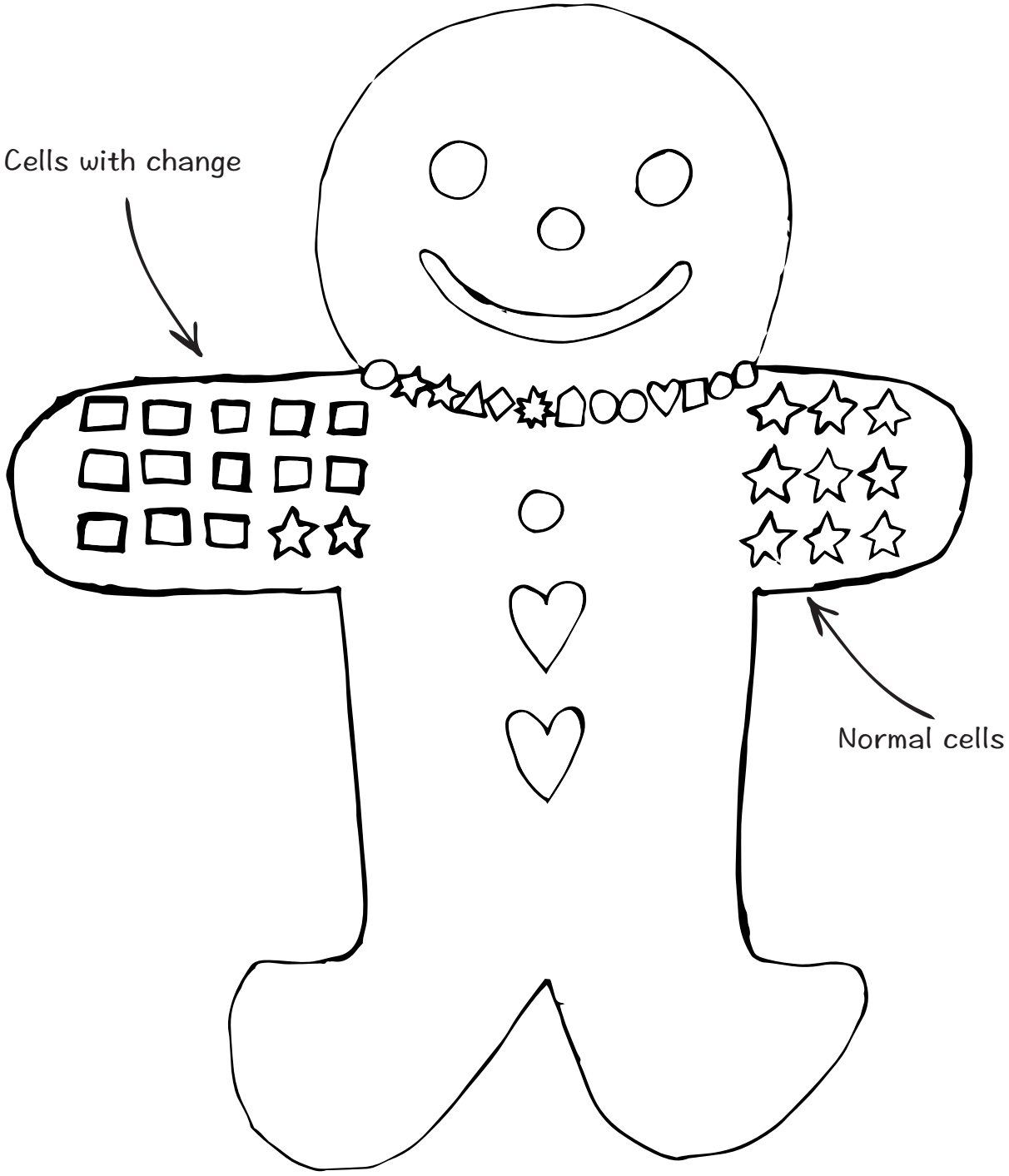
This is what chromosome 11 looks like under the microscope. The p-arm is the shorter arm and the q-arm is the longer arm.

The kinds of epigenetic changes that lead to syndromes like Beckwith-Wiedemann can happen at different times while an embryo develops into a baby. The timing of these changes can affect how many cells in a child's body contain the change. An earlier change means that more cells in the body will be affected while a later change means that fewer cells will be affected.

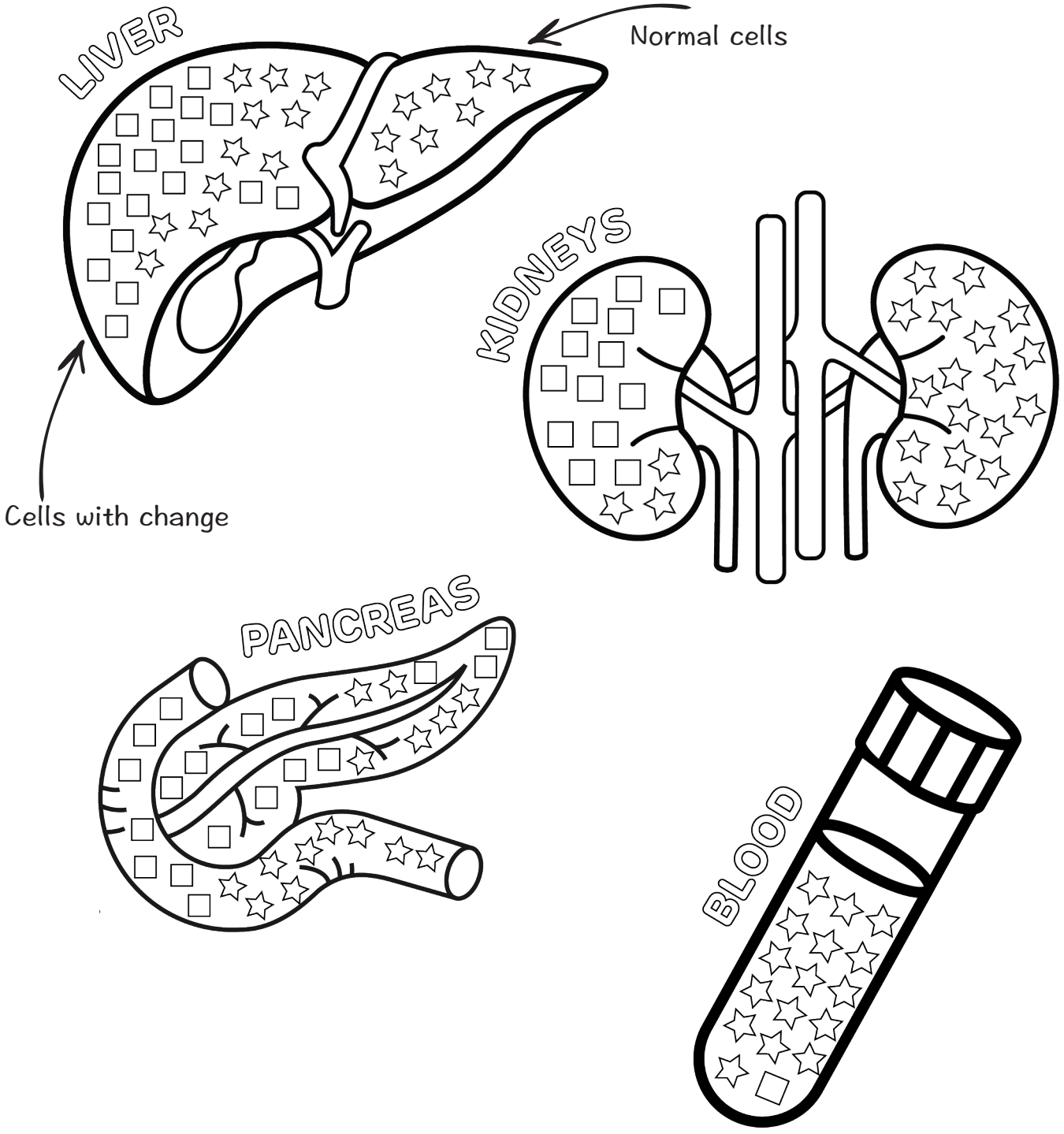


The Genetics and Epigenetics of BWS

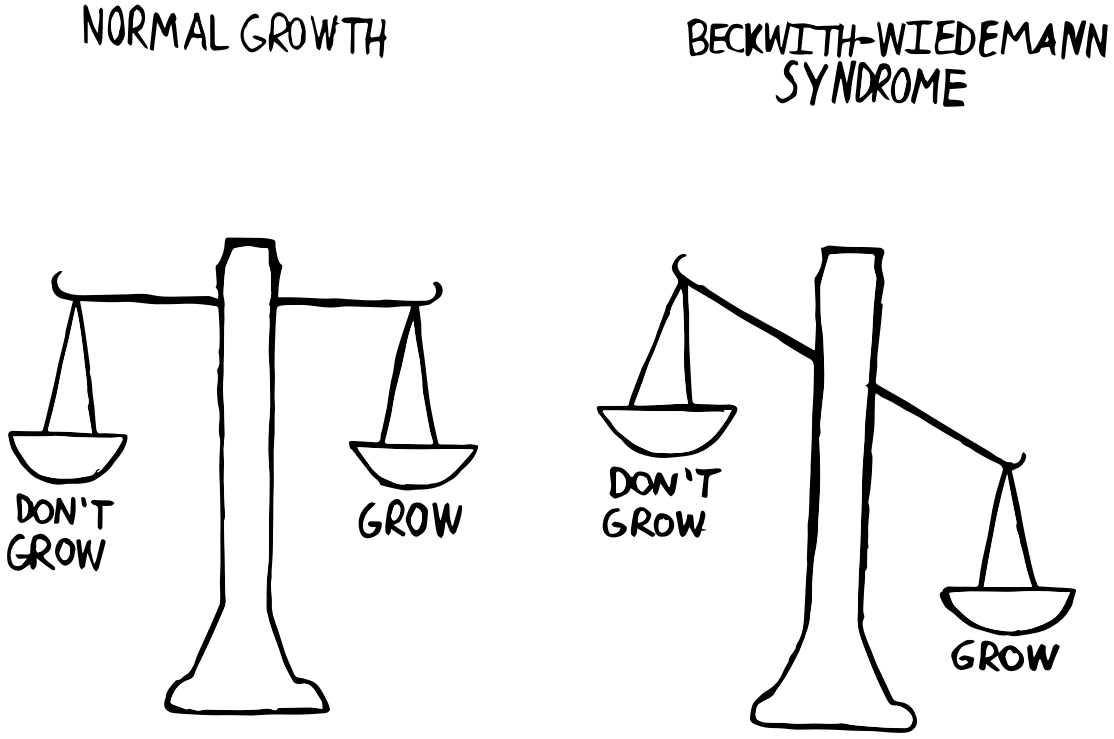
Beckwith-Wiedemann syndrome is often a "mosaic" condition. Mosaicism is when the genetic change on chromosome 11 occurs in some, but not every cell in the body. The features of Beckwith-Wiedemann Syndrome are a result of some cells of the body having a normal chromosome 11 while other cells have a change on chromosome 11.



Mosaicism can also affect the cells in a child's organs. In these cases, organs such as the liver, kidneys, or pancreas may be made up of a combination of cells -- some without a change on chromosome 11 and others with a change on chromosome 11. While this kind of mosaicism is common in Beckwith-Wiedemann Syndrome, it can sometimes make the syndrome difficult to detect depending on the cells tested.

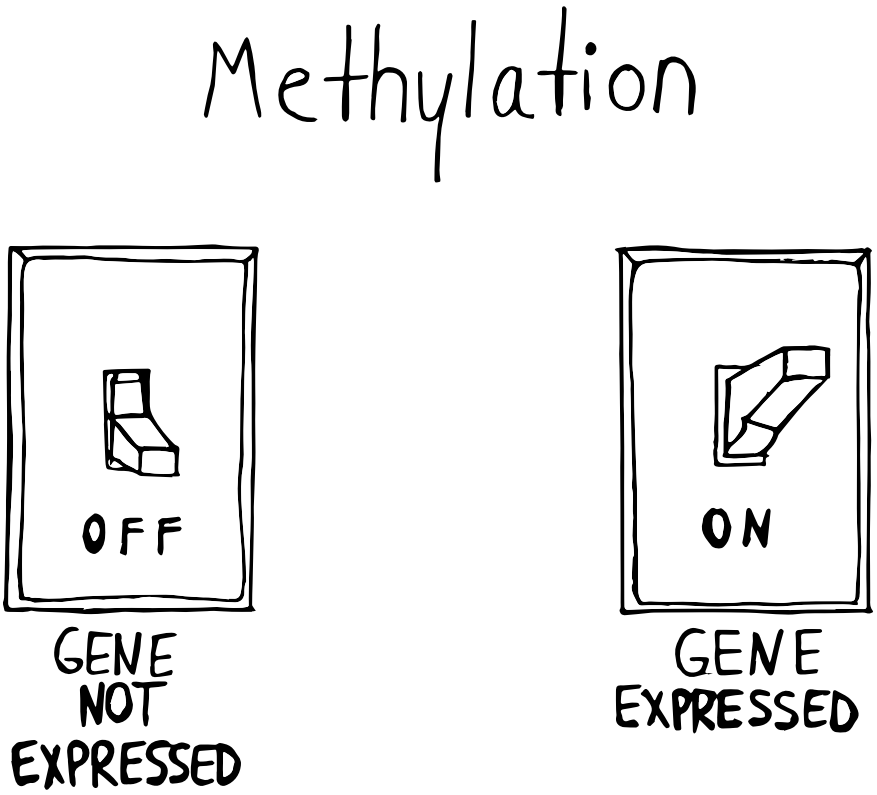


The growth of a baby with Beckwith-Wiedemann Syndrome is different from the usual growth of a baby. The diagram of the scale on the left shows how a typical child has a balance between genes that cause growth and genes that limit growth. The diagram of the scale on the right shows how a child who has Beckwith-Wiedemann Syndrome has an imbalance between genes that cause growth and genes that limit growth. This imbalance results in the child having too many genes that cause growth and not enough that limit growth.



People have two copies of chromosome 11, one from the egg and one from the sperm. Each copy of the chromosome that the child receives is different. One copy may express certain genes that control growth that the other does not.

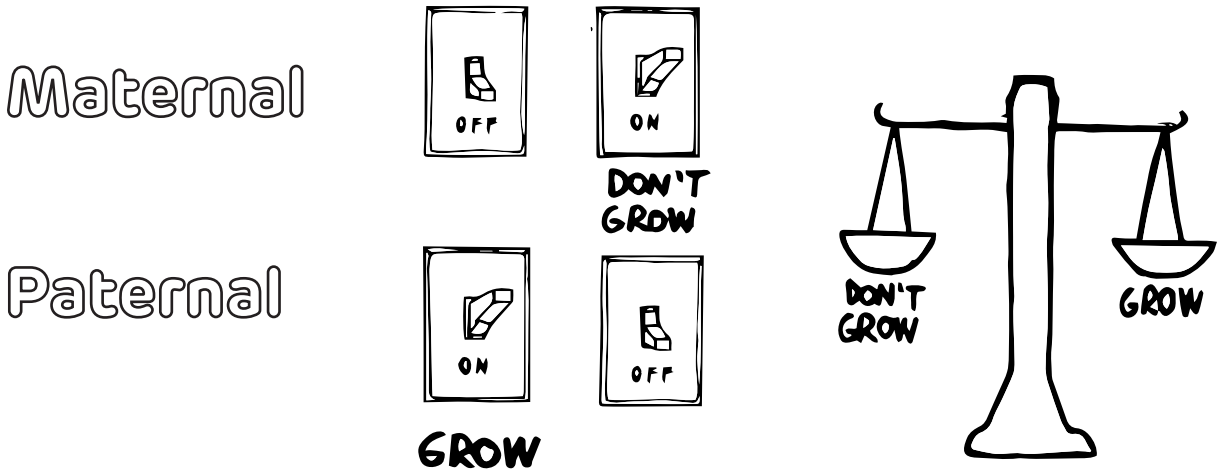
This process is called imprinting and is caused by something called methylation. Methylation is a mark on a chromosome that can be thought of as a light switch. This marks the DNA to turn certain genes on or off. When the "light switch" for methylation is on, that means that the signal is "on." When the "light switch" for methylation is off, that means that the signal is "off." Having a balance between the "switches" that are on and off is what creates a baby that grows at a normal rate.



Children with Beckwith-Wiedemann Syndrome have changes on chromosome 11 where the "light switches" of methylation are turned on or off in a different way than a child without BWS. There are several different changes on chromosome 11 that are known to cause Beckwith-Wiedemann Syndrome.

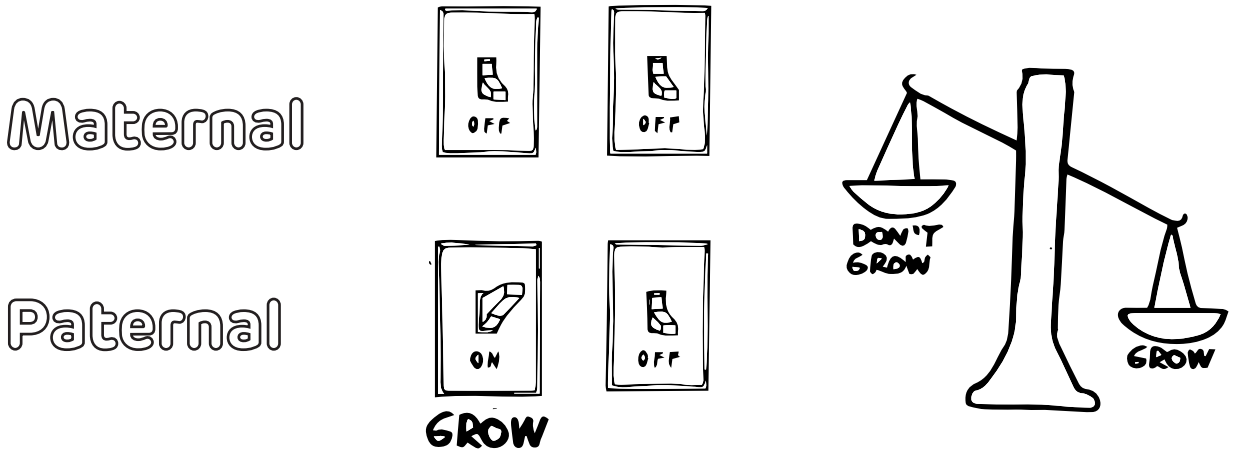
The Genetics and Epigenetics of BWS

Normally, a child has a balance of genes that cause growth and genes that limit growth. The DNA is marked so that the maternal genes make the "don't grow" signal and the paternal genes make the "grow" signal.

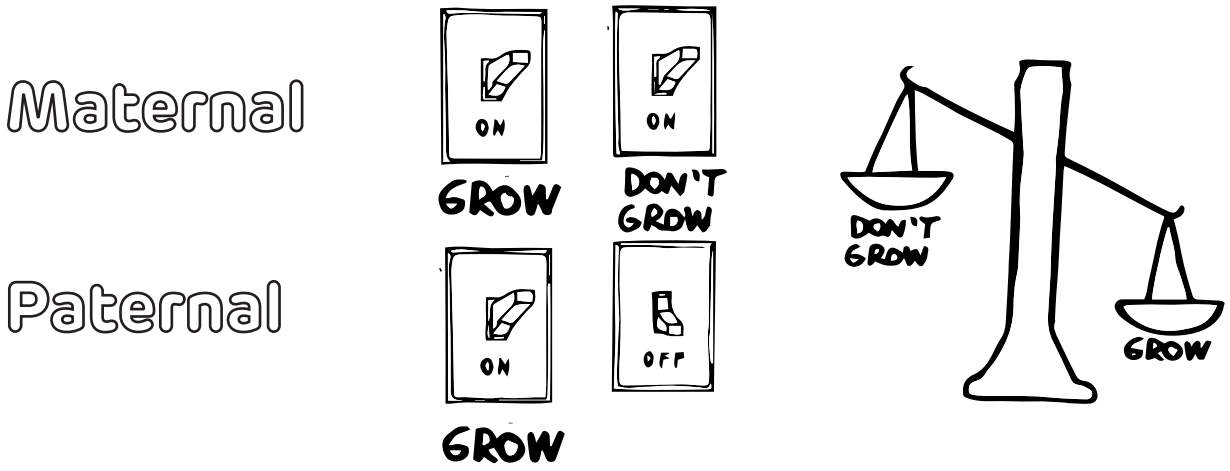


Some types of changes on chromosome 11 that occur with Beckwith-Wiedemann Syndrome may include:

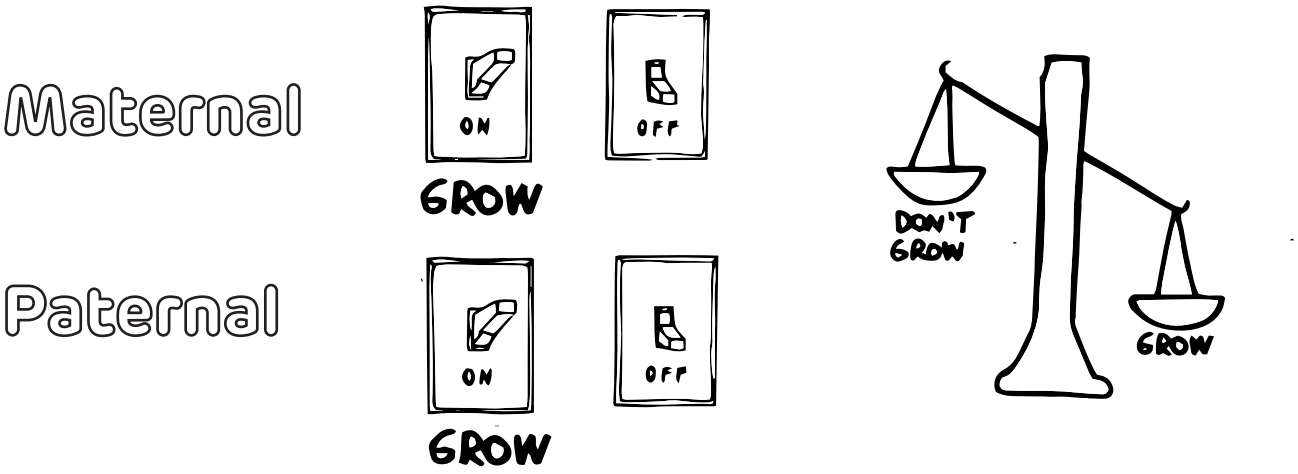
IC2, LIT1, KvDMR, loss of methylation



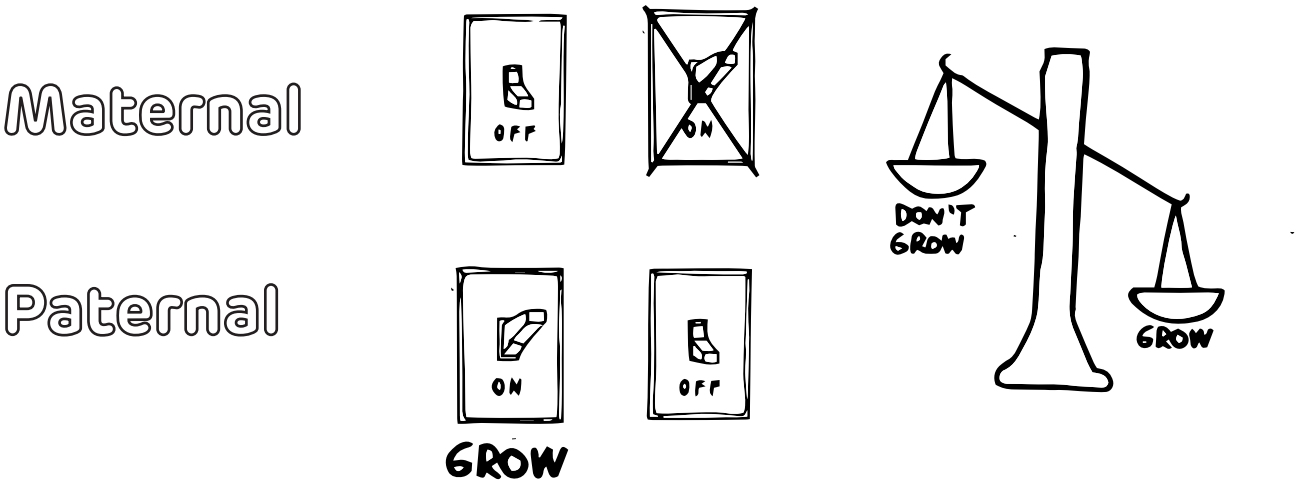
IC1, H19DMR, gain of methylation



Paternal uniparental isodisomy (pUPD11)

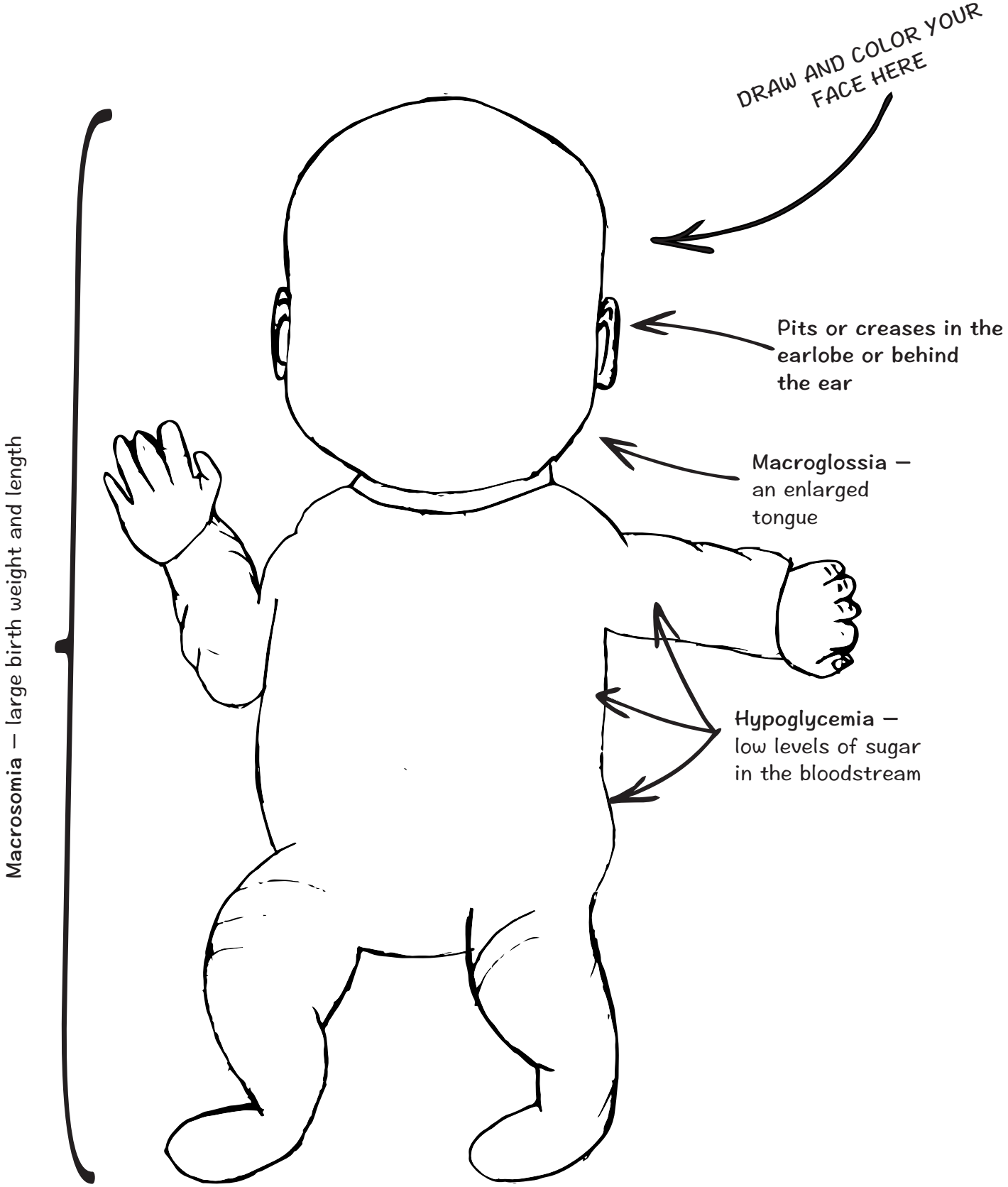


CDKN1C mutations

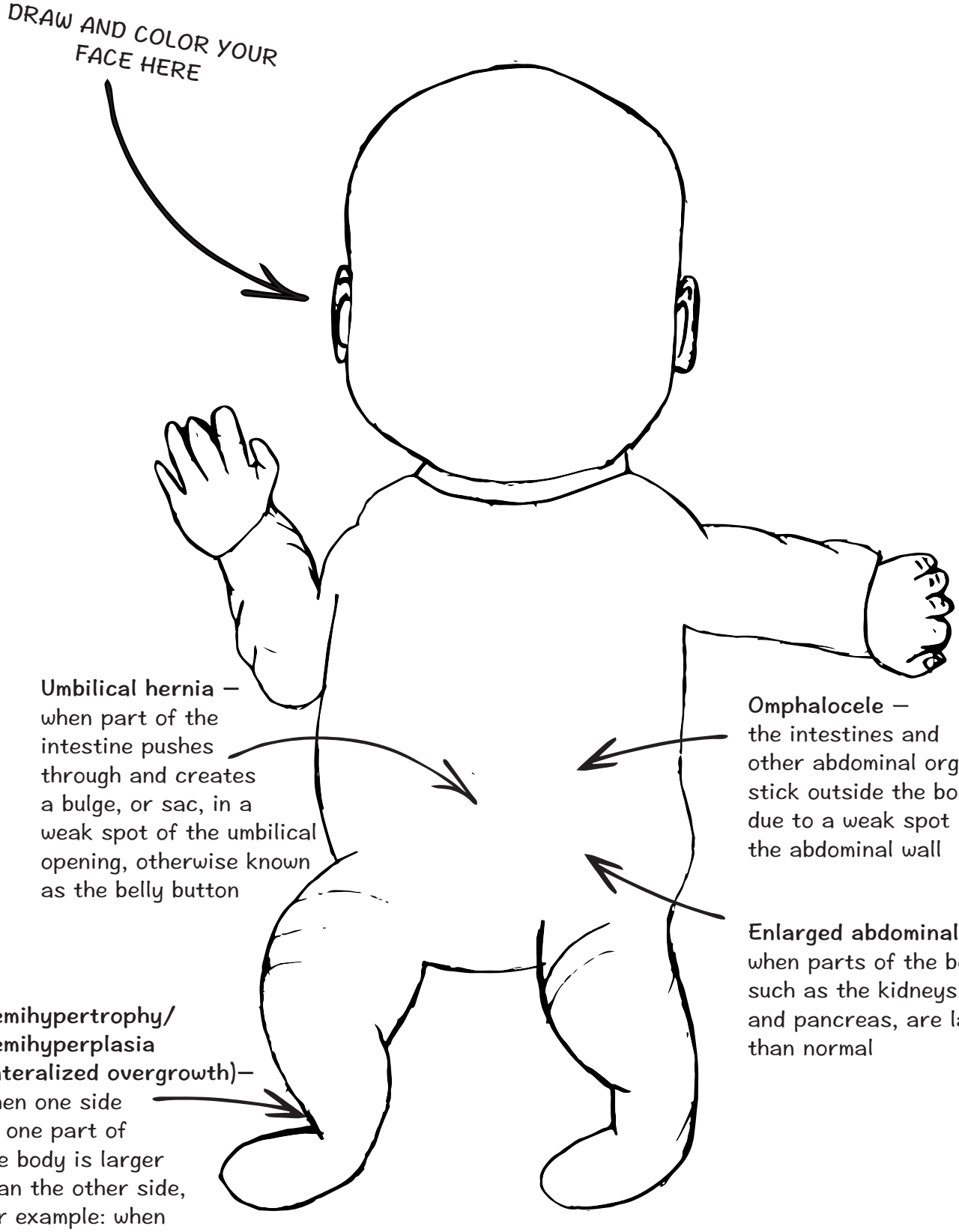


There are also rarer causes such as duplications, deletions, or chromosomal rearrangements that lead to an increase in "grow" signal and/or a decrease in "don't grow" signal.

Some physical differences that may be present in children with Beckwith-Wiedemann Syndrome include:

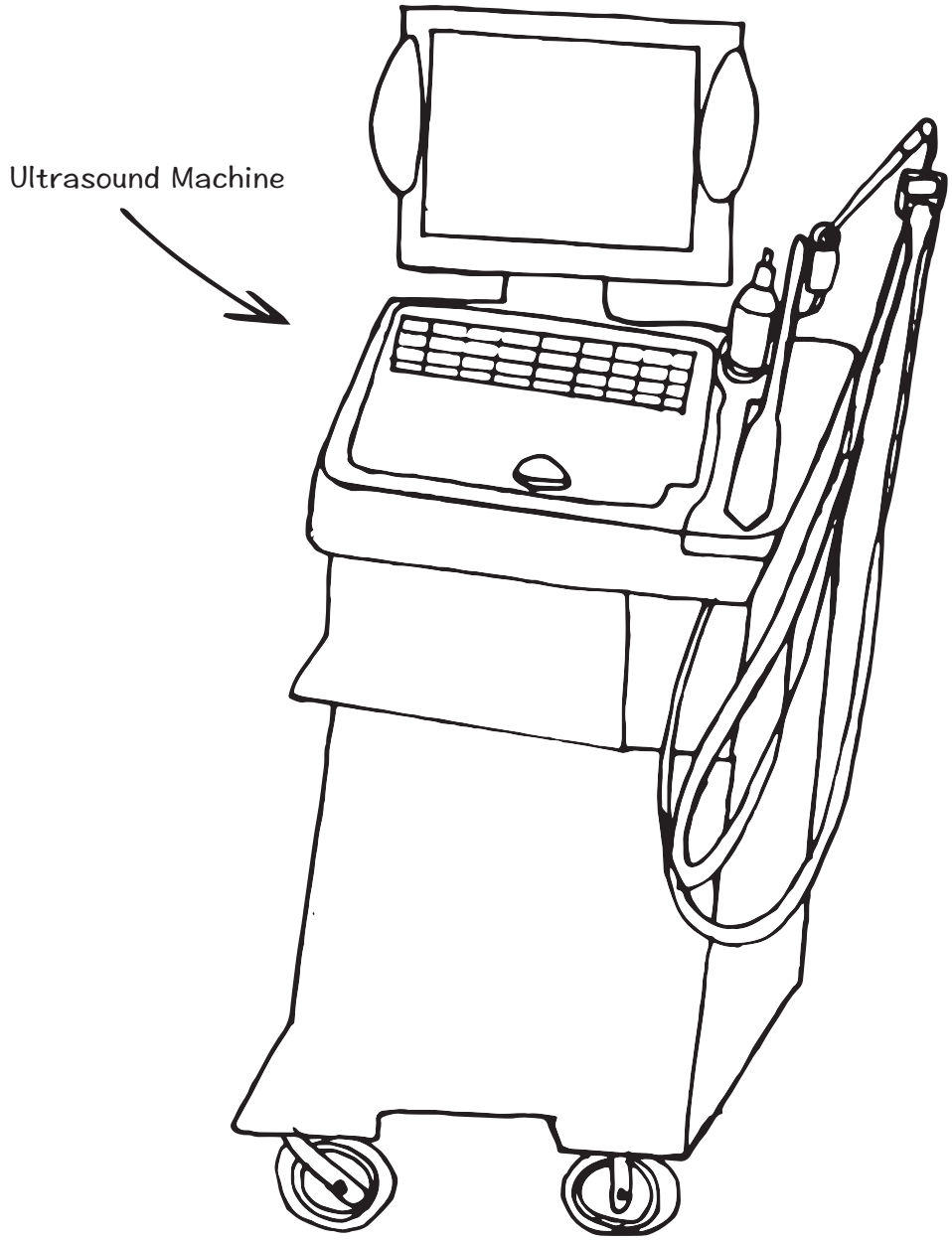


Some physical differences that may be present in children with Beckwith-Wiedemann Syndrome include:

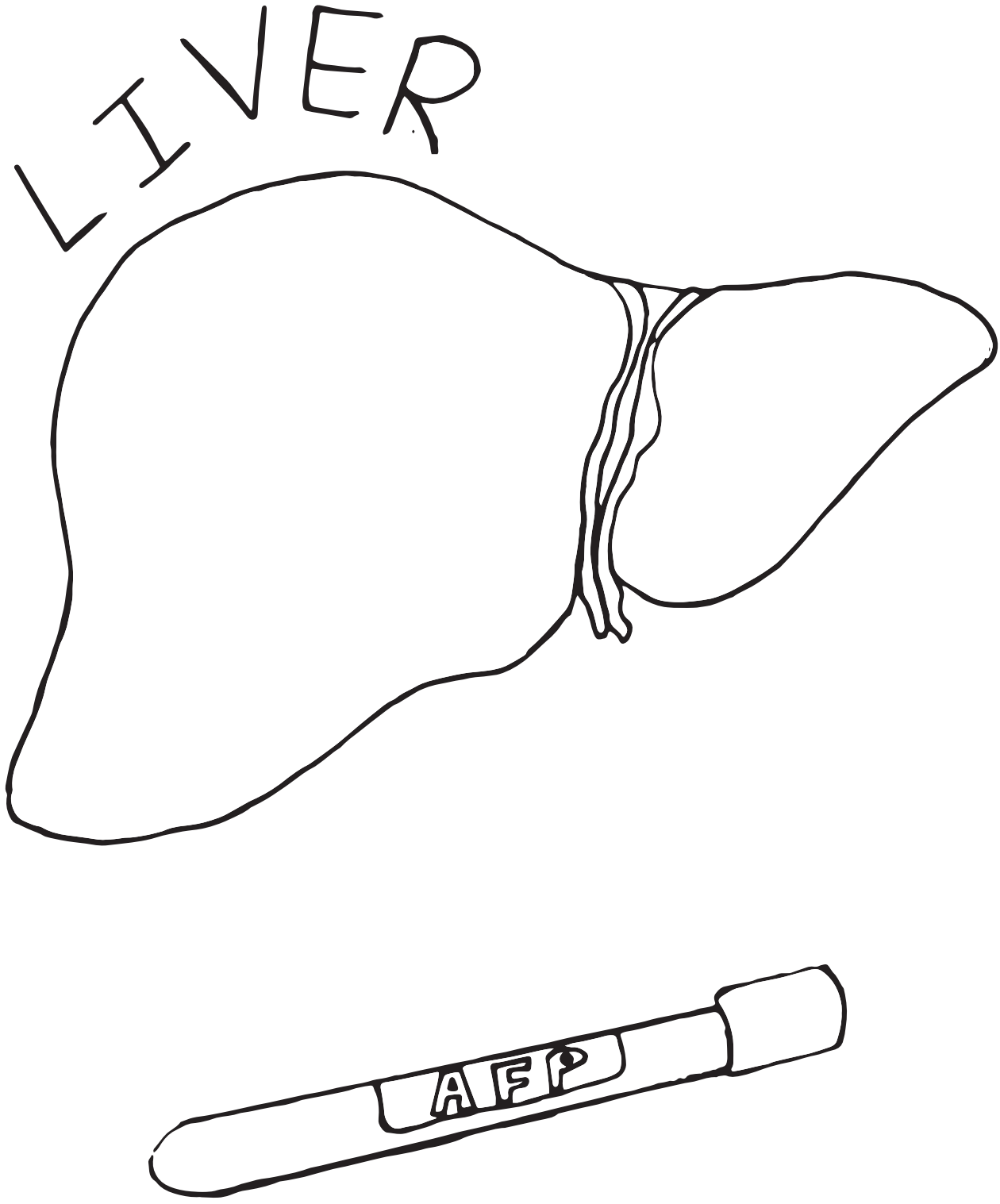


Given that children with Beckwith-Wiedemann Syndrome have an increased risk of developing tumors during childhood, it is recommended that they have regular screenings.

Two types of tumor screenings that are recommended for children with Beckwith-Wiedemann Syndrome are the abdominal ultrasound and having a blood test to measure their alpha-fetoprotein (AFP) concentration.



The abdominal ultrasound is an imaging test that uses sound waves to display views of internal organs.



Alpha-fetoprotein (AFP) is a protein that is released by the live. AFP is released at higher levels by hepatoblastoma (a liver tumor) cells, and AFP levels are normally high when the child is first born and trend downwards towards normal. It is important to follow the trend over time. This test should be ordered and reviewed by pediatricians, geneticists or pediatric oncologists who are familiar with Beckwith-Wiedemann Syndrome.

Some children with Beckwith-Wiedemann Syndrome may need to see other medical specialists.

These may include:

Endocrinologists – Doctors who treat children that have hypoglycemia (low blood sugar)

Geneticists – Doctors who make the clinical diagnosis, order testing and coordinate care

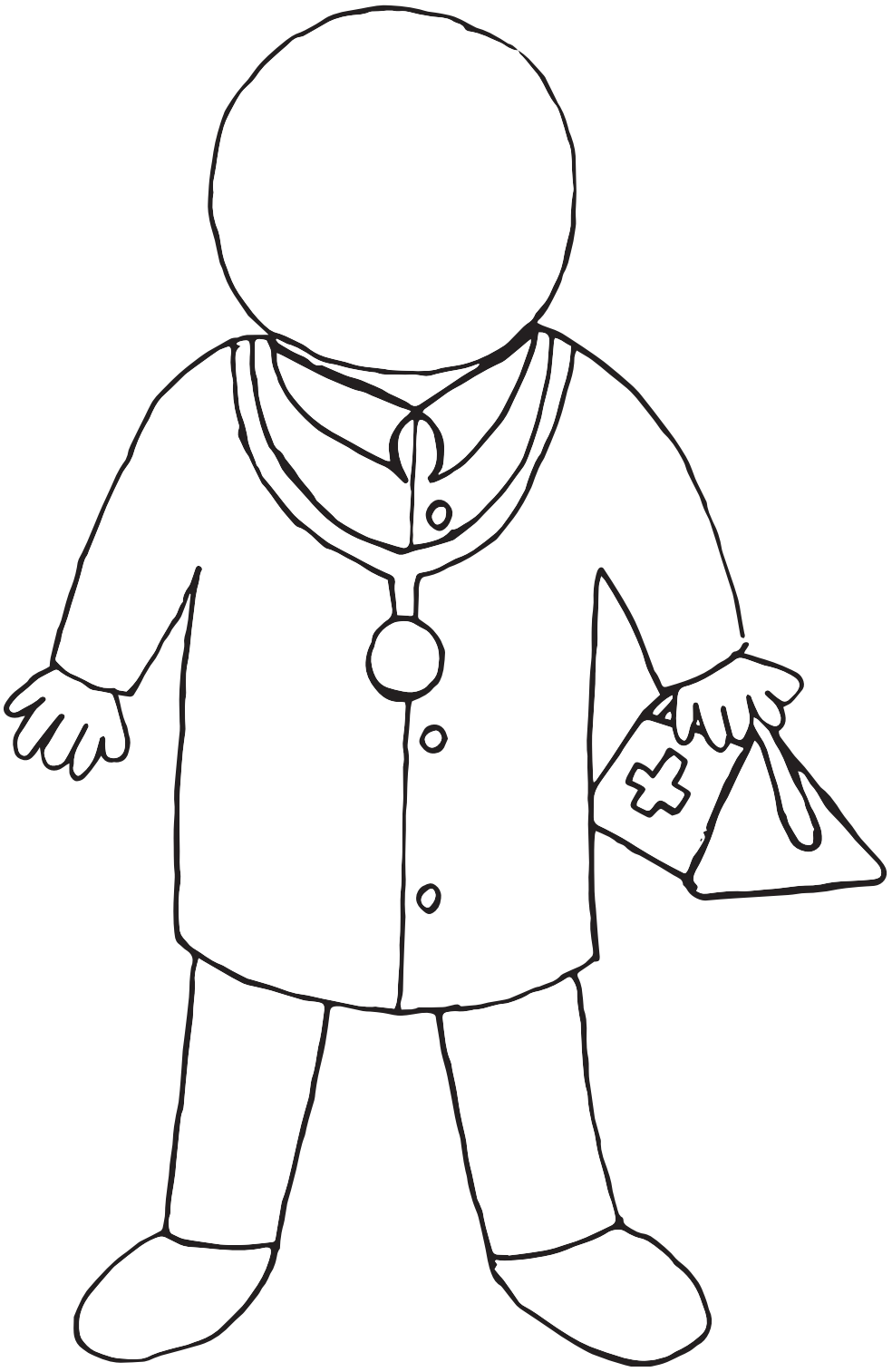
Oncologists – Doctors who manage the diagnosis and treatment of tumors

Orthopedists – Doctors who manage bone differences in children who have a difference in the size of their legs

Pediatricians – Doctors who treat babies and children

Plastic Surgeons – Doctors who treat children who have an enlarged tongue (macroglossia)

Pulmonologists – Doctors who manage breathing differences



Abdominal ultrasound / *ab-dom-uh-nl uhl-truh-sound* / — an imaging test that uses sound waves to display views of internal organs

Alpha-fetoprotein (AFP) / *al-fuh fē'tə-prō'tēn* / — a protein that is released by the liver

Cells / *sels* / — the smallest machines in your body and the basic unit of all living things

Chromosomes / *kroh-muh-sohms* / — the parts of cells that contain genes

11p15 on chromosome 11 / *ə'levən - p - one - five/* — this specific chromosome region regulates growth

DNA / *dee-ok-si-rahy-boh-noo-klee-ik as-id* / — or deoxyribonucleic acid, is a substance that carries genes from biological parents to their children

Endocrinologists / *en-doh-kruh-nol-uh-jists* / — Doctors who treat children that have hypoglycemia (low blood sugar)

Enlarged abdominal organs / *en-lahrjd ab-dom-uh-nl awr-guh ns* / — when parts of the body, such as the kidneys, liver, and pancreas, are larger than normal

Epigenetics / *ep-i-juh-net-iks* / — the study of how the function of a person's genes change, where some genes may or may not express certain traits; changes occur after conception as the embryo turns into a baby

Genes / *jeens* / — pieces of DNA that are passed down from biological parents to their children and represent traits or characteristics, such as hair color or growth

Geneticists / *juh-net-uh-sists* / — Doctors who make the clinical diagnosis, order testing, and coordinate care

Genetics / *juh-net-iks* / — the study of the process when biological mothers and fathers pass down genes to their children

Hemihypertrophy/Hemihyperplasia / *hĕm'ĭ-hī-pûr'trə-fē, hĕm'ĭ-hī-pûr pley-zhee-uh* / — when one side or one part of the body is larger than the other side, for example: when one leg is bigger than the other

Hypoglycemia / *hahy-poh-glahy-see-mee- uh* / — low levels of sugar in the bloodstream

Macroglossia / *māk'rō-glô'sē-ə* / — an enlarged tongue

Macrosomia / *māk'rə-sō'mē-ə* / — large birth weight and length

Methylation / *meth-uh-ley-shuh n* / — when DNA is marked to turn genes "on" or "off"

Mosaicism / *moh-zey-uh-siz-uh m* / — when some cells of the body have normal chromosome 11 and other cells of the body have a change on chromosome 11

Omphalocele / *m-fāl'ə-sēl* / — the intestines and other abdominal organs stick outside the body due to a weak spot in the abdominal wall

Oncologists / *ong-kol-uh-jists* / — Doctors who manage the diagnosis and treatment of tumors

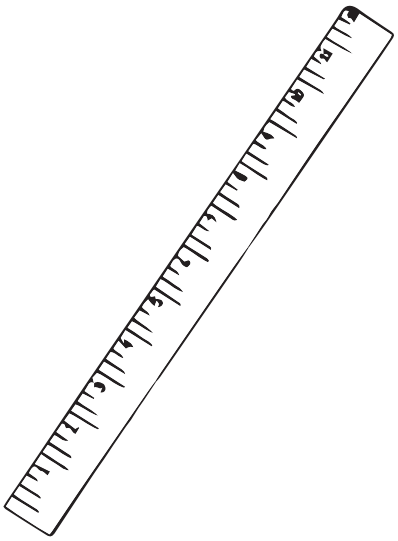
Orthopedists / *awr-thuh-pee-dists* / — Doctors who manage bone differences in children who have a difference in the size of their legs

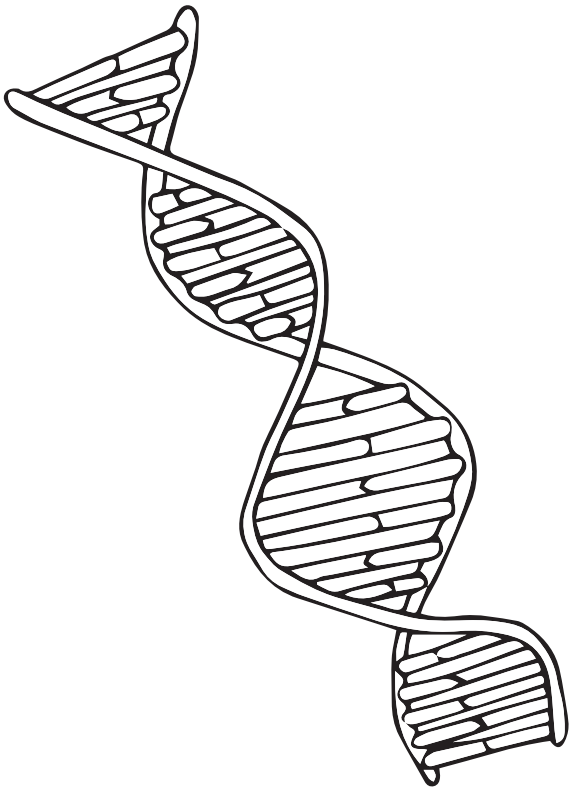
Pediatricians / *pēdēə'triSHən* / — Doctors who treat babies and children

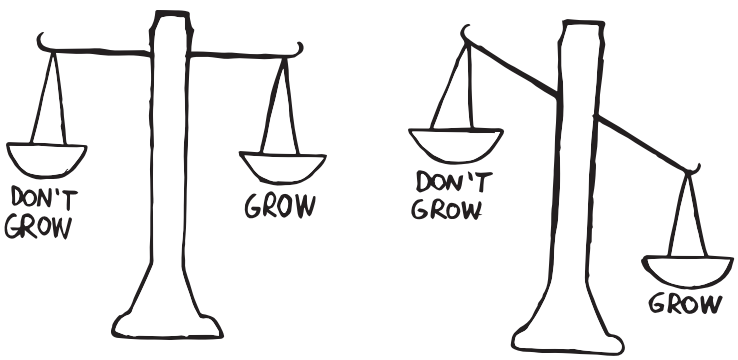
Plastic Surgeons / *plas-tik sur-juh ns* / — Doctors who treat children who have an enlarged tongue (macroglossia)

Pulmonologists / *pu̇l-mə-'nä-lə-jəsts* / — Doctors who manage breathing differences

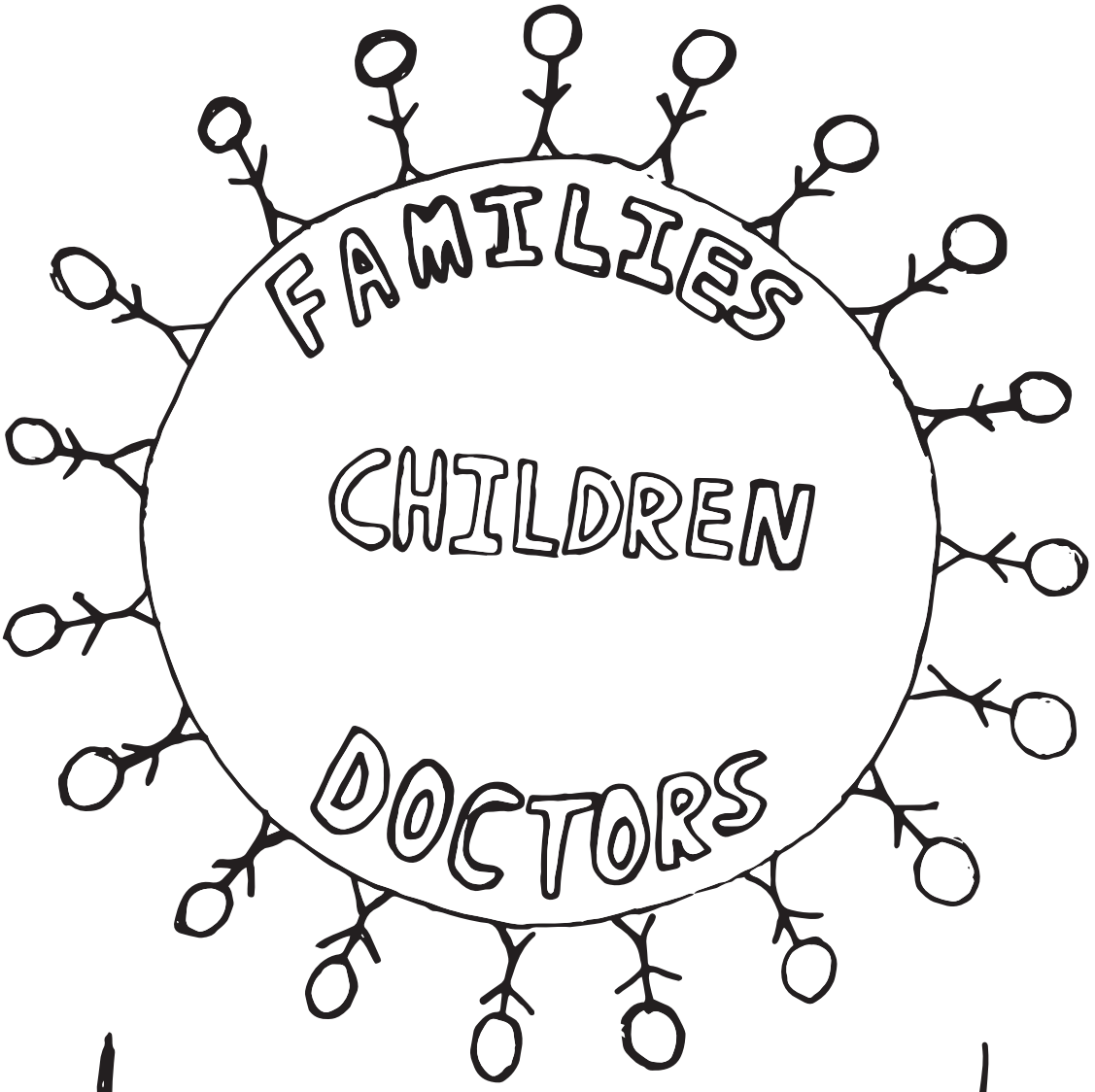
Umbilical hernia / *əm-'bi-li-kəl hər-nē-ə* / — when part of the intestine pushes through and creates a bulge, or sac, in a weak spot of the umbilical opening, otherwise known as the belly button







Let's work together



to spread BWS Awareness

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