

# DNAi Site Guide

# **Timeline**

# Pre 1920's

Johann Gregor Mendel, Friedrich Miescher, Carl Erich Correns, Hugo De Vries, Erich Von Tschermak-Seysenegg, Thomas Hunt Morgan

# 1920-49

Hermann Muller, Barbara McClintock, George Wells Beadle, Edward Lawrie Tatum, Joshua Lederberg, Oswald Theodore Avery

### 1950-54

Erwin Chargaff, Rosalind Elsie Franklin, Martha Chase, Alfred Day Hershey, Linus Pauling, James Dewey Watson, Francis Harry Compton Crick, Seymour Benzer

### 1955-59

Francis Harry Compton Crick, Paul Charles Zamecnik, Mahlon Hoagland, Matthew Stanley Meselson, Franklin William Stahl, Arthur Kornberg

# 1960's

Sydney Brenner, Marshall Warren Nirenberg, François Jacob, Jacques Lucien Monod, Roy John Britten

# 1970's

David Baltimore, Howard Martin Temin, Stanley Norman Cohen, Herbert W. Boyer, Richard John Roberts, Phillip Allen Sharp, Roger Kornberg, Frederick Sanger

# 1980's

Christiane Nüsslein-Volhard, Eric Francis Wieschaus, Kary Mullis, Thomas Robert Cech, Sidney Altman, Mario Renato Capecchi

### 1990-2000

Mary-Claire King, Stephen P.A. Fodor, Patrick Henry Brown, John Craig Venter Francis Collins, John Sulston

# Code

# Finding the structure

### **Problem**

What is the structure of DNA?





### **Players**

Erwin Chargaff, Rosalind Franklin, Linus Pauling, James Watson and Francis Crick, Maurice Wilkins

## Pieces of the puzzle

Wilkins' X-ray, Pauling's triple helix, Franklin's X-ray, Watson's base pairing, Chargaff's ratios

### Putting it together

DNA is a double-stranded helix.

# Copying the code

#### **Problem**

How is DNA copied?

### **Players**

James Watson and Francis Crick, Sydney Brenner, François Jacob, Matthew Meselson, Arthur Kornberg

## Pieces of the puzzle

The Central Dogma, Semi-conservative replication Models of DNA replication, The RNA experiment, DNA synthesis

# **Putting it together**

DNA is used as a template for copying information.

# Reading the code

#### **Problem**

How is the DNA code read?

### **Players**

Paul Zamecnik and Mahlon Hoagland, Sydney Brenner, Marshall Nirenberg, Marshall Nirenberg and collaborators, Har Gobind Khorana

### Pieces of the puzzle

Breaking the code, Cell-free extracts, The genetic code, The other codons, Defining the gene

### **Putting it together**

The DNA code is read in triplets.





# Controlling the code

#### **Problem**

How is the DNA code controlled?

# **Players**

François Jacob and Jacques Monod, Walter Gilbert

### Pieces of the puzzle

DNA packaging, The lac operon

### **Putting it together**

The DNA code is regulated by proteins

# **Manipulation**

## **Revolution**

#### **Problem**

How do you study a gene?

### **Players**

James Watson, Paul Berg, Herbert Boyer and Stanley Cohen, The controversy

#### Pieces of the puzzle

Restriction enzymes, DNA ligation, The first recombinant DNA, DNA transformation

### Putting it together

rDNA: more risk than reward?

# **Techniques**

### **Cutting & pasting**

Using enzymes to manipulate DNA

### **Sorting & sequencing**

Delivering foreign DNA into a cell

### **Transferring & storing**

Analyzing the activity of thousands of genes

### **Amplifying**

Determining the size and sequence of DNA fragments





### Large-scale analysis

Making many copies of DNA

## **Model organisms**

Using model organisms in research

### **Production**

#### **Problem**

Making insulin with recombinant DNA technology

# **Players**

Herbert Boyer, David Goeddel, Walter Gilbert

### Pieces of the puzzle

Synthetic insulin, Synthesizing the DNA, Isolating the DNA, The P4 facility

# **Putting it together**

Synthetic insulin was made using recombinant DNA.

### Genome

#### **Tour**

#### **Flyover**

The landscape of a chromosome

#### **Chromosome close-up**

Chromosome coiling and contents

### **Genome FISHing**

FISH for information about your chromosomes: Centromeres, Telomeres, Variation

#### Genome spots

Click on a "spot" to find out about the gene or genes at that location

# The Project

#### **Problem**

How do you map, sequence, and find all the genes in the human genome?

## **Players**

Pros & cons, Public consortium, Private project, Money, Technology, Competition and the media







### Pieces of the puzzle

Maps and markers, Storing DNA, Sequencing head to toe, Whole genome shotgun, Sequencing DNA, Dealing with the data, Finding genes

### Putting it together

Viewing our code for the first time

# **Genome Mining**

### **Meaning**

Meaningful sequences

### **DNA** analysis

Analyzing DNA

#### Gene features

What makes up a gene?

# **Gene finding**

Finding genes in DNA

### **Gene Boy**

A multi-function sequence analysis tool

# **Applications**

## **Human identification**

#### **Fingerprint**

DNA variations and fingerprints, The first DNA fingerprints, Today's DNA profile

### Case study 1

Sarbah vs. Home Office, Ghana Immigration Case, 1985

### Case study 2

State of Florida vs. Jones and Reesh, Murder at Rodman Dam, 1988

### Case study 3

The Innocence Project





# **Recovering the Romanovs**

## The Romanov family

The history of the Romanovs, the last Imperial family of Tsarist Russia

### The mystery of Anna Anderson

Anna Anderson claimed to be Anastasia, the missing Anastasia Romanov

## Science solves a mystery

DNA science was used to determine whether Anna Anderson was Anastasia

### Genes and medicine

### **Gene hunting**

Mary-Claire King, Mark Skolnick, Markers, The finish line

# **Gene testing**

Barbara Weber, Denise, Making a pedigree, Testing

### Genetic profiling

Patrick (Pat) Brown, Stephen Fodor, David Botstein, Techniques

### Drug design

Brian Druker, The Philadelphia chromosome, Bud's story, How Gleevec™ works

### Gene targeting

Mario Capecchi, Animal models, Techniques, Possibilities

# **Human origins**

### Our family tree

Meet the extended family

### **Comparisons**

Bones, Behavior, DNA

### Gene genealogy

Mitochondrial DNA, Y Chromosome, Other genome regions, A molecular clock?, Tracing ancestries

### **Migrations**

Follow the paths, Hear the stories







### Variation

Primate diversity, Interviews, Variation activity

# Chronicle

### Threat of the Unfit

### **Founders**

Bringing the eugenics movement to prominence

#### The fit and unfit

Pedigrees of the fit and unfit

#### **Threats**

The eugenicists' views on the socially "unfit"

### **Epilogue**

Eugenics as the "solution" to social problems

### **Trial of Carrie Buck**

### **Prologue**

Upholding the "legality" of sterilization

# **Players**

Carrie Buck, Emma Buck, Vivian Dobbs, Albert Priddy, Aubrey Strode, Irving Whitehead, Arthur Estabrook, Harry Laughlin, Oliver Wendell Holmes

### **Trials**

Buck vs. Bell: forced sterilization of the "feebleminded"

### **Outcome**

The Supreme Court decision

### **Epilogue**

The truth about Buck vs. Bell

### In the Third Reich

### Taking the torch

Nazi eugenics

#### The final solution

"The final solution" to mental illness





# **Applying the solution**

The concentration camps

## **Epilogue**

After World War II

# **Living with Eugenics**

## Living with depression

The highs and lows of manic depression

### Kallikak revisited

Comparing family pedigrees

## The diagnosis

Dealing with the diagnosis

# **Eplilogue**

The "eugenic quandary," prenatal testing for manic depression

