

LESSON 4:

The Process of Scientific Research

INTRODUCTION

In this lesson, students arrange sets of cards to show their understanding of the process of biomedical research. Students see how **basic research** may lead to studies involving both animals and humans and may culminate in the availability of new treatments and medications. Students then apply their understanding of the overall progression of biomedical research to early **chromosomal** studies and the story of Gleevec, a drug approved by the Food and Drug Administration (FDA) in 2001 to treat **chronic myelogenous leukemia** (CML). Lastly, students consider the ethical guidelines that scientists follow in every stage of research. This lesson includes instructions on how to arrange the cards using a **foldable**, if desired.

CLASS TIME

One class period of 55 minutes.

KEY CONCEPTS

- Many years of basic research may or may not lead to new treatments and medications.
- Beginning with a known medication and working backwards to its origin does not give appropriate weight to knowledge gained from the false starts, dead ends, and blind alleys along the path.
- Ethical guidelines inform every stage of biomedical research.
- New technologies drive scientific discovery.

LEARNING OBJECTIVES

Students will know:

- The biomedical research process resulting in new drugs and treatments involves modeling, **in vitro** work, the use of animals, and human trials.
- Drug development can be a slow process, often requiring years of basic research and technological advancements.

Students will be able to:

- Create a flowchart using cards summarizing the process of biomedical research for drug development.

MATERIALS

Materials	Quantity
Student Handout 4.1— <i>Card Set #1: Translational Research Process</i>	1 set per group
Student Handout 4.2— <i>Card Set #2: The Story of Gleevec</i>	1 set per group
Student Handout 4.3— <i>Card Set #3: Ethical Guidelines</i>	1 set per group
Scissors	At least 1 per group
3 x 5 index cards (if not making a foldable)	4 per group
Teacher Resource 4.1— <i>Notes for Card Set #1: Translational Research Process</i>	1
Teacher Resource 4.2— <i>Ordered Card Set #2: The Story of Gleevec</i>	1
Teacher Resource 4.3— <i>Making a Foldable</i>	1
Computer with PowerPoint and overhead projection	1
<i>The Process of Scientific Research Slide Set</i> , found at http://nwabr.org .	1

NOTE TO THE TEACHER

The story of Gleevec is particularly interesting because it was the first drug designed to target and disrupt a specific **enzyme** found in patients with **chronic myelogenous leukemia (CML)**. CML is a relatively rare type of leukemia, and one of the few cancers that can be linked to a single **oncogene**. The making of Gleevec is wonderfully intertwined with a fifty-year history of chromosomal research and discovery.

The oncogene responsible for the vast majority of CML cases is caused by a **translocation** between **chromosomes 9** and **22**. Scientists first described the resulting abnormal chromosome in 1960 and called it the **Philadelphia chromosome**. Years later, using progressively better technology, the genetic impact of the translocation was shown to be the Abelson tyrosine kinase gene (*Abl*) of chromosome 9 becoming fused with the break point cluster gene (*Bcr*) of chromosome 22. The resulting Bcr-Abl combination makes an abnormal enzyme (a kinase) that stimulates cancer-causing cells to overproduce.

When the Bcr-Abl enzyme was identified as the cause of CML, researchers worked backwards to find a drug that would disable Bcr-Abl. Picturing Bcr-Abl as the lock, researchers designed and synthesized over 400 molecular keys to fit the lock. The successful key was the molecule STI571 (named Imatinib), marketed by Novartis as Gleevec.

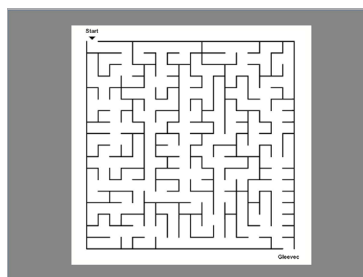
TEACHER PREPARATION

- Make copies of *Student Handouts*. You will need one copy of each handout (three total card sets) for each student group.
- Decide whether you want students to reuse the card sets or make them into foldables. If you would like to **reuse the card sets** for multiple classes, students may arrange the cards on the table and use index cards as labels (which will be further described in the Procedure section). If you do not need to reuse the cards, students may arrange the cards into a **foldable** (see Teacher Resource 4.3—*Making a Foldable*). Additional materials include two pieces of blank paper for each group, tape, and glue.
- For showing the PowerPoint slide set, prepare the computer and projection unit. Download *The Process of Scientific Research Slide Set*.

PROCEDURE

Introduction

1. Show students a picture of a complicated maze (found in *The Process of Scientific Research Slide Set*) with many openings. Ask students, “What is the easiest way to find the path of the maze?” Point out that there are many dead ends, false starts, and an element of trial and error. Once you’ve found the path, however, it is easy to retrace the steps back out.



2. Ask students to name any medicine, treatment, therapy, and/or device that improves human health and function. Tell students that considering these things is like starting at the center of a maze—the path to get to any of these products of biomedical research is often unclear. The end product may have been years in the making, with many wrong turns along the way, and may have relied on research from surprising resources.
3. Also point out to students that, in many cases, there is no center of the maze to be found—there is no one linear path that always leads towards success. Furthermore, any of these products in use right now can be improved upon and changed in the face of new evidence and research.
4. Tell students that today’s lesson will focus on the process of biomedical research by exploring the route one medicine—Gleevec—took to reach the market. Gleevec is used to treat a form of **leukemia** called chronic myelogenous leukemia (CML).

Part I: Card Set #1—The Process of Translational Research

5. Ask students, “How do you think drugs, treatments, or medical devices are developed?”
6. Have each student spend a few moments drawing a “Drug Development Process Flow Chart” of how they think a drug is developed before it is marketed to the public. Explain that they will compare this initial flow chart to a second one they will generate during the lesson. Tell them not to be discouraged if they are having difficulty, but to make their best attempt.

7. Ask students to consider some questions when developing their flow charts:
 - a. Where do scientists find new drugs?
 - b. How do they determine that the new drugs will work and are safe in humans?
 - c. What, if any, regulations and policies guide the process?
8. Elicit answers from students and write them on the board.
9. Teachers wishing to frame this activity using a foldable should follow the directions on Teacher Resource 4.3—*Making a Foldable*.
10. Divide the class into groups of two to four students each. Hand out copies of Student Handout 4.1—*Card Set #1: Translational Research Process*, one per group. The cards are not in order on the handout. Ask students to cut out the cards.
11. Have students put the cards in order—from the beginning to the end of the process as best they can. Tell students that multiple cards may go at the same “level.”
12. When each group is finished arranging the cards, have a “Gallery Walk” to allow the students to see if other groups arrived at the same order.
13. As a class, discuss the basic order of cards using the original order found on Teacher Resource 4.1—*Notes for Card Set #1: Translational Research Process*.

[**Note:** The first five cards, representing basic research, can go in different orders since the process is cyclical. Students should be able to justify the order they chose.]
14. Keeping the cards arranged in order, have students classify the cards into four categories **Basic Research**, **Animal Research**, **Humans in Research**, and **New Treatments**.
15. Write each category name on a 3x5 index card and place the card in the correct position next to the arranged cards. Alternatively, students can label these categories on the foldable.
16. Tell students that the three cards in the **Humans in Research** section showing increasing numbers of human volunteers represent the **clinical trials phases**. These can be labeled **Phase I**, **Phase II**, and **Phase III**.
17. **Do not** have students clear the **Translational Research** process cards. They will be adding to the set in *Part II*.

Part II: Card Set #2—The Story of Gleevec

[**Note:** A graphic showing the Philadelphia chromosome and blood cell development can be found at: <http://www.cancer.gov/cancertopics/pdq/treatment/CML/Patient>.]

18. Now that students have the general framework for the order of biomedical research, tell them that they will receive a second set of cards detailing the drug discovery process for a specific drug.

The drug they will be exploring is **Gleevec**. Gleevec is made and marketed by the pharmaceutical company Novartis to treat chronic myelogenous leukemia (CML). CML is a relatively rare cancer of the blood. Prior to Gleevec, fewer than half of patients with CML lived seven years. With Gleevec, nearly 90% are alive seven years later.
19. Pass out Student Handout 4.2—*Card Set #2: The Story of Gleevec* and ask students to cut out the cards. These cards give the history of chromosomal research and the discovery of Gleevec. Dates for some milestone discoveries are in parentheses on some of the cards to help students put them in order.
20. With *Card Set #1* still in place, have students arrange the cards from *Set #2* in chronological order (the dates of milestone events on some cards will help students do this). Make sure that students are tying the Gleevec cards back to the process cards from *Card Set #1*. The correct order for the cards can be found on Teacher Resource 4.2—*Ordered Card Set #2: The Story of Gleevec*.
21. When students have finished arranging *Card Set #2*, ask them:
 - a. In which category (**Basic Research**, **Animal Research**, **Humans in Research**, and **New Treatments**) are most of the Gleevec cards? Why?
 - b. Which category represents the longest period of time? Why?
 - c. In what way do new technologies drive scientific discovery?
22. Remind students of the maze analogy from the beginning of the class. Reiterate that we are tracing backwards from the beginning, knowing the path that worked. This activity does not show all the false starts, dead ends, and blind alleys that were part of the journey.

23. Tell students that *Card Set #1* represents the standard, conventional order for the development for drugs and treatments—in some ways it is an “idealized” model. The development of Gleevec differs from this model in some important ways:
- CML is considered an **orphan disease** because it is rare. Drugs to treat orphan diseases undergo a shorter clinical trial phase.
 - In **Phase I trials**, the drug was given to people with CML, not healthy volunteers.
24. Students may also be interested in knowing that the cost of Gleevec can run between \$40,000 and \$90,000 a year and must be taken for the rest of the patient’s life.

Part III: Card Set #3—Ethical Guidelines

25. Tell students that research at every level follows ethical guidelines and legal regulations. Point out that the two cards from *Card Set #1* marked with stop signs symbolize federal involvement through the Food and Drug Administration (FDA).
26. Ask students, “When doing basic research, what should the rules be?” Encourage students to think about the processes they used when conducting their gummy bear lab in *Lesson One*, such as peer review, collaboration, using repeatable trials and multiple trials, and not falsifying data. These are all aspects of ethical research.
27. Ask students, “When doing research with animals, what should the rules be?” Encourage students to recognize the importance of treating animals humanely by enhancing animal welfare and ensuring the best conditions possible, using as few animals as possible, using the least developed organisms possible, and replacing living organisms with cell/tissue cultures or computer models when possible.

[**Note:** Additional support for talking with students about animal research can be found in the curriculum, *The Science and Ethics of Animal Research*, available from NWABR’s website at: <http://nwabr.org/curriculum/animals-research>. A poster detailing the **3Rs of animal research** is also available to download.]

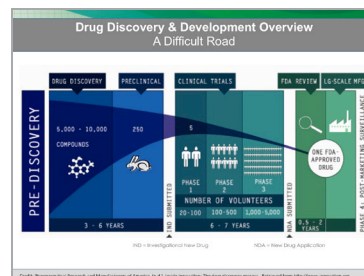
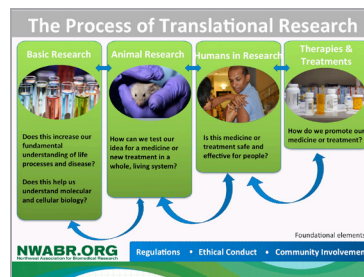
28. Ask students, “When doing research with humans, what should the rules be?” Encourage students to consider the importance of asking people their permission through an informed consent process, treating participants with respect, being fair in selecting participants, and considering the potential harms and benefits of research with humans.

[**Note:** A more in-depth look at humans in research can be found in the curriculum, *The Science and Ethics of Humans in Research*, available from NWABR’s website at: <http://nwabr.org/curriculum/humans-research>.]

29. Hand out copies of Student Handout 4.3—*Card Set #3: Ethical Oversight*, one per group. Students should cut out the cards and add them to their research process and Gleevec card sets. Alternately, students can write the information about the ethical guidelines on the back of the index card representing the correct category. If using the foldable, students should turn their paper over and glue the cards on to the back.

Closure

30. Show students the accompanying PowerPoint slides: “The Process of Translational Research” and “Drug Discovery & Development Overview: A Difficult Road.” Clarify any questions about the process.



31. Ask students to write down one question or comment about the slide, “Drug Discovery & Development Overview: A Difficult Road” to share with the class. Elicit responses from a few students, and then ask if anybody has anything to add to the discussion. Make sure that somebody points out the number of compounds that are considered for every one drug that makes it to the market.
32. Lastly, have students retrieve their *Unit Graphic Organizer* handouts and look at the third column, titled “Translational Research.” Ask students, “What is the process through

which new drugs and treatments are made available to treat disease?" Students should write down the steps in the process:

Basic Research → New Discoveries → Animal Research → Humans in Research → New Treatments.

Point out that ethical guidelines exist at every level. Although the arrows point to the right and show a simplified progression, the process is multidirectional, complex, and may end up in a blind alley or dead end at any point.

33. In addition, draw students' attention to the last column, "Being a Scientifically Literate Citizen." Ask students how their understanding of **translational research** impacts them as consumers and/or users of medications and treatments. Discuss their responsibility to be scientifically literate in their role as **consumers** and add that word to the graphic organizer.

HOMework

Teachers may assign either the Peter Nowell or Jane Brody article mentioned in the *Extension* section as homework.

EXTENSION

- To further study chromosomes, CellServ sells a kit that allow students to prepare a chromosome spread using human cells. The kits are made using HeLa cells, which links nicely to a case study about HeLa cells found in *Lesson One* of NWABR's *The Science and Ethics of Humans in Research* curriculum. Kits are available to purchase at:

CellServ

<http://www.cellserv.org/Kits/Kit4.html>

- A number of articles and retrospectives have been written about the impact of the discovery of the Philadelphia chromosome. The following articles are accessible for upper-level students and freely downloadable:

"Discovery of the Philadelphia chromosome" by Peter Nowell, one of the original researchers
<http://www.jci.org/articles/view/31771>.

"Living with a formerly fatal blood cancer"
http://www.nytimes.com/2010/01/19/health/19brod.html?_r=1

- Fox Chase Cancer Center held a 50th anniversary symposium on the Philadelphia chromosome. Many of the associated materials can be found here:

Philadelphia Chromosome: 50th Anniversary Symposium

<http://pubweb.fccc.edu/philadelphiachromosome/history.html>

GLOSSARY

Applied research: Research that relates to human health care in the form of treatments or cures of human diseases. Applied research is often conducted by for-profit companies.

Basic research: Research that furthers general scientific understanding of how the natural world works. This is often academic research.

Belmont Principles inform and guide researchers working with human participants. They are:

- Respect for Persons:** Respect for individuals and their **autonomy**; obtain informed consent.
- Maximize Benefits/Minimize Harms:** This stresses "doing good" and "doing no harm" by minimizing potential harm(s) and maximizing potential benefit(s) to the subject as well as potential benefit to society.
- Justice:** Be fair in distributing the benefits and burdens of research.

Chromosome: A strand of DNA and associated proteins that contains genetic information.

Clinical trials phases: Clinical trials are conducted in three or four phases. Each phase has a different purpose to help researchers answer different questions. Following is an overview of each phase:

- Phase I**—An experimental drug or treatment is tried on a small group of people (fewer than 100). The purpose is to evaluate its safety, potential dosage, and identify any side effects.
- Phase II**—The experimental drug or treatment is administered to a larger group of people (several hundred) to further assess safety, and to address issues such as optimal dosing and frequency of dose administration.
- Phase III**—The experimental drug or treatment is administered to large groups of people (several thousand) to determine its effectiveness, further monitor safety, and compare it with standard or equivalent treatments.

- **Phase IV**—After a drug is licensed by the FDA, researchers track its safety, seeking more information about its risks, benefits, and best use in “real-world” settings.

CML: Chronic Myelogenous Leukemia. A specific form of cancer that affects white blood cells.

Enzyme: A protein or molecule that speeds up a chemical reaction in a living cell.

In vitro: “In glass,” referring to an experiment done in a test tube or an artificial, non-living system.

Leukemia: Any cancer that affects normal production of blood cells.

Oncogene: A gene that contributes to the production of a cancer; usually a mutated form of a normal gene.

Orphan disease: In the U.S. an orphan disease, or rare disease, affects fewer than 1 in 1,500 people. They are mostly genetic conditions passed on from parent to child.

Translational research: The process of connecting basic research to applied medicine or treatment; sometimes described as “From Bench to Bedside.”

Translocation: Movement of a fragment of one chromosome to a different chromosome.

3 Rs of animal research:

- **Replacement:** Replacing conscious, living vertebrates with cell or tissue cultures, computer models, simulation models, and/or less developed animal species.
- **Reduction:** Using the fewest number of animals possible in a research project to gain valid results.
- **Refinement:** Using any technique or procedure that minimizes distress or enriches the life of an animal used in research.

SOURCES

Brody, J. E. (2010, January 18). Living with a formerly fatal blood cancer. *The New York Times*. Retrieved from http://www.nytimes.com/2010/01/19/health/19brod.html?_r=1

Clinical Trial Image (Man Receiving a H1N1 Vaccine Injection). Courtesy U.S. Navy, # 091119-N-1825E-253. U.S. Navy photo by Mass Communication Specialist 2nd Class Joseph Eballo/Released. http://www.navy.mil/view_image.asp?id=78844

Computer Modeling Image (Researcher with 3-D Model of Protein). Courtesy of Wellcome Images. Mol. Biophysics, Oxford Univ., Wellcome Images, #B000388. <http://wellcomeimages.org>

Drug Containers Image. Courtesy of Microsoft Clipart. <http://office.microsoft.com/en-us/images/results.aspx?qu=00402126&ex=2>

Drug Discovery & Development: Understanding the R&D Process. Retrieved from <http://www.innovation.org>

Imatinib. (2012, June 4). In *Wikipedia, The Free Encyclopedia*. Retrieved from <http://en.wikipedia.org/w/index.php?title=Imatinib&oldid=495877778>

In vitro Image of Hand Holding Petri Dish. Courtesy of Wikimedia Commons, Umberto Salvagnin. http://commons.wikimedia.org/wiki/File:Cell_culture.jpg#file

In vitro Image of Test Tubes. Courtesy of Microsoft Clipart. <http://office.microsoft.com/en-us/images/results.aspx?qu=research&ex=1&AxInstalled=copy&Download=MP900406576&ext=JPG&c=0#ai:MP900406576|mt:2|>

Li, J. J. (2006). *Laughing gas, Viagra, and Lipitor: The human stories behind the drugs we use*. New York, NY: Oxford University Press.

Maze Image. Courtesy of Wikimedia Commons, Nandhp. http://commons.wikimedia.org/wiki/File:Prim_Maze.svg

Microscope Image. Courtesy of Microsoft Clipart. <http://office.microsoft.com/en-us/images/results.aspx?qu=microscope&ex=2#ai:MP900305708|mt:2>

Nowell, P. C. (2007). Discovery of the Philadelphia chromosome: A personal perspective. *The Journal of Clinical Investigation*, 117 (8) 2033-2035. Retrieved from <http://www.jci.org/articles/view/31771>


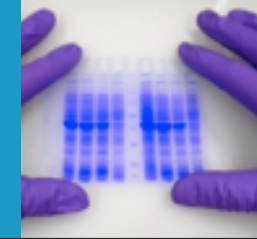




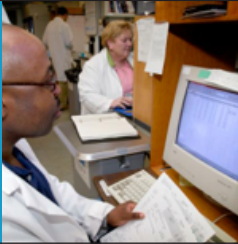




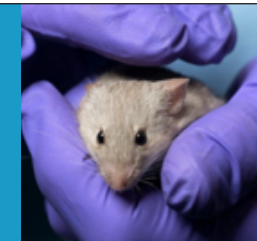
Researcher Holding a Mouse Image. Courtesy of Wellcome Images. <http://wellcomeimages.org/indexplus/image/C0018221.html>

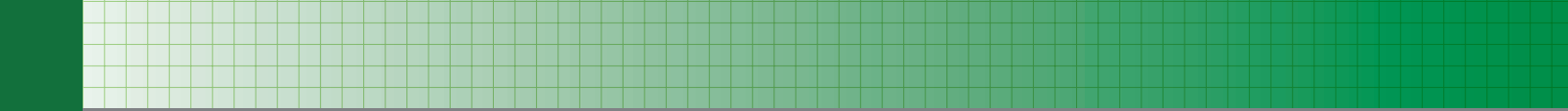
STUDENT HANDOUT 4.1

Card Set #1: Translational Research Process

Name _____ Date _____ Period _____

Instructions: Cut out the cards and put them in chronological order.

 <p>The Food and Administration (FDA) requires information on the results of animal studies, manufacturing information, and procedures for upcoming clinical trials before humans can be used in drug research.</p>	 <p>New and improved technologies drive the process of scientific discovery.</p>
 <p>Drug given to a larger number (100-300) of volunteers with the disease to see how effective the drug is in treating the disease and to look for side effects.</p>	 <p>Drug tested <i>in vitro</i> on target molecules to determine effectiveness.</p>
 <p>The Food and Drug Administration (FDA) requires that research results are reviewed and approved before releasing the drug to the market.</p>	 <p>Computer modeling shows possible interactions of the drug with the body.</p>
 <p>Computers are used to design possible candidate drugs that will "fit" with a target, such as an enzyme involved in a known disease pathway.</p>	 <p>Drug given to larger numbers (1,000-3,000) of volunteers with the disease to confirm its effectiveness and to continue to look for risks and side effects from longer use.</p>
 <p>Final product approved for market.</p>	 <p>Drug tested <i>in vitro</i> on cells or tissues to determine effectiveness.</p>
 <p>Drug given to small number (20-80) of healthy volunteers to evaluate safety and identify side effects.</p>	 <p>Drug tested in animal models.</p>



TEACHER RESOURCE 4.1

Notes for Card Set #1: Translational Research Process

These cards are in the correct order (see **Teacher Notes**).

	New and improved technologies drive the process of scientific discovery.
	Computers are used to design possible candidate drugs that will “fit” with a target, such as an enzyme involved in a known disease pathway.
	Computer modeling shows possible interactions of the drug with the body.
	Drug tested <i>in vitro</i> on target molecules to determine effectiveness.
	Drug tested <i>in vitro</i> on cells or tissues to determine effectiveness.
	Drug tested in animal models.

BASIC RESEARCH

ANIMAL RESEARCH

Teacher Notes:

This card set: The process of connecting basic research to **applied research** is called **translational research**. This is sometimes described as “From Bench to Bedside”—from the scientist’s laboratory bench to the physician’s bedside care of a patient.

The group of five cards on this page represent scientific discovery through **basic research**. Basic research (sometimes called bench science) furthers general scientific understanding of how the natural world works. This is often academic research.

While these five cards are shown in generally the ‘correct’ order, they can be arranged in different orders as this is a cyclical process that informs and changes itself over time.

These cards are in the correct order (see *Teacher Notes*).

	<p>The Food and Administration (FDA) requires information on the results of animal studies, manufacturing information, and procedures for upcoming clinical trials before humans can be used in drug research.</p>	<p>HUMANS IN RESEARCH</p>	<p>Teacher Notes:</p> <p>Applied research is when knowledge gained from basic research is used to improve human or animal health with treatments or cures for diseases. This is often done by for-profit companies.</p>
	<p>Drug given to small number (20-80) of healthy volunteers to evaluate safety and identify side effects.</p>		
	<p>Drug given to a larger number (100-300) of volunteers with the disease to see how effective the drug is in treating the disease and to look for side effects.</p>		
	<p>Drug given to larger numbers (1,000-3,000) of volunteers with the disease to confirm its effectiveness and to continue to look for risks and side effects from longer use.</p>		
	<p>The Food and Drug Administration (FDA) requires that research results are reviewed and approved before releasing the drug to the market.</p>		
	<p>Final product approved for market.</p>	<p>NEW TREATMENTS</p>	

STUDENT HANDOUT 4.2

Card Set #2: The Story of Gleevec

Name _____ Date _____ Period _____

Instructions: Cut out the cards and put them in order of events.

After more than 400 *in vitro* tests using different shapes of molecules, one molecule is found to inactivate the BA enzyme. This will later be named Gleevec.

Phase I clinical trials begin with the drug. In this case, the drug was given to people with CML, not healthy volunteers. The study found that one daily pill was sufficient.

Phase III clinical trials begin.

Animal trials begin with the drug. The molecule is well-tolerated in rodents.

Later studies show the drug to be very effective in animals with CML.

The drug is approved for market in 2001. It is named Gleevec in the U.S.

Post-marketing research finds it to be safe and effective for treatment of ten different cancers.

Thanks to new **gene mapping** techniques, scientists learn that the translocation in the Philadelphia chromosome puts two genes, B and A, next to each other. (1984)

Phase II clinical trials are successful in showing the drug to be effective. (1999)

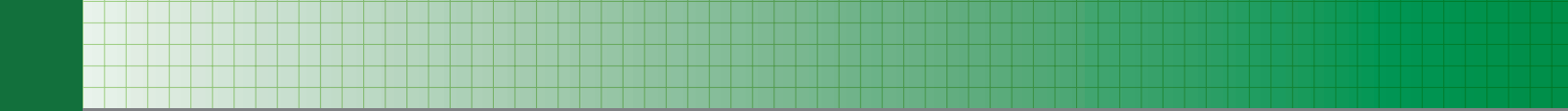
A chromosomal abnormality called the Philadelphia chromosome is found after new air drying techniques for cell preparation allow chromosomes to be seen more clearly. People with CML are found to have this abnormality.

The gene combination is found to make an abnormal BA **enzyme** that triggers cells to divide uncontrollably. This is the genetic cause of CML.

Scientists have a specific target: to inactivate the BA enzyme. They design and test hundreds of molecules *in vitro* to find one that shuts down BA. (1990-1992)

Advances in cell culture techniques allow scientists to study human leukemia cells. (1955)

The Philadelphia chromosome is found to result from chromosomes 9 and 22 trading genetic information in a **chromosomal translocation**.



TEACHER RESOURCE 4.2

Ordered Card Set #2: The Story of Gleevec

This card set is in the correct order with dates included.

Advances in cell culture techniques allow scientists to study human leukemia cells. (1955)

After more than 400 *in vitro* tests using different shapes of molecules, one molecule is found to inactivate the BA enzyme. This will later be named Gleevec. (1992)

A chromosomal abnormality called the Philadelphia chromosome is found after new air drying techniques for cell preparation allow chromosomes to be seen more clearly. People with CML are found to have this abnormality. (1960)

Animal trials begin with the drug. The molecule is well-tolerated in rodents. (1992)

Later studies show the drug to be very effective in animals with CML.

The Philadelphia chromosome is found to result from chromosomes 9 and 22 trading genetic information in a **chromosomal translocation**. (1972)

Phase I clinical trials begin with the drug. In this case, the drug was given to people with CML, not healthy volunteers. The study found that one daily pill was sufficient. (1998)

Thanks to new **gene mapping** techniques, scientists learn that the translocation in the Philadelphia chromosome puts two genes, B and A, next to each other. (1984)

Phase II clinical trials are successful in showing the drug to be effective. (1999)

The gene combination is found to make an abnormal BA **enzyme** that triggers cells to divide uncontrollably. This is the genetic cause of CML. (1987)

Phase III clinical trials begin.

Scientists have a specific target: to inactivate the BA enzyme. They design and test hundreds of molecules *in vitro* to find one that shuts down BA. (1990-1992)

The drug is approved for market in 2001. It is named Gleevec in the U.S.

Post-marketing research finds it to be safe and effective for treatment of ten different cancers.

Name _____ Date _____ Period _____

Ethical Guidelines Supporting Basic Research

Scientists and researchers at every level are trained in the ethical conduct of research which entails the use of and need for:

collaboration, peer review, multiple trials, repeatable trials,
skepticism, persistence despite setbacks, transparency,
rules against falsifying data

Ethical Guidelines Supporting Research with Animals

People working with animals follow **The 3 Rs** as ethical guidelines when working with animals:

- **Replacement:** Replacing conscious, living vertebrates with cell or tissue cultures, computer models, simulation models, and/or less developed animal species to the extent possible.
- **Reduction:** Using the fewest number of animals possible in a research project to gain valid results.
- **Refinement:** Using any technique or procedure that minimizes distress or enriches the life of an animal used in research.

Any institution that involves animals in research must also have an ***Institutional Animal Care and Use Committee (IACUC)***. This committee evaluates and oversees all aspects of the animal care and use program for that research facility.

Ethical Guidelines Supporting Humans in Research

The **Belmont Principles** inform and guide researchers working with human participants. They are:

- **Respect for Persons:** Respect for individuals and their ***autonomy***; obtain informed consent.
- **Maximize Benefits/Minimize Harms:** This stresses “doing good” and “doing no harm” by minimizing all potential harm(s) and maximizing potential benefit(s) to the subject as well as potential benefit to society.
- **Justice:** Be fair in distributing the benefits and burdens of research.

Research involving human participants must also be reviewed, monitored, and approved by an ***Institutional Review Board (IRB)***. IRBs are sometimes called “ethics committees.”

TEACHER RESOURCE 4.3

Making a Foldable

1. Tape two 8.5 x 11" sheets of paper together along the long end.
2. Fold the left margin in about 1.5" along the dotted line. Reopen it.
3. To the right of the fold, arrange *Card Set #1: Translational Research Process*. Tape/glue these in place when finished.
4. Fold the left margin in. On both sides of the flap, write BASIC RESEARCH, ANIMAL RESEARCH, HUMANS IN RESEARCH, and NEW TREATMENTS in the appropriate places (see below).
5. Arrange *Card Set #2: The Story of Gleevec* to the right of *Card Set #1*. Make sure the cards fall into the correct categories labeled in #4. Tape/glue in place.
6. Turn the foldable over and open the flap. Write in or glue the ethical guidelines (*Card Set #3*) that underlie each stage of biomedical research.

