OVERVIEW OF THE ACTIVITY

Genome generation is a card-based activity, designed to encourage discussions about the social and ethical issues associated with genetic and genomic science. The activity has 8 scenarios which can be explored and discussed. Each scenario has the following cards:

- **Story card**
  An A4 card featuring a story relating to genetic testing, usually based around one character. The Story card also features quotes from three characters involved in the story, along with a question. Once groups have read the Story card, they will use this question to start discussions.

- **Info cards**
  Cards featuring factual information relating to the Story card. These cards should be distributed to all participants, who will share the information on the card with the rest of their group. This information is used to help them understand some of the details of the story and provide additional knowledge to help them to develop their own view. Groups should use this information to continue discussing the situation presented in the Story card.

- **Issue cards**
  Cards featuring questions designed to drive discussions and take the conversation in new directions. Once the Info cards have been shared, Issue cards are placed face down on the table. The group take it in turns to take an Issue card and share it with the rest of the group.

Participants work in small groups to read and discuss the Story cards. The Info and Issue cards are introduced in stages. The session is run by a facilitator, whose role is to introduce the session, guide participants through the process and guide discussions. The facilitator will circulate between the groups to clarify information and prompt discussion. Groups are given the opportunity to discuss one story and will then share what they have discussed with the other groups. The session concludes with each group sharing their top issues with the other groups.

AIM OF THE ACTIVITY

The aim of the activity is to encourage students to discuss the social and ethical issues associated with genetic and genomic science. Students debate the issues presented in the different scenarios and make their own informed decisions about the ethical issues.

Estimated time: 60 minutes

Group size: Students can work in groups of up to 5 or 6

ACTIVITY PREPARATION

The following tasks need to be completed before starting the activity:

Decide on your scenarios

Decide which scenario(s) you will be using. You have the option of giving all groups the same scenario or giving each group a different scenario to discuss. Read through the supporting information on your chosen scenario(s), along with the Story card, Info cards and Issue cards to familiarise yourself with the potential discussions.

Prepare your introductory PowerPoint

Introductory PowerPoint slides are provided that give a brief introduction to genetics and some of the science involved in the scenario(s). The slides also provide guidance on how to participate in the activity. Decide which slides you want to use from the PowerPoint, hide any slides (right click and select hide slide) that are not necessary for your lesson.

Background reading

Read through the background information to familiarise yourself with the science and current genomic research. Prepare a few prompting questions or additional issues in case you are required to help drive discussions forward.

Print and prepare materials

Print and laminate the Story card, Info cards and Issue cards for your chosen scenario(s). Make sure that you have enough sets of cards for each group. Print and laminate one copy of the Glossary of terms for each group. Alternatively, you can arrange for it to be displayed on the white board. Print out a top issues sheet; make sure there is at least one per group.

RUNNING THE ACTIVITY

To run the activity you will require:

- Facilitators (this can be you plus any assistants)
- Teacher's notes and Scenario guide(s)
- Genomegeneration_intro.ppt slides
- Story cards, each with their accompanying sets of Info and Issue cards
- Top issues sheet or A1 flipchart sheet
- Pens
- A glossary of terms (enough for each group)
- A clock or watch so that you can keep an eye on timings
- A flipchart and pens (or whiteboard and pens) to record issues at the end

Overview of timings:

Time	Steps
00.00	1. Get students into groups
00.05	2. Introduction and ground rules
00.15	3. Group reads and discuss Story cards
00.25	4. Info cards shared amongst members of each group
00.35	5. Groups take Issue cards as prompts for further discussions
00.45	6. Groups discuss their top two key issues
00.50	7. Sharing of key issues
00.60	8. Ends

1. Getting into groups (5 minutes)

Divide the class into groups of 5-6 students. Either allocate students to groups or get the students to form their own groups. Make sure each group has a full set of cards, glossary of terms and top issues sheet.

2. Introducing the activity (10 minutes)

Using your PowerPoint presentation, introduce the students to the session. Provide an overview of the session format, the purpose of the session and the key concepts, i.e. genes, genotyping and the

personal genome. Also briefly run through the ground rules of discussion, such as listening to and respecting others.

At this point it is necessary for students to choose a member of the group to act as scribe. This person will make a note of the major topics discussed on the Top issues sheet provided. Remind them that they will need to do this throughout discussion as they need to identify the two most important issues at the end of the activity.

3. Story cards (10 minutes)

Each group has a Story card which they should read together, along with quotes from three characters detailed on the card. The groups may wish to nominate one member of the group to read out the Story card, while others take it in turns to read the three character quotes. Once the group has read and understood the story, they should have an initial discussion in reaction to the question on the card.

Circulate the room to ensure that students understand what they are doing. Remind them to read the character quotes and prompt them to answer the question on the card. Keep an eye on timings – once discussions are in full flow, prepare the Info cards for each group.

4. Info cards (10 minutes)

After about 10 minutes, provide each group with a set of Info cards. All of the Info cards should be distributed to members of the group, each of whom will read and summarise their information for the rest of the group. Groups should continue their discussions based on the new information provided.

Circulate the room to provide additional information and to help participants if they are having difficulty understanding the information. Encourage them to keep the scenario in mind and to continue discussions based on the new information. Once discussions are in full flow, place the relevant Issue cards face down on each group's table.

5. Issue cards (10 minutes)

After about 10 minutes, announce that it is time to move on to the Issue cards which have been placed face down on each of their tables. The students should take one Issue card at a time, pausing to continue discussions between each card. The Issue cards will provide questions, detailing a particular dilemma or implication which should help the discussion to progress. It is important that they record the main points from their discussions for the next step in the activity.

Circulate the room to provide additional information and, if necessary, ask questions to help participants challenge the points raised and think about all of the potential implications.

6. Reflection on the key issues (5 minutes)

Encourage the students to wind down their discussions and to agree upon the two key issues they wish to share with the rest of the group. Refer them to the notes that they have made throughout

the discussion to help them identify these issues. If some of the students are nervous about speaking in front of the class, encourage the groups to nominate a speaker who will feedback the issues from their discussions.

7. Feedback and discussion (10 minutes)

To conclude the session, ask all of the groups to summarise the scenario that they have discussed (if different to the other groups) and to provide the two headline issues arising from their discussions.

Note down the issues on a flipchart or whiteboard. If there is time, lead the groups in a discussion about these and other issues arising.

QUICK GUIDE TO THE SCENARIOS

Genome generation contains 8 scenarios. There are two options for running the activity with students. Provide each group with the same Story card or provide each group of students with a different Story card to discuss. Only give each group one Story card to discuss.

Some of the scenarios on the Story cards are more complex, or carry issues which may be sensitive to some students. As a rough guide, the scenarios are numbered to indicate complexity. The earlier numbers (1-4) may be more appropriate for younger students, whereas the higher numbers (5-8) are more complex and may be more suitable for older students.

Each scenario has its own detailed guidance notes. These notes provide suggested questions to ask so that students can explore the issues and highlight topics that may be sensitive to some students. It is recommended that you take the time to read through the cards, as these contain the most vital information.

Note: All of the information presented in the Info cards is factual (as understood in February 2012). Some of the Story cards are hypothetical, and may be based in the future, but they are developments that could potentially occur. Any genetic factors relating to the conditions included are based on accurate scientific information. It is possible that participants will be confronted with some of these issues during their lifetime.

A summary of the scenarios is given below:

Scenario 1: Amy and the breast cancer test

This scenario is set in the present day.

Summary: Scenario 1 deals with a 15 year old girl (Amy) who has a family history of breast cancer. Her paternal aunt has been diagnosed with the disease and tests have shown that she is a carrier of the *BRCA1* mutation associated with breast cancer. There is a dispute within the family about whether Amy's father should be tested to find out whether he is also a carrier of the *BRCA1*

mutation, and may have passed the risk to Amy. Her mother does not want the test to take place. The decision is Amy's. The group has to decide whether Amy should ask her father to take the test.

Initial question: Should Amy insist on her father being tested for the *BRCA1* mutation?

Key issues: Would you want to know? Impact on families

Scenario 2: Jill and the schizophrenia risk

This scenario is set in the future and assumes that people will be able to find out this information through a recreational genotyping kit.

Summary: Scenario 2 deals with a woman (Jill) who has no knowledge of her father's family history. She has a husband and a young baby and pays to be genotyped to get a better understanding of her genetics. She does not know that the test will reveal that she has a rare chromosome deletion, associated with a higher than normal risk of developing schizophrenia.

Initial question: If you were Jill would you want to know that you have an increased risk of schizophrenia?

Key issues: Incidental or unexpected findings; Would you want to know? Impact on families

Scenario 3: Sam and the insurance company

This scenario is set in the future and assumes that insurance companies will be able to use genetic information to determine insurance premiums.

Summary: Scenario 3 deals with a middle-aged man (Sam) with a family history of heart attacks. He wishes to purchase insurance but the insurers ask him to be genotyped. Sam's brother (who has had heart problems himself) is keen for Sam to be tested. He feels that knowing if Sam is at high risk of heart disease will help him to take steps to avoid severe heart problems. Sam fears he will be refused insurance if he takes the test and is not certain he wants to know the results. His wife is firmly against genotyping. The group have to decide if Sam should take the test.

Initial question: Should Sam take the test?

Key issues: Who should have access to data? Would you want to know? Impact on families

Scenario 4: Heather, her risk of Alzheimer's and her reluctant twin

This scenario is set in the future and assumes that recreational genotyping has become commonplace.

Summary: This scenario presents a young woman (Heather) who has an identical twin. Heather wishes to start a family with her husband and has decided to get herself genotyped. Her twin objects to the test and does not wish to know the results. The results show that the twins are carriers of two copies of the gene variant ApoE-e4, which puts them at high risk of developing

Alzheimer's disease. The group has to decide whether Heather should tell her sister or parents about the results.

As the twins are identical whatever is revealed about the genotype for one twin will match the genotype of the other. If the twins were non-identical the genetic similarities would only be as close as that of any other pair of siblings.

Initial question: Who should Heather tell about her results?

Key issues: Incidental or unexpected findings; Impact on families; Who should have access to data? Issues of consent

Scenario 5: Pete's potential adverse drug reaction

This scenario is set in the future. A test for the genes linked to this drug reaction does currently exist, but is not currently widely available to patients.

Summary: This scenario is centred on (Pete) whose doctor would like to prescribe the antibiotic flucloxacillin, since it is particularly effective for his type of infection. However, in rare cases flucloxacillin can cause a serious liver injury, and Pete is offered a test to determine whether he has a particular genotype associated with this severe reaction. Pete is concerned about the cost but his wife is keen for him to take the safe option. His teenage son is concerned about misuse of the data if it becomes part of his medical records. The group has to decide whether Pete should take the test.

Initial question: Should Pete take the test?

Key issues: Access to data and data storage issues; Impacts on families; Issue of who should pay

Scenario 6: Should a baby have its genome sequenced?

This scenario is set in the future. It assumes that we are at a point where whole genome sequencing can be carried out cheaply and quickly.

Summary: In this scenario expectant parents are asked whether they would like to have their child's genome sequenced after it is born. The information would form part of the child's ID card.

Initial question: Should the parents have their child's genome sequenced?

Key issues: Incidental findings; Access to data; Impact on families; Would you want to know?

Scenario 7: Andy's unexpected paternity results

This scenario is set in the future and assumes that recreational genotyping has reached the point that it is affordable for most people to purchase a genotyping kit as a gift.

Summary: This scenario involves Andy, who buys a genotyping kit online. He finds it fun and therefore decides to buy one for his father. Looking through their results together, Andy notices that there are different markers on the Y chromosomes of him and his father, indicating that he is not

Andy's biological father. The group has to decide whether Andy should tell his father what he's found.

Initial question: Should Andy tell his father the results?

Key issues: Incidental or unexpected findings; Impact on families; Access to data

Scenario 8: Should researchers share incidental findings?

This scenario is set in the present day.

Summary: This scenario is about a researcher (Lin) who is working on a study into childhood developmental disorders. She discovers that one of the children in the study has a mutation associated with the cancer retinoblastoma. The study has a strict policy not to share incidental findings with participants. The group has to decide whether Lin should tell the child's parents.

Initial question: Should Lin share the results with the participant's parents?

Key issues: Unexpected or incidental findings; Access to data; Use of research data

SUPPORTING NOTES ABOUT THE HUMAN GENOME

The human genome

A genome is an organism's complete set of DNA. It contains all the instructions required to make the organism. The human genome therefore contains all the information required to make a human. Although any two human beings are more than 99% alike in their DNA, the differences in the other 1% of the DNA are what make us unique. These differences can be changes in a single DNA letter, or larger chunks of DNA that are copied, missing or flipped round. Only identical twins are exactly alike at the DNA level; although changes to the DNA may occur over the course of a lifetime which will shape each individual twin. Scientists are working to identify places in the human genome where the DNA varies and are studying these areas to discover their relationship to different characteristics and diseases.

The Human Genome Project

The Human Genome Project was an international collaboration to work out the sequence of chemical letters, known as bases, in the DNA code of humans. In 2003, after 13 years of work, the 3 billion chemical letters of the human genome were published. The DNA sequence published represents the combined genomes from a small number of donors.

The technology that allowed the Human Genome Project to take place is advancing rapidly. In 2001, it cost a little under $100 million to sequence a human genome. It is now possible to sequence an entire human genome in just a few days at a cost of less than $10,000 and it is predicted that it will soon be possible to sequence a whole human genome for less than $1,000. Some experts anticipate that the process will soon become affordable for everyone and will eventually become available as

part of everyday health care. This will become increasingly important as our understanding of the role of genetics in health and disease improves.

There are already commercial organisations that offer recreational genotyping – looking within the DNA sequence for single letter changes, known as SNPs (or single nucleotide polymorphisms). Genotyping looks at a small proportion of the estimated 10 million single letter changes in the entire human genome. However, these tests can indicate a person's risk for developing some diseases (compared to the average population) or a genetic basis for particular physical characteristics. It is possible to purchase genotyping online for about $200 (February 2012).

DNA, chromosomes and genes

Our bodies are made up of around 50 trillion **cells**. Most of these cells contain a person's genetic information within a long molecule called DNA (deoxyribonucleic acid). This DNA contains the genetic information that we inherit from our parents.

Our DNA is made up of specific sequences of letters or **bases** that encode instructions on how to make proteins. These bases [Adenine (A), Guanine (G), Cytosine (C) and, Thymine (T)] are lined up along two strands of DNA. This DNA is coiled into a double helix structure that resembles a twisted ladder. The bases in the two strands of DNA pair up to form the rungs of the ladder. A always pairs with T and C always pairs with G, e.g.

A - T

T - A

C - G

G - C

The side by side arrangement of these bases along a strand of DNA, e.g. ATTCGATCGTAGGA, is known as the DNA **sequence**.

What do our genes do?

In humans most of the **DNA** is contained in 23 pairs of **chromosomes**. One set of chromosomes is inherited from the mother and one set from the father. There are 22 pairs of autosomes (chromosomes that do not determine gender) and one pair of sex chromosomes (the chromosomes which determine gender): XX (female) or XY (male).

Each chromosome contains **genes**. It is estimated that the human genome contains 20,000-25,000 genes. Genes are lengths of DNA which carry the instructions to make molecules, usually **proteins**. Proteins carry out most of the functions in a cell. You could think of DNA as the recipe book and proteins as the ingredients. These ingredients create our unique physical characteristics and carry out the different processes that keep our bodies ticking along.

However, not all of the DNA in our genome is in the form of genes that are used to make proteins. Only approximately 2% of the human genome is made up of genes; the rest is made up of noncoding regions. Much of what these noncoding regions do is unknown but some is involved in providing the structure of the chromosome or regulating when a gene is switched on or off.

Mutations and genetic variations

Our genomes change during our lifetime. To function properly, each cell depends on thousands of proteins doing the right job, in the right place, at the right time. It is a fine balance, which can be disrupted by small changes that may make big differences to our bodies. A mutation is a permanent change in the DNA sequence.

Mutations happen in our cells all the time but they are usually either repaired or completely harmless. However, some may lead to a difference in the amount or structure of the protein produced. Some mutations may switch genes on at the wrong time.

Mutations, or genetic variations, come in many forms including:

- **SNPs (single nucleotide polymorphisms):** Referred to as "snips", SNPs are changes to a single letter in the sequence of DNA, e.g. AAGGT becomes AACGT. SNPs make up approximately 90% of all human genetic variation. Many SNPs do not affect cell function but others can result in changes that may predispose people to disease or influence their response to a particular drug.

- **Translocation/inversions:** Sometimes an entire section of DNA may be flipped over or reversed. Some may be swapped between different chromosomes.

- **Insertions:** An insertion is the presence of an additional base or piece of DNA, which changes the number of DNA bases in a gene.

- **Deletions:** A deletion is a missing sequence of DNA; ranging from the deletion of a single base through to the loss of a section of DNA or an entire gene.

- **Duplications:** Small or large sections of DNA can be repeated.

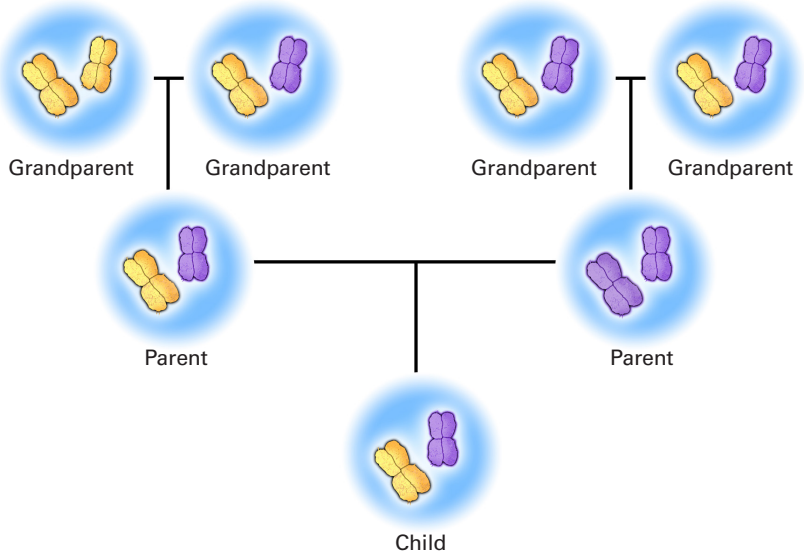
These deletions, insertions and duplications are collectively known as copy number variations (CNVs).

Genetic inheritance

Our 23 pairs of chromosomes are inherited from our parents. For each pair we get one chromosome from our father (carried in a sperm cell) and one chromosome from our mother (carried in an egg cell). When a sperm cell and an egg cell join together the genetic material from each parent is combined to create one new person, with their own, unique genome.

Some mutations are also passed on from parent to child, along with the rest of the genome, which explains why some diseases can run in families. However, since each parent only provides a copy of one half of their genome, it is possible that some traits or genetic disorders will not be passed to their offspring.

Inheritance basics



Recessive versus dominant genes

There are a number of factors which determine how our genes are expressed (i.e. which characteristics or traits they produce), but some gene variants (alleles) are 'dominant' or 'recessive'.

If we receive two dominant alleles, then we will get the characteristic that the dominant allele codes for. If we receive one dominant and one recessive allele, the dominant one will be expressed. However if we inherit two recessive alleles – one from each parent – the recessive characteristic will be expressed.

Predisposition and the polygenic nature of disorders

Although changes to some genes, or genotypes, will mean that a person will definitely develop a disease, with most diseases particular gene variants are only associated with an increased risk of developing the disease. This means those people with that genotype will not necessarily go on to develop the condition. A predisposition means that people with a particular genetic makeup tend to have an increased risk of developing a disease compared to the average population. Those with a predisposition may never go on to develop the disease. On the other hand, those who do not have the genotype associated with that increased risk may still develop the condition.

Lifestyle plays a significant role in increasing the risk of developing some diseases. Disorders caused by changes in a single gene are rare. Common diseases, such as Alzheimer's disease, heart disease, diabetes and cancer, are complex and are likely to be caused by a combination of genetic and environmental factors.

TOP TIPS FOR FACILITATING A DISCUSSION

Discussion about issues that affect us, particularly sensitive issues such as inherited disease, should be handled very carefully. Here are some tips for facilitating effective discussions:

1. Before discussions begin, set ground rules of mutual respect and tolerance. If you have time, encourage the group to set the rules themselves – ask them to suggest what the rules should be and write them down on a flipchart or whiteboard. For example, groups should agree not to talk over one another, not to be dismissive of other people's views, and not to personalise their comments. Comments should be aimed at arguments, not people.

2. Make sure you familiarise yourself with the Story cards, and with the background information provided. Be ready to explain the key concepts regarding genetic inheritance, genotyping and genetic disease.

3. Make sure that you are familiar with the issues arising and plan some questions to get discussions going if a group is not fully engaging with a scenario. It is important that you don't tell them everything! Remember that your role is to facilitate the discussion, not to direct it. Allow the students the space and opportunity to bring up issues and ideas for themselves.

4. Be wary of presenting your own opinions. Be respectful of all opinions and retain an element of objectivity so others feel that they are able to put their point of view across. You may also be required to present a viewpoint which differs to your own position, in order to prompt discussion of certain issues.

5. Be aware that some students may have personal experiences or background knowledge (such as family history of a disease) that makes them more sensitive or opinionated about certain issues.

6. There may be strongly held or deeply ingrained views regarding the subject matter. If these opinions are rejected by others, it may lead to defensiveness or participants may feel that they are being criticised. People with strong views may also make other members of the group reluctant to express their own viewpoint. Try to encourage everyone to explore their own views and those of others by asking questions.

7. Allow space for all participants to express their views, but don't allow the loudest voices to dominate the discussion. You could consider introducing a yellow card scheme that the students manage themselves. If one person is dominating discussions or being disruptive the group can vote to yellow card them, so they have to stop talking for a few minutes. This will also alert you of potential trouble.

8. Some members of the group may not feel confident enough to share their views but do not force members to contribute opinions if they do not wish to. Less confident participants can still benefit from listening to, and considering, the issues raised by others.

9. If discussions are becoming too heated and personal, steer discussions back to the scenario. If you encourage the group to think about the characters (and a situation from which they are removed), they should be able to retain a more objective viewpoint.

10. Encourage participants to examine their own opinions by looking at opposing views and exploring their own reasons for drawing their conclusions. Ask why they feel the way they do, and encourage them to put themselves in the position of other people.

11. Ask questions to draw out deeper discussions, for example:
    - Why do you think that?
    - What is the reason for that?
    - How do you know?
    - Can you think of an argument against your view?
    - Is there another argument to support that?
    - What affect would that have on other people?
    - If [introduce a scenario] were to happen, how would that make you feel?
    - What would be the consequences of that?

RECOMMENDED SUPPORT RESOURCES

Websites

To find out more about the science behind genetics and genomics:

yourgenome: www.yourgenome.org

Inside DNA: www.insidedna.org.uk

To find out more about the issues surrounding personal genome sequencing:

The Nuffield Council on Bioethics is an independent body that examines and reports on ethical issues in biology and medicine: www.nuffieldbioethics.org

Recent news

$1000 genome – are we there yet? – Nature News 10th January 2012
http://blogs.nature.com/news/2012/01/the-1000-genome-are-we-there-yet.html

Analysis: Human genome hype or reality? – BBC News 10th January 2012
www.bbc.co.uk/news/health-16347116

Has decoding the genome lived up to hype? – BBC News 25th June 2010
www.bbc.co.uk/news/10337585

HUMAN GENOME AT TEN: 5 Breakthroughs, 5 Predictions – National Geographic 31st March 2010
http://news.nationalgeographic.com/news/human-genome-project-tenth-anniversary/

Videos/animations

How the human genome was sequenced:
www.yourgenome.org/video/how-the-human-genome-was-sequenced

Direct to consumer testing:
www.yourgenome.org/video/direct-to-consumer-genetic-testing

FURTHER READING

Scott S. Ten years on: The Human Genome Project today. Catalyst December 2010; 6-8.
www.stem.org.uk/system/files/elibrary-resources/legacy_files_migrated/8430-catalyst_21_2_469.pdf