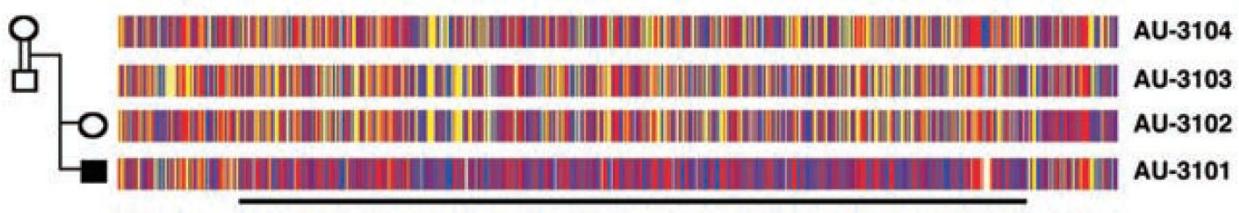
HOW TO USE THIS RESOURCE

Show the following figure and caption to your students. The accompanying "Student Handout" provides space below the caption for "Observations, Notes, and Questions" and space next to the "Background Information" for "Big Ideas, Notes, and Questions." The "Interpreting the Figure" and "Discussion Questions" sections of the "Educator Materials" provide additional information and suggested questions that you can use to prompt student thinking, increase engagement, or guide a class discussion about the characteristics of the figure and what it shows.

Additional information related to pedagogy and implementation can be found on this resource's webpage, including suggested audience, estimated time, and curriculum connections.



Caption: The diagram is a pedigree of a mother (AU-3104), father (AU-3103), daughter (AU-3102), and son (AU-3101). Women are represented by circles and men by squares. Nonautistic individuals are shown as open symbols and autistic individuals as shaded symbols. The double line connecting the two parents indicates that they are related. Each horizontal bar represents a map of single nucleotide polymorphisms (SNPs) along one arm of chromosome 3 of the family members. Red and blue vertical stripes indicate homozygous SNPs for either one of two alleles, yellow stripes represent heterozygous SNPs, and white gaps represent genetic deletions. The horizontal black line demarcates a region with a pattern of homozygosity found in the autistic individual but not in the nonautistic individuals.

BACKGROUND INFORMATION

Autism is a disability that involves differences in development that can manifest in a variety of ways. Autistic individuals may engage in repetitive behaviors, have intensely focused interests, and have differences in communicating and interacting with others in social situations. The differences associated with autism can be strengths, neutral traits, or impairments depending on the social context in which they occur.

Autism has a strong genetic component. Researchers who study autism genetics should work closely with the autistic community to make sure that their research will benefit autistic people. In general, the autistic community does *not* want to prevent or "cure" autistic differences, since those are not inherently bad, just another way of being. Instead, they may want to identify genes related to autism to help treat co-occurring genetic conditions that decrease quality of life (for example, epilepsy, a condition that causes seizures). However, it has been difficult to identify specific genes related to autism, likely because many different genes are involved.

When parents share recent ancestry (for example, if cousins have a child together), their children are more likely to have conditions caused by recessive genetic mutations. This is because relatives are more likely to have the same recessive mutations, which may be rare in the population as a whole, and they can pass these mutations on to their children, who will then be homozygous for the mutations. In these families, scientists use a technique called "homozygosity mapping" to identify the locations of mutations associated with a recessive genetic

condition. The technique basically involves finding regions in the genome where the DNA of an individual with the recessive condition is homozygous. Scientists can then further study those regions to determine which genes and mutations are there.

To identify regions of homozygosity, scientists map single nucleotide polymorphisms (SNPs), which are positions throughout the human genome where individuals are known to have different nucleotides. For each SNP, researchers determine whether an individual is heterozygous or homozygous at that location. If an individual is homozygous for two adjacent SNPs, which are typically mapped an average of 6,000 base pairs apart, then one can reasonably assume that the entire stretch of DNA between the two SNPs will also be homozygous. Scientists then determine which regions of homozygosity are in the genome of the person with the condition but not in the genomes of their relatives without the condition. Such regions are likely to hold genes related to the individual's condition.

Eric Morrow and colleagues mapped SNPs on chromosome 3 in a family in which the parents shared recent ancestry and had an autistic son and a nonautistic daughter.

INTERPRETING THE FIGURE

The four horizontal bars represent maps of SNPs in a father, mother, and two children, one of whom is autistic (AU-3101). Blue and red vertical stripes mark homozygous SNPs for either one of two alleles, yellow vertical stripes mark heterozygous SNPs, and white gaps mark genetic deletions. The autistic individual has a large section of DNA that is homozygous (the region is marked by the black line), which is different from those of his nonautistic parents and sibling. We can infer, then, that (a) this region of DNA may contain a gene that, when mutated, may contribute to autism, and (b) each parent has one copy of this recessive mutation. Researchers can now focus on this region to identify the gene that contains this mutation. Within this region of the genome of the autistic individual (AU-3101), the white gap indicates the deletion of an entire gene, called *C3orf58*. Based on the locations of the SNPs, the deletion is about 886,000 base pairs in size and likely to represent the autism-associated mutation.

TEACHING TIPS

Prompt your students to explain the parts of the figure as applicable:

- Graph type: Map of SNPs created by microarray analysis
- SNP map (bars): The horizontal bars represent SNPs from chromosome 3 of four family members. The vertical stripes represent individual SNPs and the colors indicate homozygosity (red and blue), heterozygosity (yellow), or genetic deletion (white).
- Pedigree: The diagram to the left of the bars shows a pedigree of parents and two offspring. Women are represented by circles and men by squares. Nonautistic individuals are shown as open symbols and autistic individuals as shaded symbols. A double line connecting the two parents indicates that they are related.

Be aware of and address potential misconceptions about autism with your students. For example:

- Students may think that autism is "bad" and that autistic people should be "cured" by having their autistic traits removed. Clarify that autism is not considered an illness or inherently bad, just another way of being, and that many autistic people do not need or want to be "fixed." Rather than trying to change autistic people, society should accommodate and remove barriers for them instead.
- Students may think that the goal of identifying autism genes should be to "cure" autism. Clarify that using genetic research to prevent autistic people from existing would be considered unethical and a form of eugenics. Instead, the goals of autism research should align with the goals of the autistic community. For

example, they may want to improve quality of life by treating co-occurring genetic conditions, such as epilepsy, or focus more on societal services and supports for autistic people.

- Bottema-Beutel et al. (2021) provide more specific suggestions for language around autism and autism research.

Acknowledge and discuss the ethical considerations of autism genetic research with students. Some points include the following:

- Science in general is not always "neutral" and often has broader societal implications, especially when the research involves humans.
- Although some autism genetic research could be used to improve the wellbeing of autistic people, it could also be misused to stigmatize or prevent them from existing — for example, a eugenics approach of terminating pregnancies based on prenatal screening for "autism genes."
- Scientists should work closely with the autistic community to align the goals of their research with those of the community and make sure that their research will benefit autistic people.
- You may wish to discuss Spectrum 10k, a large and controversial autism genetic study that was paused due to ethical concerns. You can learn more about the study and concerns from the following sources:
  - "Spectrum 10k: The Fallacy of Genetic Autism Studies" from NeuroClastic
  - "Spectrum 10K and cognitive dissonance in autism research" from Thinking Person's Guide to Autism
  - "Spectrum 10K, autism, autistic people, and the controversy of SBC" from The Autistic Advocate

DISCUSSION QUESTIONS

- How are the maps of the parents and siblings similar to or different from each other?
- Is it important to include the pedigree when looking at the SNP map? Why?
- What does the double line in the pedigree indicate about the relationship between the parents? Why is this important for this technique?
- Using this map, where would you begin your search for genes that may be related to autism?
- Why do you think the autistic individual, AU-3101, has such a large section of DNA that has a pattern of SNPs that differ from those of his nonautistic family members? In other words, how did this pattern of SNPs arise in his genome?
- Identify a genetic deletion in the region demarcated by the black line in AU-3101. How could this deletion be associated with autism?
- Autism genetic research has many ethical considerations. Although it can be used to improve the wellbeing of autistic people, it can also be misused to stigmatize autistic people and prevent them from existing.
  - How could the results of this study be used to help autistic people?
  - How could the results of this study be misused and harm autistic people? What steps could the scientists take to keep this from happening?

SOURCE

Figure 1A from:
Morrow, Eric M., Seung-Yun Yoo, Steven W. Flavell, Tae-Kyung Kim, Yingxi Lin, Robert Sean Hill, Nahit M. Mukaddes, et al. 2008. "Identifying Autism Loci and Genes by Tracing Recent Shared Ancestry." *Science* 321, 5886: 218–223. https://doi.org/10.1126/science.1157657.

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