GENETICS OF

Autism Spectrum Disorders

COUNSELLING FLIPBOOK

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INTRODUCTION

This counselling flipbook was developed by Ny Hoang (certified genetic counsellor) and the ***Genetics of Autism Spectrum Disorder*** research team led by Dr. Stephen Scherer at The Hospital for Sick Children (SickKids).

This counselling tool is meant to be printed on double-sided paper. The front pages provide visual aids to help explain concepts related to the genetics of autism spectrum disorder (ASD). On the back pages, we have provided additional information to facilitate an interactive discussion with patients, participants and families.

We hope you find this tool useful and welcome your feedback. To leave comments or questions about this counselling flipbook, contact the ASD research team at:

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416-813-8748
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CAUSES OF ASD

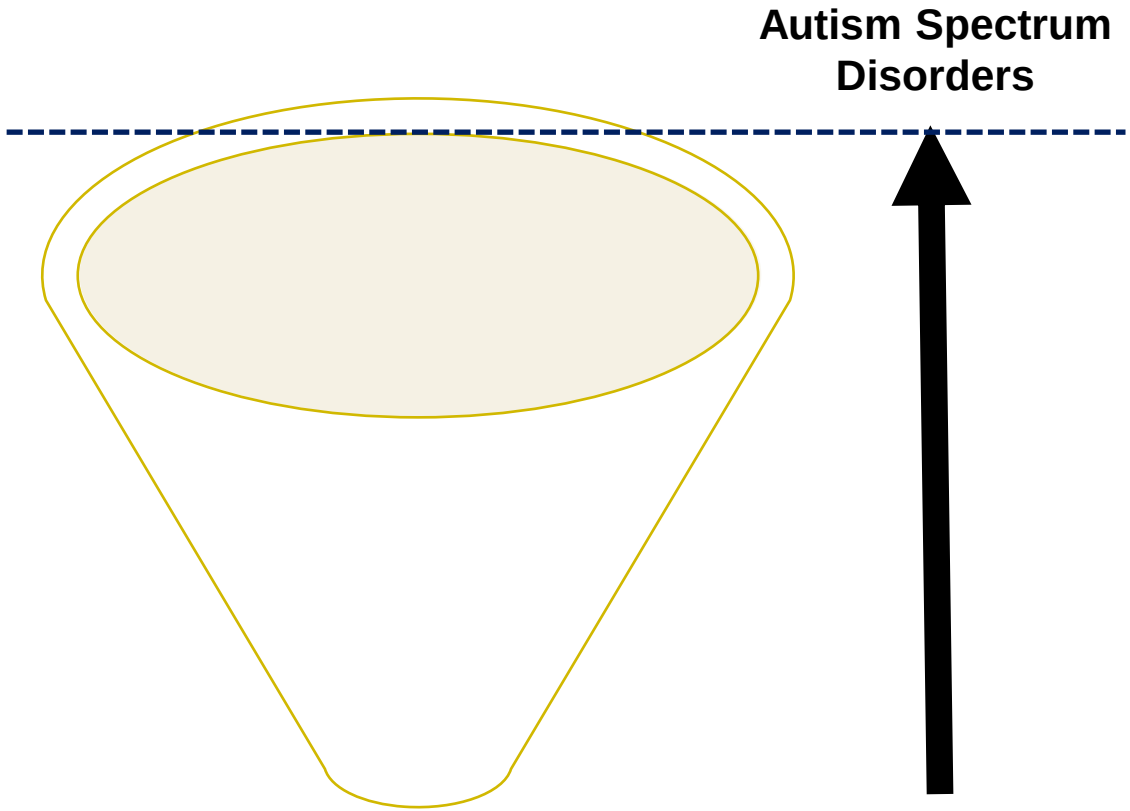
ASD is a multifactorial condition where genetic factors and environmental factors contribute to the risk of developing ASD.

How much a factor contributes to the risk varies:

- **Strong genetic factor:** some genetic factors confer a very high risk of developing ASD. Examples include genetic factors that are associated with known syndromes where ASD is a feature (e.g. Fragile X, Rett, tuberous sclerosis).
- **Weak genetic factor:** most ASD associated genetic factors confer some risk for developing ASD, but are not sufficient to cause ASD on their own.
- **Environmental factors** have varying degrees of influence, but are generally thought to contribute less to ASD risk compared to genetic factors.

- ASD is not usually due to a single genetic or environmental cause, but rather due to the combination of both types of risk factors
- Risk factors have different strengths of impact represented by the size of the risk balls

Multifactorial condition



Cup represents an individual's ASD risk

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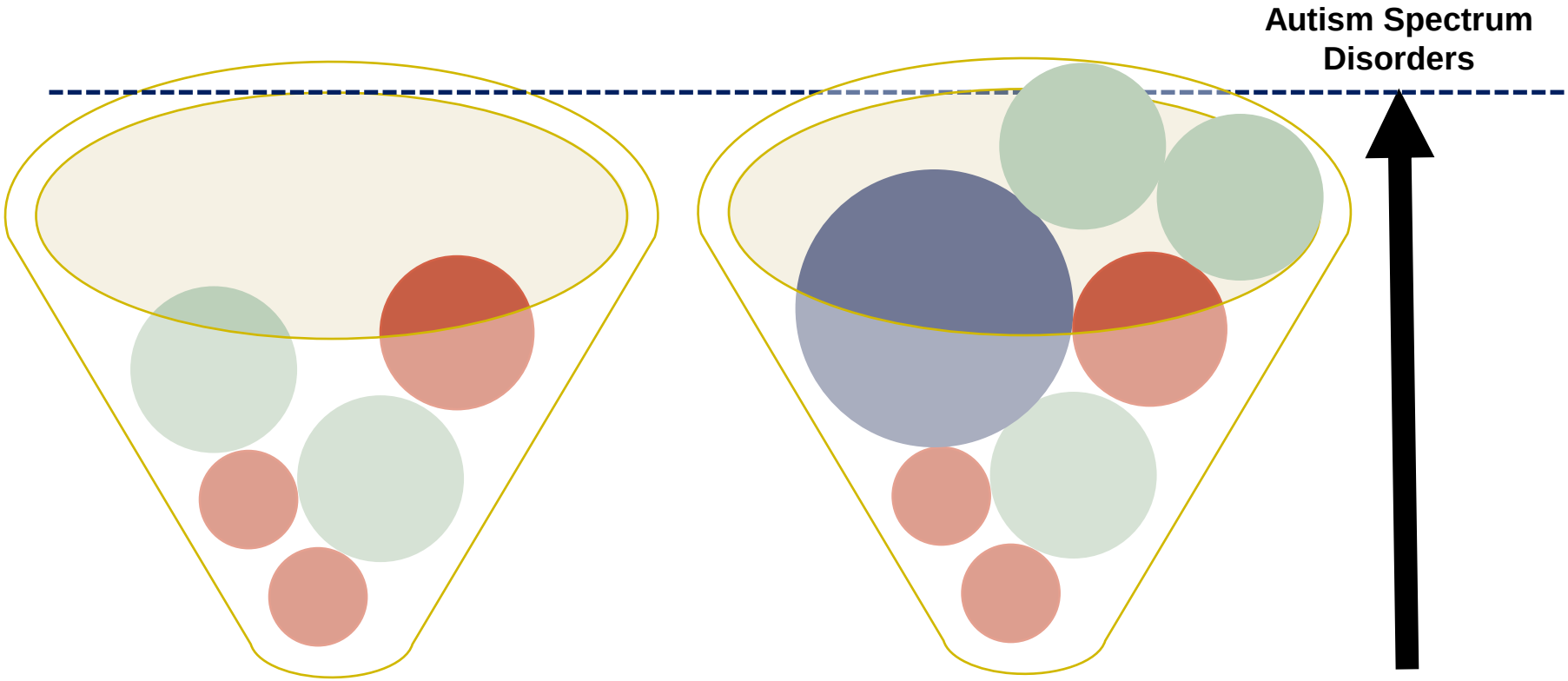
ASD THRESHOLD

Every individual has an ASD risk cup that represents their risk for developing ASD. An individual would have ASD only if there are enough risk factors to fill the cup to reach a critical threshold.

- If the ASD risk cup has some risk factors but not enough to reach the threshold, the individual would not have ASD.
- If the ASD risk cup is filled with enough risk factors to reach the threshold, the individual would have ASD.

Once the threshold is reached, an individual who develops ASD is not likely to lose their diagnosis. Even if environmental risk factors can be removed, impact during the critical window of development has already occurred.

- ❖ Everyone has some risk factors for ASD
- ❖ Once threshold is reached risk factors cannot be removed



Threshold not reached
No ASD

Threshold reached
ASD

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UNIQUE RISK PROFILE

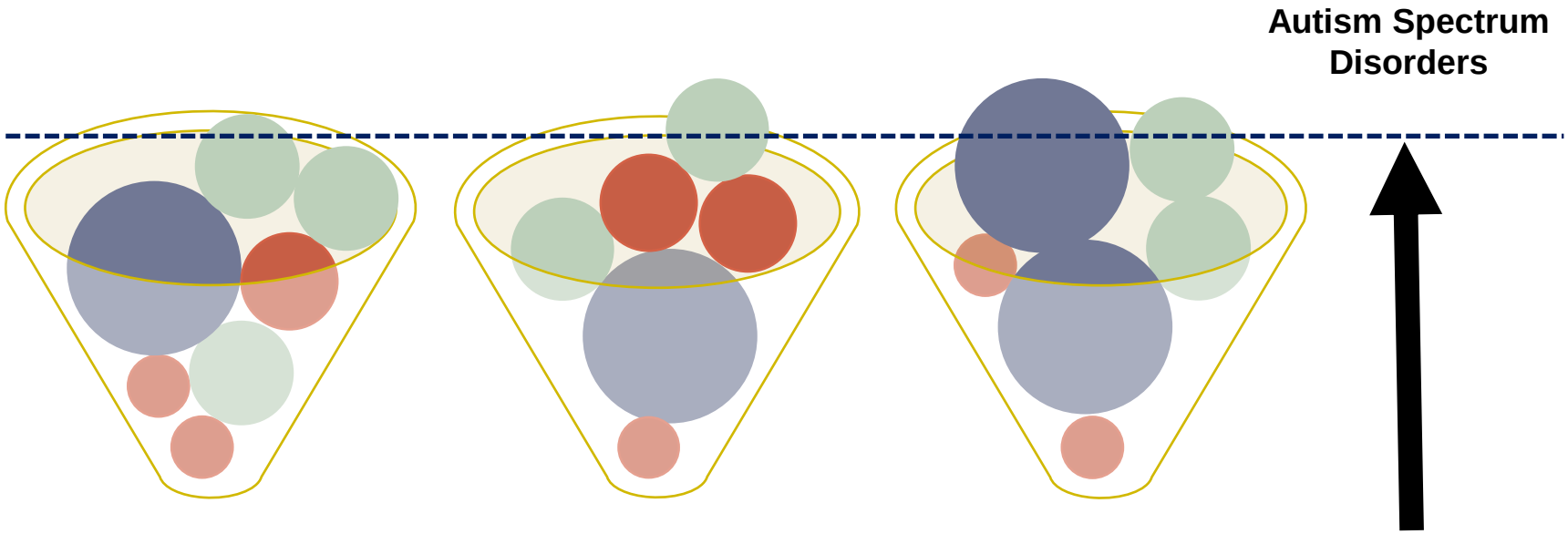
Individuals with ASD have a unique combination of risk factors.

- No two risk cups have the same combination of genetic and environmental risk factors.
- No two individuals with ASD present in the same way.

Even members of the same family with ASD have different risk profiles and clinical presentations.

❖ ASD is genetically and clinically variable

Each individual with ASD has a unique combination of risk factors



Threshold reached **ASD**

Threshold reached **ASD**

Threshold reached **ASD**

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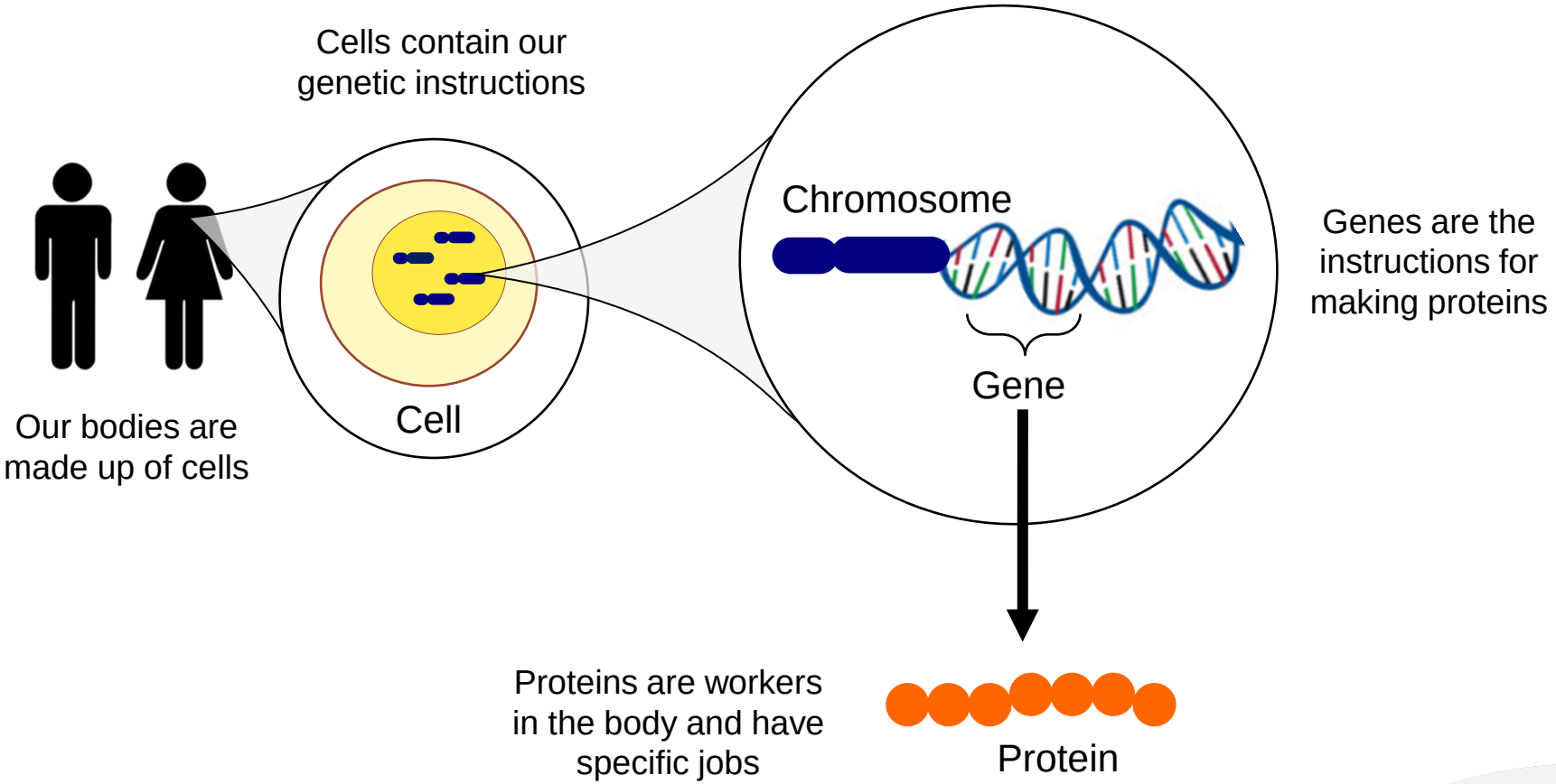
REVIEW OF GENETICS

To understand what genetic risk factors are, a review of genetic concepts is important.

- Our bodies are made up of trillions of cells: skin cells, blood cells, brain cells, heart cells, etc.
- In nearly all the cells of our body are the same set of instructions that tell it how to grow and function properly
- These instructions are packaged into structures called chromosomes
- If you unwind the chromosomes, there are sections of our genetic information called genes
- Genes are important because they code for proteins
- Proteins are workers in the body that have specific jobs and are crucial for normal development and function

❖ Genes are the instructions that tell our bodies how to grow and function properly



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GENETIC VARIANTS

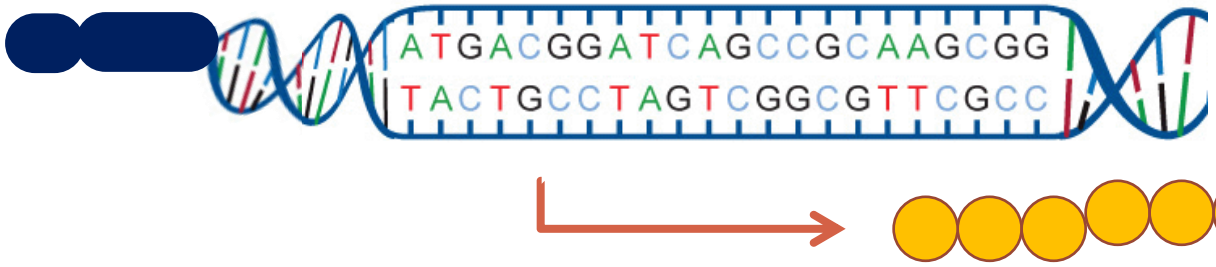
If genetic information is changed or disrupted, it could have a downstream impact on the protein. Changes or disruptions to the genetic information are called “variants”. Variants may or may not impact the production of a protein.

- Some variants can cause the protein to be made improperly, which could affect its ability to do its job in the body.
- Some variants can cause the protein to not be made at all, so it cannot do its job in the body.
- Some variants do not change how the protein is made, so it can still do its job in the body.

Genetic variants in certain genes associated with ASD are the genetic risk factors for ASD. These genes typically code for proteins that play a role in the development and/or function of the brain.

- Disruptions in certain genes associated with brain development and function contribute to ASD risk
- Hundreds of genes have been implicated in ASD

Gene



Protein

Genetic variant

Changes or disruptions to the genetic instructions

Protein is not made properly or not made at all

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VARIANT CLASSIFICATION

It is important to note that we all have genetic variants. Some variants impact health and development, while others do not. Variants are typically classified as:

- **Pathogenic or significant variant:** there is enough data to show the variant causes a health and/or developmental condition.
- **Variant of unknown significant**: there is not enough data to determine whether or not the variant contributes to a condition, so its significance is unclear. This classification may be further subdivided to highlight the amount of evidence available.
- **Benign or normal variant:** there is enough data to show the variant does not impact growth and development and is a normal variation found in the general population.

- We all have genetic variants
- Classification of variants may change over time as new information becomes available

PATHOGENIC or SIGNIFICANT VARIANT

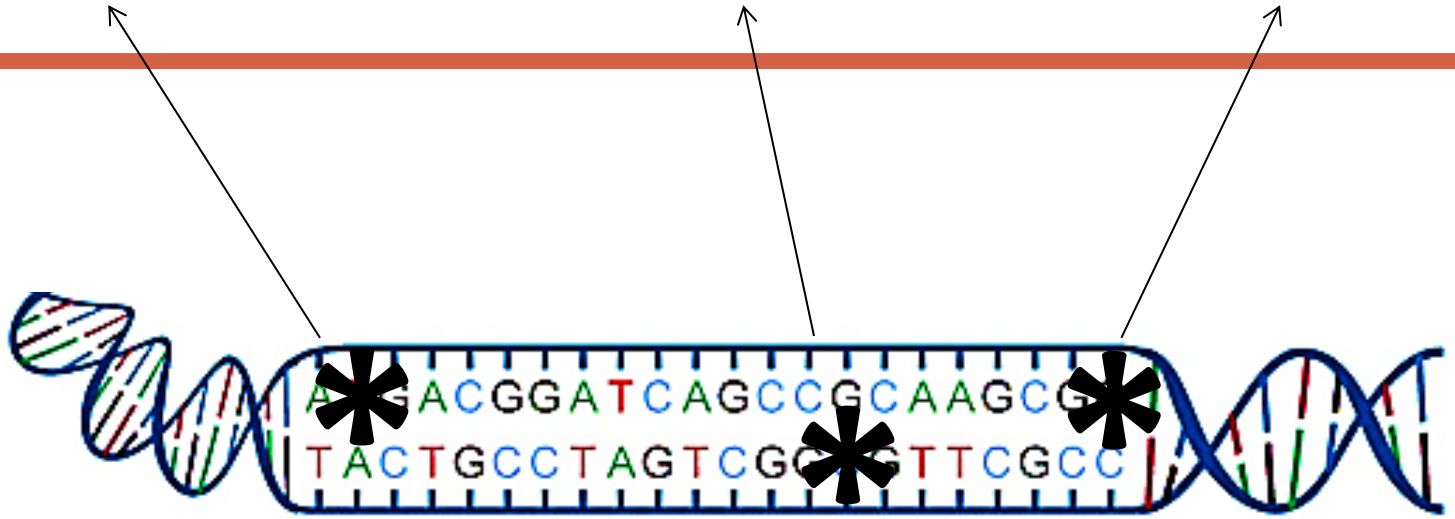
cause health or developmental conditions

VARIANT OF UNKNOWN SIGNIFICANT

not enough information to determine if it contributes

BENIGN or NORMAL VARIANT

does not impact health or development



We all have genetic variants

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INHERITED & NEW GENETIC VARIANTS

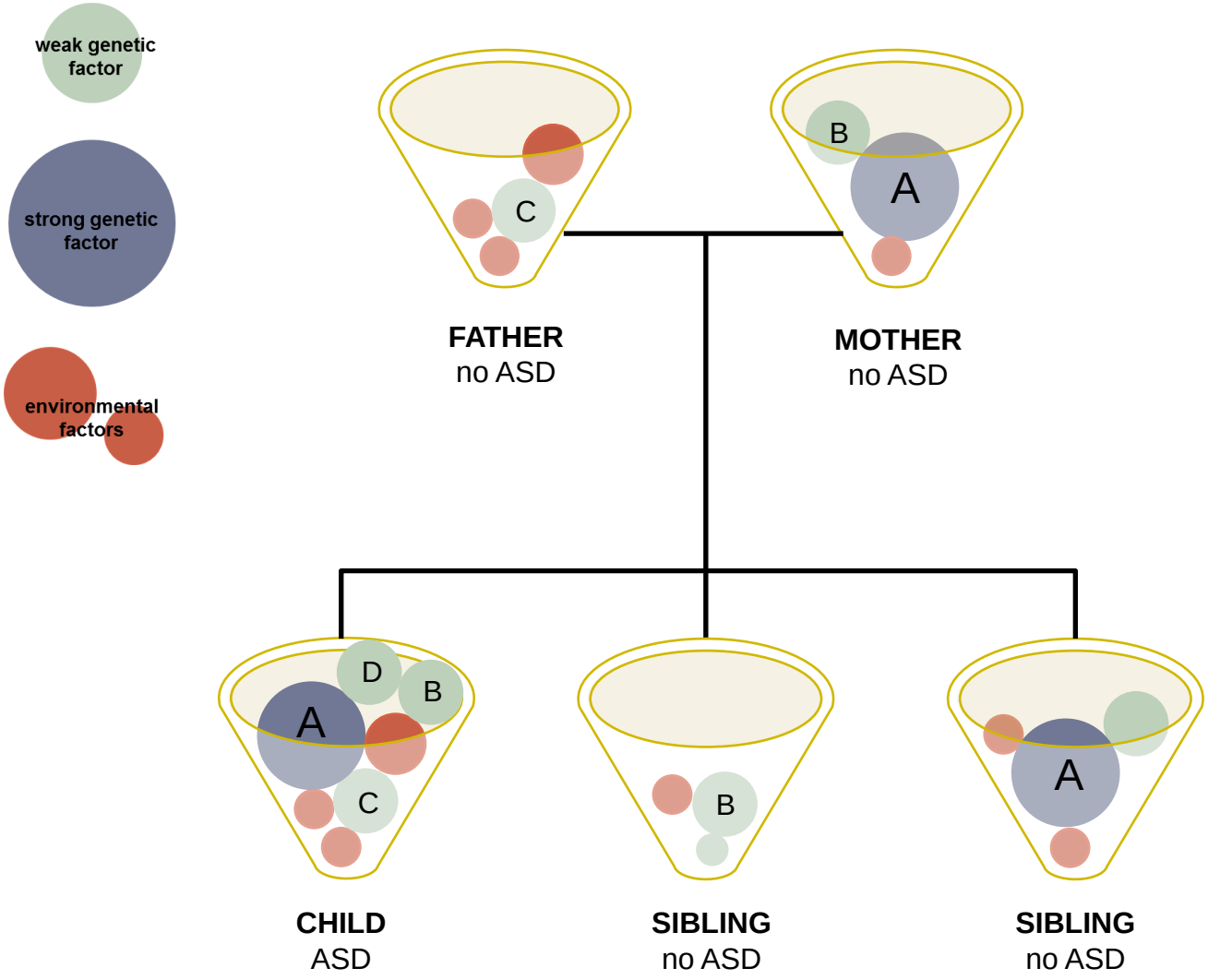
In this family, the child with ASD has a risk cup filled with both inherited and new *(de novo)* genetic risk factors:

- **Strong risk ball labelled A:** genetic variant inherited from the mother who does not have ASD. The risk ball occupies half of the cup, but not enough to overflow it.
- **Weaker risk ball labelled B and C:** genetic variants inherited from the unaffected parents that contribute to the risk cup.
- **Weaker risk ball labelled D**: genetic variant that is not inherited from either parent that contributes to the risk cup.

Along with environmental risk factors, the genetic risk factors push the child's risk above the threshold.

Other family members do not have enough inherited and *de novo* risk factors to reach the ASD threshold.

- Genetic risk factors for ASD can be inherited or *de novo*
- Genetic variants that contribute an increased risk for ASD can also be found in individuals without ASD



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GENETIC TESTING IN ASD

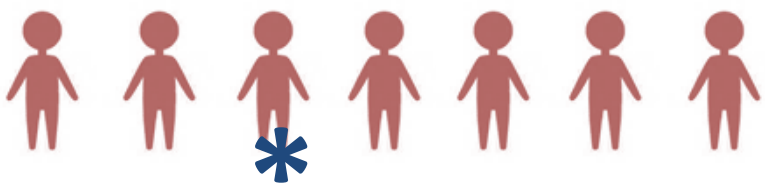
Most individuals with ASD have no other health conditions (e.g. heart defects, seizures, etc.) and are referred to as idiopathic, isolated or essential ASD (75% of cases). Individuals where their ASD is part of a syndrome and can include other physical differences and/or health conditions are referred to as syndromic, complex or ASDplus (25% of cases).

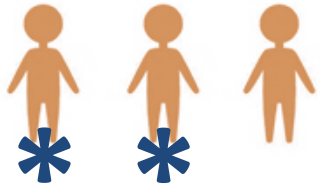
Genetic testing detects a contributory genetic variant in 20-30% of individuals with ASD.

- Most of the genetic variants identified are associated with a known genetic syndrome (e.g. Fragile X syndrome, Rett syndrome).
- Some of the genetic variants identified are in brain related genes that contribute to idiopathic ASD.
- No single genetic variant accounts for more than 1% of ASD.

- ❖ Majority of individuals with ASD have ASD and no other health conditions
- ❖ Majority of families who undergo genetic testing do not receive a causal genetic result

75% of ASD	25% of ASD
IDIOPATHIC	**SYNDROMIC**
ASD diagnosis with no other health condition	ASD diagnosis with physical differences and/or health condition





* **Genetic testing identifies a contributory genetic variant in 20% to 30% of individuals with ASD**

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