‘HOW TO BE A RIBOSOME’: THE DEVELOPMENT OF A NOVEL METHOD OF TEACHING PROTEIN TRANSLATION IN THE HIGH SCHOOL CLASSROOM

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by

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ABSTRACT

As part of its educational outreach department, The Cornell Centre for Materials Research (CCMR) maintains a library of experiment kits that can be loaned free of charge to any science teacher in the United States. These kits allow teachers to deliver innovative lessons on a wide variety of Science topics aligned to the Next Generation Science Standards. This project aimed to develop a new kit for high school Biology, a subject which is currently lacking in the lending library. This kit, which teaches the central biochemical process of protein translation, was built around the development of a novel set of 3D-printed classroom manipulatives- jigsaw-like pieces which allow students to actively translate an mRNA code to an amino acid sequence. A set of these pieces, a module guiding teachers through the lesson, student activity sheets, and an accompanying PowerPoint presentation are presented as the components of the completed kit.

BIOGRAPHICAL SKETCH

Rachel Gray is a graduate student from Edinburgh, Scotland. She graduated with a B.Sc. (Hons) in Biomolecular Science from the University of St Andrews in June 2018.

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I would like to extend my sincere thanks to the following people for their assistance with this project;

- To Mark Walsh, Cornell Centre for Materials Research (CCMR) Outreach department, for project guidance and resources.

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INTRODUCTION

The Cornell Centre for Materials Research (CCMR) Educational Programs Office maintains a 'Lending Library of Experiments'.[1] From this resource, any school teacher in the United States can access lesson plans and student activity sheets to allow them to deliver engaging Science lessons that have been designed by Cornell faculty and graduate students. For many of these lessons, kits containing the required equipment and/or materials are also available and can be sent to any school free of charge. Such kits have proven to be popular in schools which lack laboratory space or resources.

The kits in the lending library are aligned to the Next Generation Science Standards. These standards are widely adopted throughout the United States and provide a framework for the teaching of Science in K-12 classrooms.[2] Of the fifty kits which are currently available from the lending library, Biology or Biochemistry standards are the focus of only three.[1] With this challenge in mind, this project aimed to create a novel method of teaching the basic Biochemistry of protein translation in the high school classroom, with the hope of developing the result into a new kit available from the CCMR lending library.

CHOICE OF LESSON TOPIC

Despite being at the heart of every living cell on earth, many Biochemistry topics taught at the middle or high school level suffer from being uninteresting and therefore difficult to teach effectively. The central biochemical processes of DNA replication, transcription to mRNA (messenger ribonucleic acid) and translation of this mRNA to peptides are no exception, particularly as there is no school-level way of observing such processes directly, so off-putting abstract explanations are frequently used.[3] Additionally, the nucleic acid bases - adenine, guanine, cytosine, thymine, and uracil- and amino acid components that are key to understanding the basics of transcription and translation are often referred to only by a single letter (A,G,C,T and U for the bases and the one-letter code for amino acids). Whilst this approach simplifies the structures of these molecules to an appropriate level, when students approach these topics for the first time, they can struggle with long strings of seemingly meaningless letters, a particular issue for those suffering from dyslexia or other learning difficulties.[4]

Whilst these topics remain challenging to teach, the human genome and proteome have come to feature more and more clearly in the public imagination over the last several years. As biologics replace small molecules as the fastest growing type of pharmaceuticals[5], and analysis of individual genomes for familial history or medical information becomes ever more commonplace[6], the need for an accurate basic understanding of our DNA and the proteins it encodes grows in importance.

Whilst replication, transcription and translation would all lend themselves to the development of hands-on activities to better engage students, a single lesson doesn't offer enough time to cover all of these topics in the required detail, and developing more than one lesson was beyond the time-constraints of this project. Because, at least at a school level, translation is viewed as the more complex subject to teach- requiring the introduction of a number of different types of biomolecules and cellular structures-, and lends itself well to providing real world examples- many human diseases are caused by mutated protein structures- this process was chosen as the most appropriate topic for a new lending library kit.

Gaining an accurate understanding of the process of protein translation will allow pupils to meet the following Next Generation Science Standards;

> “**HS-LS1-1** From Molecules to Organisms: Structures and Processes
> Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins, which carry out the essential functions of life through systems of specialized cells
>
> **HS-LS3-1** Heredity: Inheritance and Variation of Traits
> Ask questions to clarify relationships about the role of DNA and chromosomes in coding the instructions for characteristic traits passed from parents to offspring.
>
> **MS-LS1-5** From Molecules to Organisms: Structures and Processes
> Construct a scientific explanation based on evidence for how environmental and genetic factors influence the growth of organisms.
>
> **MS-LS3-1** Heredity: Inheritance and Variation of Traits
> Develop and use a model to describe why structural changes to genes (mutations) located on chromosomes may affect proteins and may result in harmful, beneficial, or neutral effects to the structure and function of the organism.” [2]

DEVELOPMENT OF THE 3D-PRINTED PIECES

From the outset, this project centered around the development a new type of classroom manipulative in order to teach protein translation in an engaging manner. Virtual and physical manipulatives from interactive computer simulations to simple counters have long been shown to be effective in increasing conceptual understanding and engagement in classes as diverse as kindergarten children and undergraduates.[3,7,8] Using manipulatives as part of active learning can encourage students to develop their own explanations in terms they fully understand, and help them to dispel misapprehensions they may have on a topic. [8] Additionally, the use of hands-on models in combination with more traditional activity types can help the teacher to engage pupils across the spectrum of sensory learning styles, particularly appealing to kinesthetic, visual and auditory learners.[9]

Understanding the process of translation at a high school level requires students to understand the roles (and to an extent, structures), of the molecules, macromolecules and cellular structures as detailed in table 1. Based on these important central concepts, the kit pieces were designed, first by hand-drawing and eventually using 3D-printing software Tinkercad[10], to represent individual nucleic acid bases and amino acid-bound tRNA (transfer ribonucleic acid) molecules. Whilst the bases and anti-codon regions of the 'tRNAs' make use of simple shapes to demonstrate that each base has a distinct physical shape that is recognised by another specific shape, the remaining portion of the tRNA pieces were designed based on the conventional 'loop' representation used to describe these molecules in existing educational resources, as shown in figure 1.[11,12]

Figures 1 and 2 compare the molecular structures, conventional representations and kit shapes of tRNA molecules and nucleic acid bases. The simplified base and anti-codon shapes offer students the ability to physically 'click' the pieces together in order to establish the amino acid sequence that would be encoded by a given mRNA sequence, hence, they ‘become the ribosome’ and actively engage[13] with the scientific content.

Table 1: The essential cellular components required for protein translation and their functions, at the level as taught in the high school classroom.[12,14]

Molecule/Macromolecule/Structure	Role in Translation/Important Terms
Ribosome	Essential in protein synthesis. Brings together the mRNA strand and the corresponding amino-acid bound tRNA molecules so that the amino acids can be joined to form a peptide.
mRNA	Carries the ‘code’ required for the protein from the nucleus to the ribosome. Consists of RNA bases. Three adjacent bases are called a codon, which pair with the anti-codon on the correct amino acid-carrying tRNA molecule.
tRNA	Act as a bridge between the mRNA strand. Contain an anticodon which pairs with the correct codon so that the amino acids are added to peptide strands in the correct order.
Amino Acids	Are the building blocks of proteins. There are 20 common amino acids that are commonly represented by single or three-letter codes.

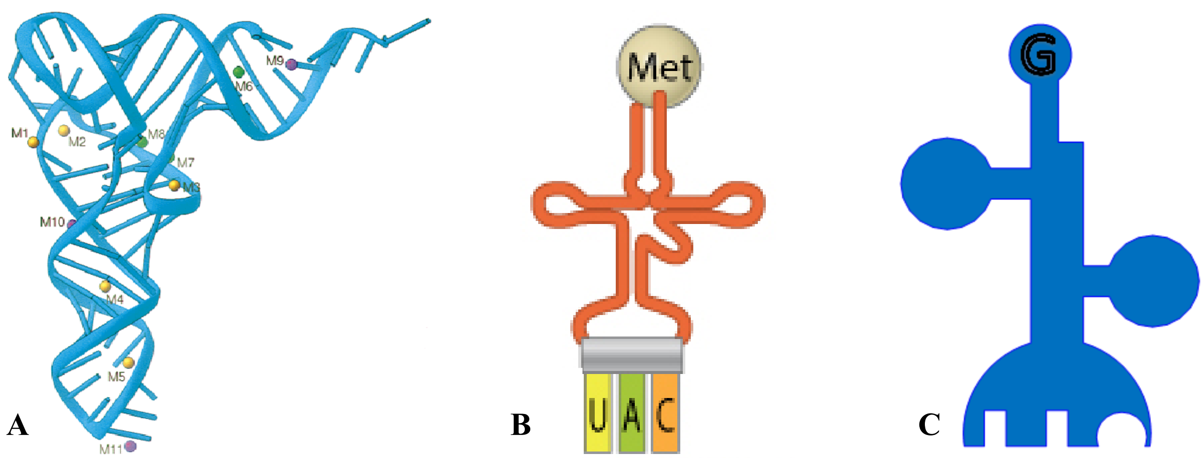

Figure 1: Representations of the structure of amino acid-bound tRNA molecules. A) the structure of yeast tRNA as determined by x-ray crystallography, shown as a ribbon diagram. Taken from[17]. B) an example of typical representation of a tRNA molecule carrying a bound amino acid that is common in high school-level resources. Adapted from[11] C) The shape of the developed kit tRNA pieces, with a ‘bound amino acid’ attached at the top and ‘anti-codon’ region represented by shapes at the bottom.

The design and 3D-printing of the kit pieces were deceptively time-consuming. Several iterations of the shapes were tested as prototypes before the final forms were produced. After several designs of the base pieces that more closely resembled the molecular structures shown in figure 2 were prototyped on paper, it was decided that these were unnecessarily complex for the level required and would be prohibitively complex to 3D print at the small size intended (approximately 2cm x 3cm). Additionally, once the simpler shapes were adopted for the base pieces, several card and 3D-printed prototypes were required in order to ensure that they would successfully fit together with the tRNA pieces.

Subtle details of the design allow for several important aspects of the protein translation process to be demonstrated. For example, the tRNA pieces have been adapted to fit directly beside each other, with the bottom 'anti-codon loops' touching. This means that the 'codons' within the mRNA strand do not need to be separated to be matched up with the corresponding tRNA piece, staying true to the fact that the mRNA strand is a continuous molecule that is 'read' in sections. A demonstration of how the pieces fit together to enable the students to translate sequences of mRNA code is shown in figure 3b.

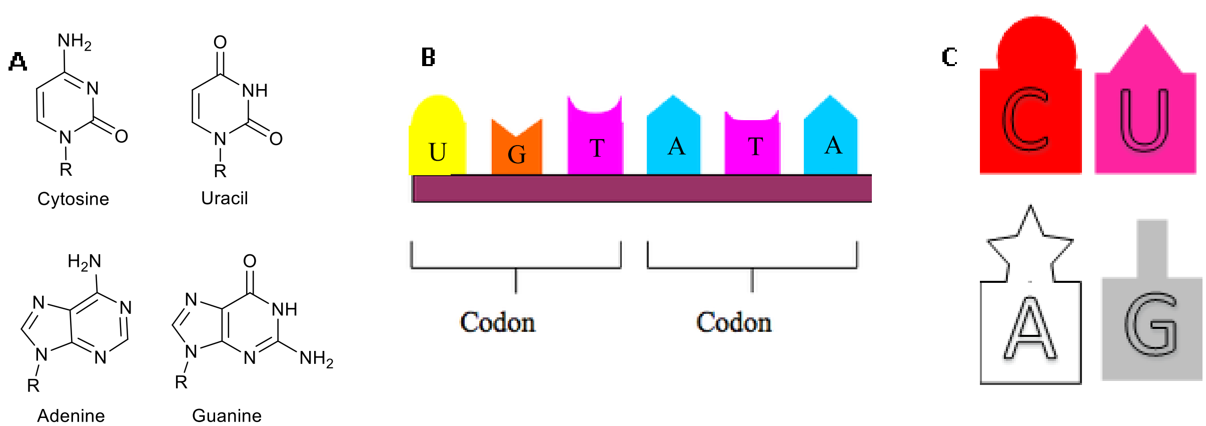

Figure 2: Representations of the RNA bases. A: molecular structures.[18] B: typical shape representations found in high school level resources, adapted from[12]. C: Shapes of the base kit pieces.

A complete set of the finalised 3D pieces consists of twenty ‘tRNA’s’, which contain an ‘anti-codon’ corresponding to each of the amino acids, fifteen of each of the ‘C’, ‘A’ and ‘G’ base pieces and twenty ‘U’ pieces. This complete set of pieces is shown in figure 3a.

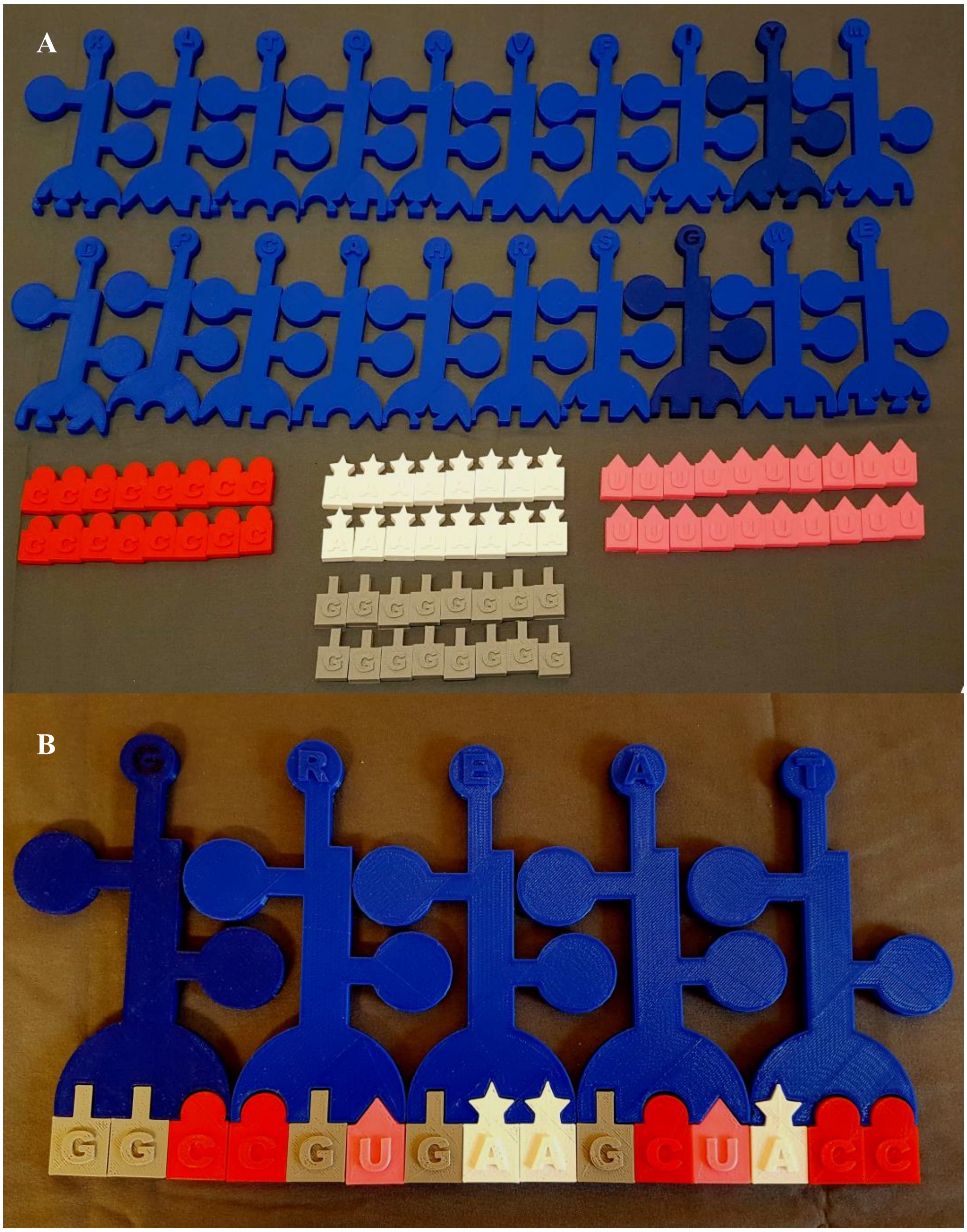

Figure 3: A) The complete set of 3D-printed pieces, designed to be shared between 2-3 students, containing twenty amino acid-bound ‘tRNAs’ and 65 ‘bases’. B) an mRNA code is brought together with the corresponding ‘tRNAs’ to translate to the peptide sequence G-R-E-A-T (see activity 3, question 2 in the student activity sheet (appendix 2)).

DEVELOPMENT OF THE LESSON ACTIVITIES

During and after the design of the 3D manipulatives, five student activities were designed to accompany their use in the classroom. These activities were created to meet the following five aims, which were developed to align with the Next Generation Science Standards given above.

Educational aims of the lesson- at the end of the lesson, students will:

A. Understand the process of protein translation from an mRNA ‘code’ to an amino acid sequence that eventually becomes a functional protein.
B. Be able to translate a selection of codons to amino acid sequences using the kit pieces.
C. Understand how small changes in the DNA and mRNA code can significantly alter the sequence of amino acids in a protein and therefore lead to problems with how the protein functions.
D. Be able to describe how insertions, deletions and substitutions can affect the amino acid sequence in a translated protein.
E. Be able to describe the simplified disease mechanism of cystic fibrosis and recognise that it is caused by a change in just one amino acid in a single protein.

In order to ensure that the information is conveyed to students in a manageable format, each activity focusses on one aspect of the translation process (or relevant processes before or after translation). The purpose and an outline of each activity are given in table 2. In the lesson plan suggested in the teacher module (appendix 1), teachers review key concepts from each activity (or pair of activities) before moving on to the next. The activities can also easily be split over more than one lesson if teachers wish to spend more time on particular aspects of the translation process. The full activities are given in the student activity sheets (appendix 2).

Table 2: Summary of the purpose and outline of each of the lesson activities.

Activity	Purpose	Outline
1: Journey Through the Cell	Students will review the relevant cell parts and the processes which must occur before translation can take place.	The students race in groups to accurately complete the 'Journey through the cell', by filling in the answers on the second and third pages of the worksheet. Answers are provided on the accompanying PowerPoint (appendix 3).
2: Introducing the Kit Pieces	Students will familiarise themselves with the kit pieces and relate them to the terms introduced at the end of the last activity.	Students use the terms in the word box to correctly label the parts of the diagram of the kit pieces. Answers to this activity are provided in the PowerPoint and module sheet (appendix 1).
3: Translation: from mRNA to Protein	Using the kit pieces, students will translate given mRNA sequences to their corresponding peptides, and relate amino acid sequences back to their mRNA codes.	The students use the small base pieces to 'write out' the codes given in their activity sheets. They can then translate this to an amino acid sequence by locating the tRNA pieces that match up with each codon and bringing the pieces together. The questions in this activity ask them to translate mRNA sequences to peptide sequences and determine the mRNA sequence that led to certain sequences of amino acids.

4: Mutations	This activity also uses the kit pieces to introduce the concepts of point mutations, insertions, deletions and substitutions. Students observe the changes in peptide sequence resulting from changing the mRNA code.	Students will answer the questions using the kit pieces, as in activity 3, but now use them to explore how changing, or mutating, the mRNA sequence effects the amino acid sequence that results from translation.
5: From DNA to Characteristics	Students will answer three short questions about cystic fibrosis and how the DNA and mRNA encoding the relevant transporter protein are affected in people with this condition.	Students answer the three questions by integrating the information in the table with what they have learned in the previous activities. Some students may find these questions more challenging, so this activity is a good way to test understanding.

In addition to meeting the educational aims and realising the benefits of using manipulatives as detailed above, the activities were also designed with other central educational ideas in mind. All of the activities (except perhaps activity 5, though this is down to teacher discretion) are designed to be undertaken by students in pairs or groups of three. Cooperative learning such as this is a popular and effective method of increasing student engagement and conceptual understanding, as well as providing students the ability to improve classroom relationships.[13,15] Additionally, activity one, a 'race through the cell', encourages intergroup competition, another strategy which has been shown to be highly beneficial to student productivity and achievement.[15]

Problem solving and enquiry-based learning are also integral parts of the activities. This is particularly apparent in activity five, which asks students to integrate the knowledge they have acquired in the previous activities with the information given to predict the symptoms of cystic fibrosis. Less obvious examples include questions three to five in activity 3, where students must use the kit ‘in reverse’, to establish the mRNA code that matches a given peptide sequences. Question five in this activity also requires the students to understand, without explicit instruction, that when amino acids appear repeatedly in a protein sequence, their codons must also appear more than once. Such questions give the teacher the opportunity to establish which students have gained a full understanding of the content and those who may require further explanation. They also encourage students to develop their problem-solving skills and relate the information to real-life examples, which can also improve engagement with the material.[16]

Additional activity suggestions that complement the content of this lesson, including a research activity, have also been included in the teacher module (appendix 1). These could be particularly useful if the teacher were to choose to split the activities over two lessons. The accompanying PowerPoint presentation (appendix 3) was designed to complement the activities and includes examples of the variety of online videos available to assist the teaching of this topic, as well providing the answers for each of the activities.

ASSESSMENT

Whilst methods of assessing the student's understanding following the lesson activities will develop as the kit is tested in the classroom environment, a preliminary rubric for this purpose is given in table 3. In this rubric, the number classification system corresponds to the extent to which individual students have met the expectations for the activity, where 4= exceeds expectations, 3= meets expectations consistently, 2= meets expectations occasionally, and 1= not meeting expectations.

Table 3: Preliminary rubric for assessing students understanding of the lesson activities.

	Engage	**Explore**	**Explain**
4	Shows leadership in the group activities and discussion and demonstrates an in depth understanding of the translation process and how mutations affect the peptide sequence.	Completes worksheet accurately while providing an explanation for the correct answers obtained.	Provides and in-depth explanation of findings and makes excellent use of vocabulary terms. Fills out worksheet clearly.
3	Participates in the groupwork and discussion and shows an understanding of translation and mutation.	Completes worksheet accurately.	Provides clear explanation of findings and uses vocabulary terms. Fills out worksheet clearly.
2	Contributes to the discussion and groupwork, making use of the kit pieces, but shows little understanding of translation and mutation.	Makes some mistakes in answering the worksheet questions.	Provides a limited explanation of findings, uses some vocabulary terms. Fills out some of the worksheet.
1	Does not participate in discussion or make use of the kit pieces. Shows no understanding of translation or mutations.	Does little to complete the worksheet.	Is not clear in explanation of findings, does not use vocabulary terms. Does not fill out worksheet.

If teachers prefer not to use the rubric, evidence of understanding of the content of lesson can also be in the form of oral communication with the teacher or observed between students. The content of the lesson also means that it lends itself well to a wide variety of existing formal or informal assessment materials which test understanding of protein translation. A lack of understanding should also be physically apparent if a student struggles to use the pieces correctly in activities three and four.

FUTURE DIRECTIONS

Funding dependent, it is hoped that this project will soon be developed into a full lesson kit that will be added to the CCMR 'Lending Library of Experiments' and will therefore be available to any high school in the country free of charge. This would require the production of nine more sets of 3D-printed pieces, assuming that pupils in a class of thirty work in groups of no more than three during the lesson.

The lesson plan and activities as they are designed at present are awaiting a classroom trial, which is planned to take place in May 2019. This will provide the springboard to develop the activities and resources based on initial feedback from students and teachers. Teachers visiting Cornell during the summer of 2019 as part of a series of STEM (Science, Technology, Engineering and Mathematics) teacher workshops will also be asked to provide feedback on the activities as part of the initial trial process. It is expected that the structure of the lesson and how the kit is used will continuously evolve as it is used in the classroom. All of the materials in the kits are also expected to be adapted to the needs of the individual classes by the teachers if necessary.

It is also hoped that the current resources, which have been designed to meet the high school curriculum, can and will be easily adapted to meet the simpler middle school standards, increasing the utility of the kit. Additionally, as is the case for many of the kits currently in the lending library, once the activities have been tested and finalised, they are frequently translated into Spanish in order to further widen their educational reach.

The design of the 3D pieces could also easily be extended to further related activities. As mentioned above, other central biochemical processes such as DNA replication and transcription also suffer from being abstract and difficult to teach. With the simple designs of the nucleic acid base pieces in the kit, it is easily imaginable that complementary sets of small pieces could be designed to form parts of ‘sister’ replication and transcription lending library kits. To this end, all of the 3D-printed shapes are available virtually, and can be easily developed and/or adapted using basic 3D modelling software. This also presents the benefit that the kit can be sent anywhere electronically, so could be reproduced on any 3D-printer for use and development by schools nationwide.

REFERENCES

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APPENDIX 1: TEACHER MODULE SHEET

How to be a Ribosome- Describing How Proteins are Made
Author(s): Rachel Gray
Date Created: March 2019
Subject: Biology
Grade Level: High School
Standards: Next Generation Science Standards (www.nextgenscience.org) **HS-LS1-1** From Molecules to Organisms: Structures and Processes Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins, which carry out the essential functions of life through systems of specialized cells **HS-LS3-1** Heredity: Inheritance and Variation of Traits Ask questions to clarify relationships about the role of DNA and chromosomes in coding the instructions for characteristic traits passed from parents to offspring.
Schedule: 60-90 Minute Class
CCMR Lending Library Connected Activities: Extracting DNA Gel Electrophoresis

Objectives:

Students will learn about how cells make proteins. They will model the process of translation from mRNA code to peptide sequence using the kit 'jigsaw' pieces. They will then explore how errors in the code can lead to disease.

Vocabulary:

- Codon
- Anti-codon
- Amino Acid (inc. one-letter code)
- tRNA
- Ribosome
- Point mutation
- Deletion
- Insertion
- substitution
- DNA
- mRNA
- Peptide
- Protein
- Transcription
- Translation
- Cystic Fibrosis

Students Will:

-Understand the process of protein translation from an mRNA 'code' to an amino acid sequence that eventually becomes a functional protein.

-Be able to translate a selection of codons to amino acid sequences using the kit pieces.

- Understand how small changes in the DNA and mRNA code can significantly alter the sequence of amino acids in a protein and therefore lead to problems with how the protein functions.

-Be able to describe how insertions, deletions and substitutions can affect the amino acid sequence in a translated protein

-Be able to describe the simplified disease mechanism of cystic fibrosis and recognise that it is caused by a change in just one amino acid in a single protein.

Materials:

For each group (1-3 students):

- Set of 'tRNAs' x 20
- 4 sets of 20 'RNA bases': 20 pieces each of G, C, U and A

For each student:

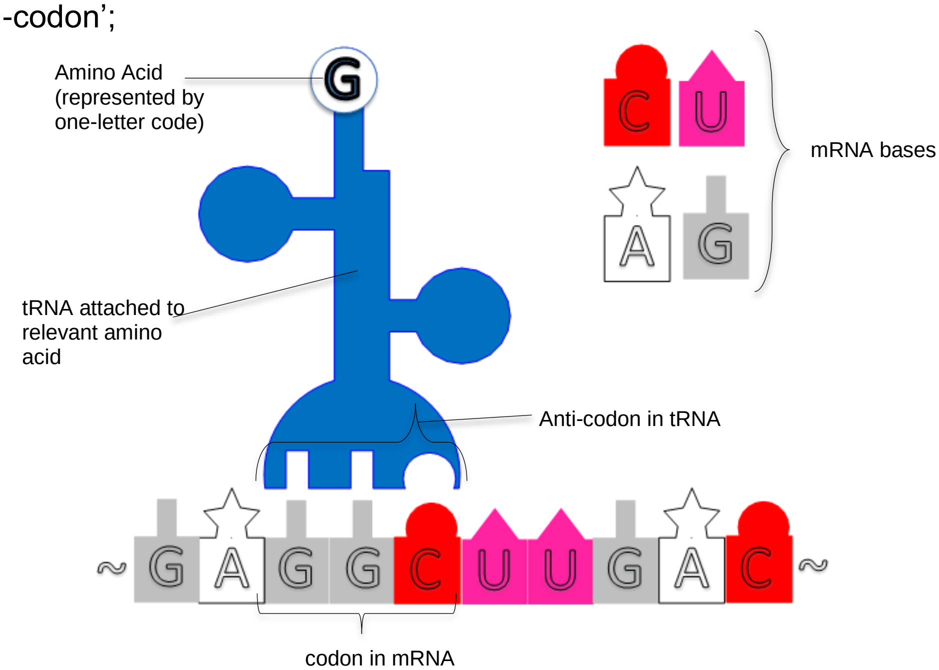
- Activity Sheet

Science Content for the Teacher:

See the following article for detailed background on protein translation:
https://www.nature.com/scitable/topicpage/translation-dna-to-mrna-to-protein-393

This activity assumes that students are already familiar with protein transcription, can successfully transcribe a DNA sequence to mRNA (see activity 1), and have an understanding of the names and roles of the cellular organelles.

In order to make the process of protein translation more accessible, this kit uses 3D-printed jigsaw-like pieces to represent a) the bases found in mRNA, A, U, G and C and b) tRNA molecules attached to the amino acid that corresponds to their 'anti-codon';



The students then take on the role of the ribosome, 'translating' a code of mRNA bases to peptides by physically bringing the code pieces together with the correct tRNA's. See the short animation in the slideshow for a visual representation of this process.

The kit can then also be used to explore the role of genetic mutation. In activity 4, the students will introduce 'mutations' to given mRNA codes and explore the effect these have on the resulting amino acid sequence.

Classroom Procedure:

The PowerPoint presentation designed to accompany the lesson activities is provided as part of this kit, but tailoring the content to the class is expected. A suggested lesson outline is as follows.

Activity 1: Journey Through the Cell Students will review the relevant cell parts and the processes which must occur before translation can take place.	
Before	Divide the students into groups of 3 and provide each group with a complete set of 'tRNAs and bases' and each student with an activity sheet. Introduce activity 1 as a 'race through the cell' and start every group at the same time.
Activity	The students race in groups to accurately complete the 'Journey through the cell', by filling in the answers on the second and third pages of the worksheet. Check students answers as they fill them in.
After	Review the answers to activity one as a class (given on the PowerPoint). Introduce or review the principles of translation. In order to successfully complete the following tasks, the students must have a basic understanding of the terms codon, anti-codon, tRNA, amino acid and peptide sequence. Videos are provided on the slides to assist explanations.

Activity 2: Introducing the Kit Pieces Students will familiarise themselves with the kit pieces and relate them to the terms introduced at the end of the last activity.	
Activity	Students use the terms in the word box to correctly label the parts of the diagram of the kit pieces. Answers to this activity are provided in the PowerPoint and shown above.

Activity 3: Translation: from mRNA to Protein Using the kit pieces, students will translate given mRNA sequences to their corresponding peptides, and relate amino acid sequences back to their mRNA codes.	
Activity	The students will need to use the small base pieces to ‘write out’ the codes given in their activity sheets. They can then translate this to an amino acid sequence by locating the tRNA pieces that match up with each codon and bringing the pieces together. The questions in this activity ask them to translate mRNA sequences to peptide sequences *and* determine the mRNA sequence that led to certain sequences of amino acids. The students should be reminded that the kit pieces must be laid out with the letters facing upwards for the activities to work correctly.
After	Review the answers to activities 2 and 3. Introduce or review the concept of DNA mutation, and how such mutations can therefore be passed on to the mRNA and protein.

Activity 4: Mutations This activity also uses the kit pieces to introduce the concepts of point mutations, insertions, deletions and substitutions. Students observe the changes in peptide sequence resulting from changing the mRNA code.	
Activity	Students will answer the questions using the kit pieces, as in activity 3, but now use them to explore how changing, or mutating, the mRNA sequence effects the amino acid sequence that results from translation.

<table>
<tr><td colspan="2">Activity 5: From DNA to Characteristics
Students will answer three short questions about cystic fibrosis and how the DNA and mRNA encoding the relevant transporter protein are affected in people with this condition.</td></tr>
<tr><td>Activity</td><td>Students answer the three questions by integrating the information in the table with what they have learned in the previous activities. Some students may find these questions more challenging, so this activity is a good way to test understanding.</td></tr>
<tr><td>After</td><td>The answers to activities 4 and 5 are also given in the PowerPoint if time allows for a review. Relevant additional activity suggestions for groups who finish early are detailed below.

At the end of the lesson, activity sheets can be collected for assessment. Please ask the students to count the pieces back into the kit to prevent losses!</td></tr>
</table>

Assessment:

The following rubric can be used to assess students during each part of the activity. The term "expectations" here refers to the content, process and attitudinal goals for this activity. Evidence for understanding may be in the form of oral as well as written communication, both with the teacher as well as observed communication with other students. Specifics are listed in the table below.

4= exceeds expectations
3= meets expectations consistently
2= meets expectations occasionally
1= not meeting expectations

	Engage	Explore	Explain
4	Shows leadership in the group activities and discussion and demonstrates an in depth understanding of the translation process and how mutations affect the peptide sequence.	Completes worksheet accurately while providing an explanation for the correct answers obtained.	Provides and in-depth explanation of findings and makes excellent use of vocabulary terms. Fills out worksheet clearly.
3	Participates in the groupwork and discussion and shows an understanding of translation and mutation.	Completes worksheet accurately.	Provides clear explanation of findings and uses vocabulary terms. Fills out worksheet clearly.
2	Contributes to the discussion and groupwork, making use of the kit pieces, but shows little understanding of translation and mutation.	Makes some mistakes in answering the worksheet questions.	Provides a limited explanation of findings, uses some vocabulary terms. Fills out some of the worksheet.
1	Does not participate in discussion or make use of the kit pieces. Shows no understanding of translation or mutations.	Does little to complete the worksheet.	Is not clear in explanation of findings, does not use vocabulary terms. Does not fill out worksheet.

Resources:

An accessible but detailed video describing protein translation:

- https://www.khanacademy.org/science/biology/gene-expression-central-dogma/translation-polypeptides/v/translation-mrna-to-protein

An overview of replication, transcription and translation:

- https://www.khanacademy.org/science/biology/gene-expression-central-dogma/translation-polypeptides/v/rna-transcription-and-translation

An accessible online module covering the basics of genetic mutation:

- https://www.bbc.com/bitesize/guides/zc499j6/revision/3

A video overview of genetic mutation and how it relates to sickle-cell disease:

- https://www.khanacademy.org/science/ap-biology/gene-expression-and-regulation/mutations-ap/v/an-introduction-to-genetic-mutations

Extra Activities:

- Research task: Give each group the name of a disease caused by just one mutated protein (suggestions are listed below) and ask them to research the following information for their disease;

    - How common the disease is and where it is most common
    - The name of the protein affected
    - How the protein is changed in individuals with the disease
    - How the disease affects the individuals that have it.

  Pupils can then present their findings to the class. This may be as part of a class discussion, or groups could prepare posters or short presentations to share with the class.

  Diseases affecting a single protein include;
  -Sickle cell anaemia -Thalassaemia -Tay-Sachs disease -Huntington's disease -Haemophilia -Polycystic kidney disease -Marfan syndrome -Lynch syndrome -Menkes disease

- Extension task- understanding the codon table. To introduce students to the concept that each amino acid can attach to more than one tRNA (so can be encoded by various codons in the mRNA), give students a copy of a codon table such as that shown below, and ask them to draw additional kit pieces that would also correspond to five of the amino acids.

Seond letter

First letter	U	C	A	G	Third letter
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

Acknowledgements:

- Prof. Melissa Hines for the introduction to CCMR outreach and for supporting the project.

- The staff of the Cornell Mann Library MakerSpace for their 3D printing advice and expertise.

APPENDIX 2: STUDENT ACTIVITY SHEET

Student Name:__________ Date:____________

Activity Sheet

How to be a Ribosome- Understanding Protein Translation

Materials:
Set of 20 tRNAs and ~65 small bases per group (2-3 students)

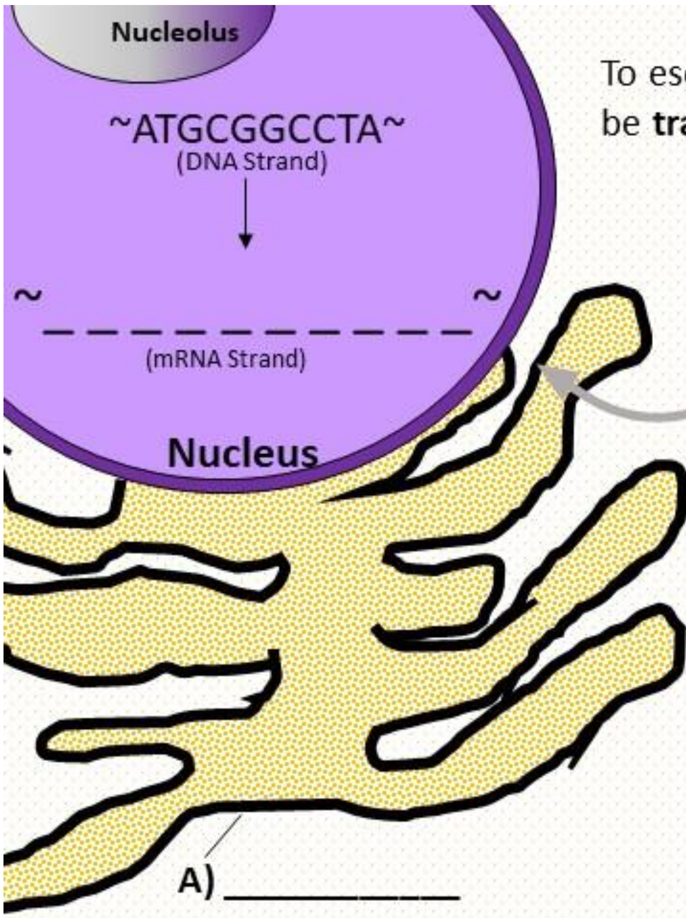
Activity 1
Journey Through the Cell

Aim: To review relevant cell parts and the processes that must occur **before** translation can happen.

What has to happen before translation (making proteins) takes place?

In your groups, race your classmates to complete the 'Journey Through the Cell' on the following page.

Ask your teacher to check each answer before you move on to the next question.



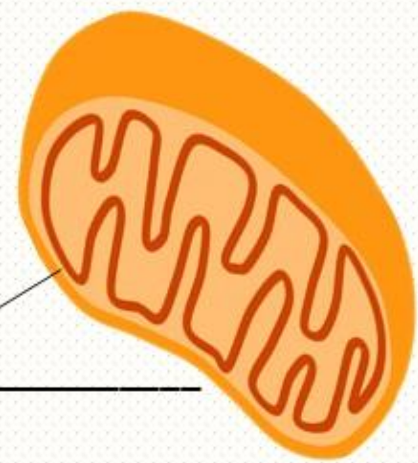
To escape the nucleus, the DNA code must be **transcribed** to mRNA.

1. Fill in the blanks and ask your teacher to check your answer before moving on to each next answer.

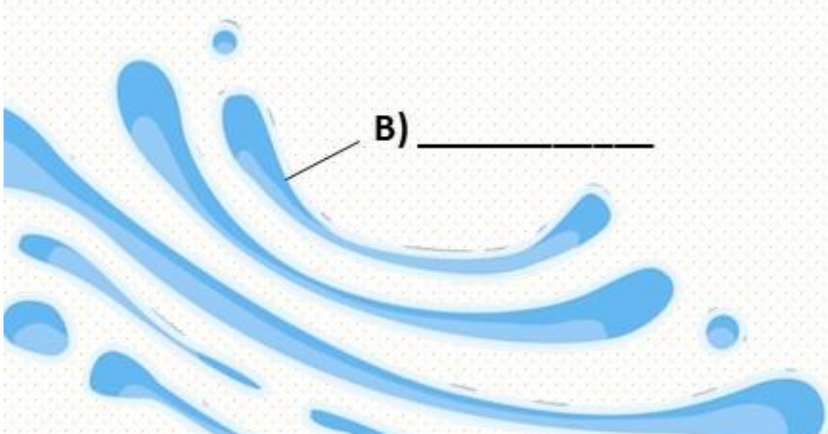
2. Label the four cell parts A, B, C and D

A) ___________

D) ___________

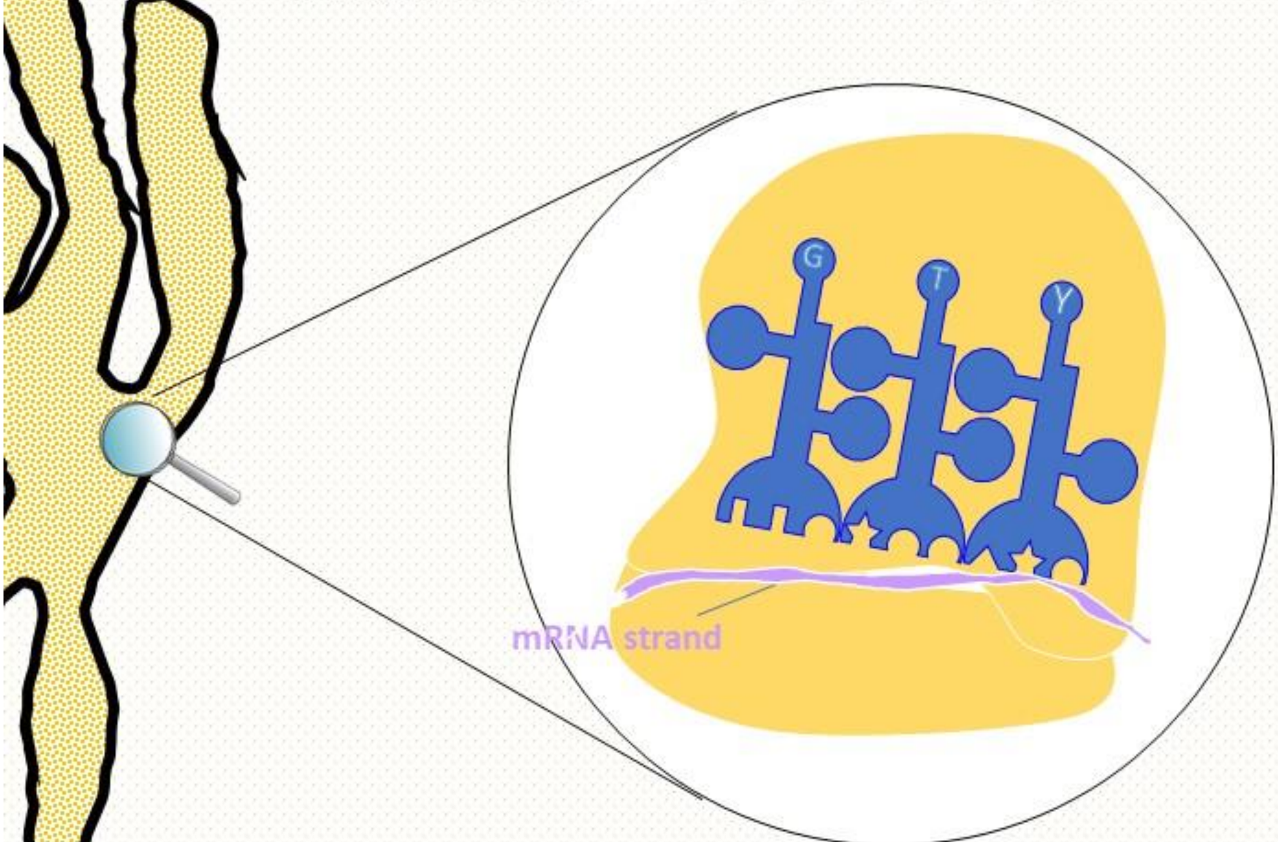


C) ___________



B) ___________

3. Structures called _______________ are required to attach to the mRNA to produce proteins. These are found either free in the _______________, or attached to the ____________________________.



4. When the ________________ is attached to the mRNA, ___________ molecules can then recognize **codons** in the RNA. Then the process of _________________ transforms the mRNA code into a protein.

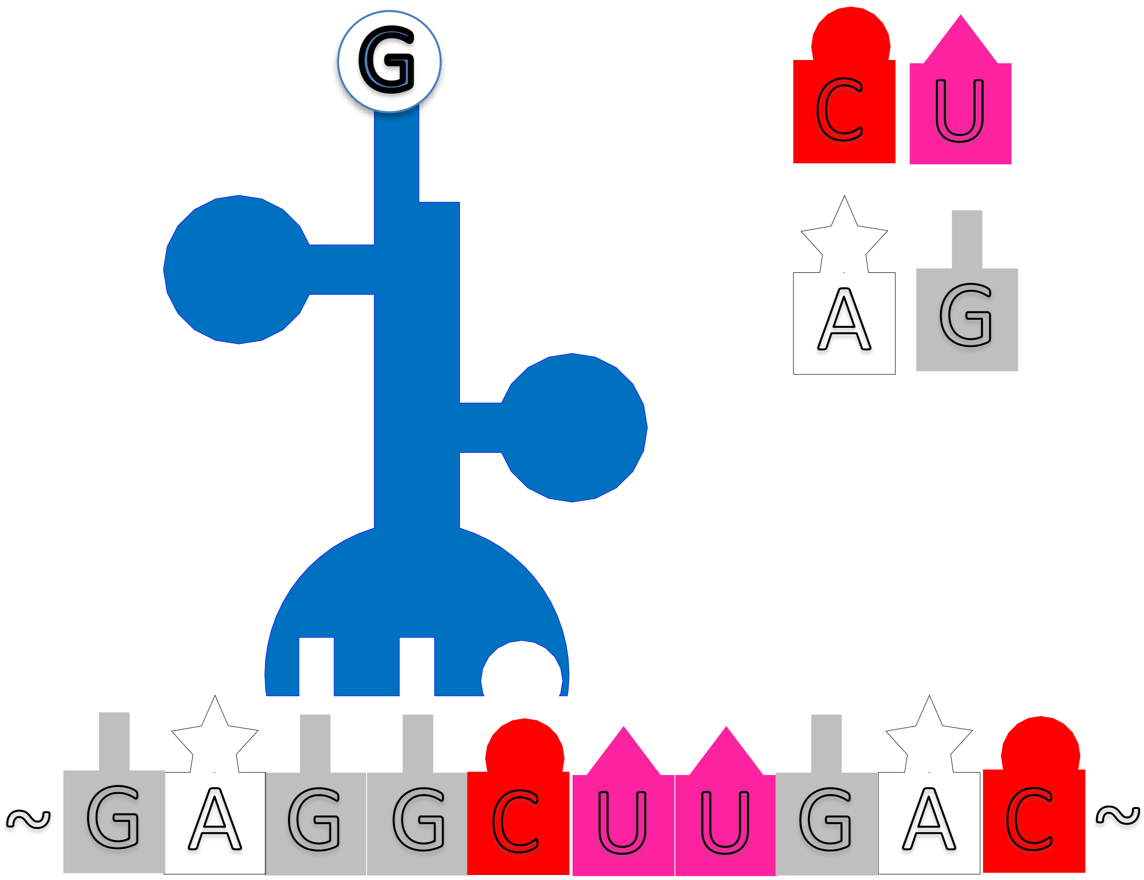
5. After a protein has been made, it is processed by two main organelles, the _____________________, and the _______________.

After processing, the finished protein is transported to the correct intracellular compartment or out of the cell to carry out its required function

Activity 2: Introducing the Kit Pieces

This kit uses 3D-printed pieces to represent the components required for translation. **Translation turns the code within a strand of mRNA into a 'string' of amino acids**, which will then be processed to become functional proteins. Remember that here, amino acids are represented by their **one-letter code**.

Label the diagram of the pieces using **all** of the words in the word bank below.



Codon	mRNA strand	tRNA
mRNA base	Amino acid	Anti-codon

Activity 3: Translation: from RNA to Protein

In this activity, you will become the ribosome. Your job is bringing the tRNAs, which are attached to the amino acid 'building blocks' for proteins, together with the mRNA code. Use the pieces to answer the following questions.

1) Use the mRNA bases to write out the following code;

CCUAUGGGCCAG

Now write down the amino acid sequence that this code **translates** to:

____

2) Translate the following code; GGCCGUGAAGCUACC

Which amino acid sequence does it translate to?

____

3) Write your own word using the amino acids. What will the mRNA code for this word be?

Word____________ mRNA Code_____________________________

4) Which mRNA code gives the following amino acid sequence?

PSIFYQVNTA

____

5) Which mRNA code gives the following amino sequence?

KGWCLRMDCHE

____

The amino acids are joined together in order by the ribosome, forming a **peptide chain**. When this chain is 100s-1000s of amino acids long, it is processed to form the complete, **functional proteins** needed in **every** living cell!

Activity 4: Mutations

Even a change in a **single** base in the DNA, and therefore the mRNA code after transcription, can cause big changes in the protein it makes by changing the sequence of amino acids.

Use the kit pieces to answer the following questions.

1) **Substituting** one base in a codon can change the amino acid it codes for, which amino acids correspond to the following codons?

GCU________________ CCU______________
AUA________________ AUG______________
UAC________________ UGC______________

2)a) which amino acid sequence results from **translation** of the following mRNA sequence? AGUACAACC: _____________

b) now **add** just one C to the beginning of the mRNA sequence. What happens to your amino acid sequence?

3) What **single change** do you have to make to the following mRNA sequence to change the amino acid sequence it makes from K-H-S to T-I-V?

AACCAUAGUU → K-H-S
_______________ → T-I-V

Required change:

4) When only a **single** base in the DNA is **substituted, inserted or deleted**, it is called a **point mutation.** Using your answers to the questions above (and the kit pieces) to complete the following sentences.

When a single DNA base is altered, transcription creates _____________ which also contains _____________ alteration.

When a base has been ______________, only one amino acid in the protein sequence is changed by the mutation.

When a base has been ________________ or ________________, every amino acid after the mutation is changed.

Activity 5: From DNA to Characteristics

An example of a disease caused by **deletions** in the DNA is **cystic fibrosis**. For an individual to have this condition, they must **inherit** mutated DNA from **both** of their parents.

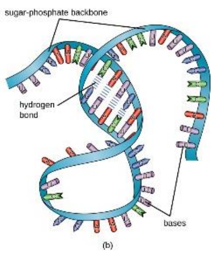
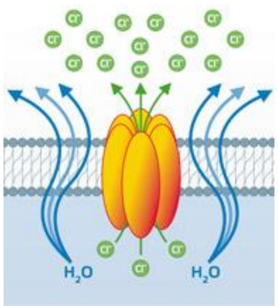
Using what you have already learned and the information in the table below, answer the following questions;

1) Would you expect the mRNA transcribed from the healthy DNA to be normal or abnormal? Why? Write your answer in the table.

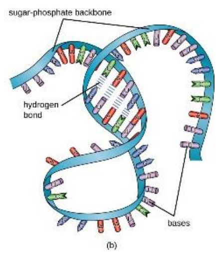
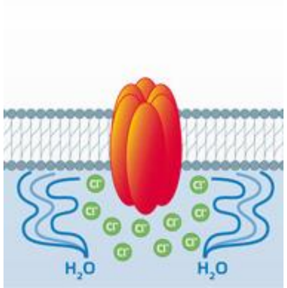
2) What will be different about the **mRNA** in the cystic fibrosis patient compared to the mRNA healthy in the healthy individual? Write your answer in the table.

3) What kind of symptoms would you expect someone who has cystic fibrosis to have? (hint: think about what might happen to the mucus in the lungs when the transporter doesn't work properly) Write your answer in the space below the table.

Healthy Individual

	DNA that encodes a **transporter protein** in the membrane of the cells that line the lungs is **normal**.
	mRNA resulting from **transcription** is ____________________
	The cell makes a healthy transporter protein by **translating** the mRNA. This is present in the membrane of the cells that line the lungs and allows ions and water to escape the cell. The water that escapes thins the mucus that coats the lungs, allowing it to move freely and stopping it from building up.

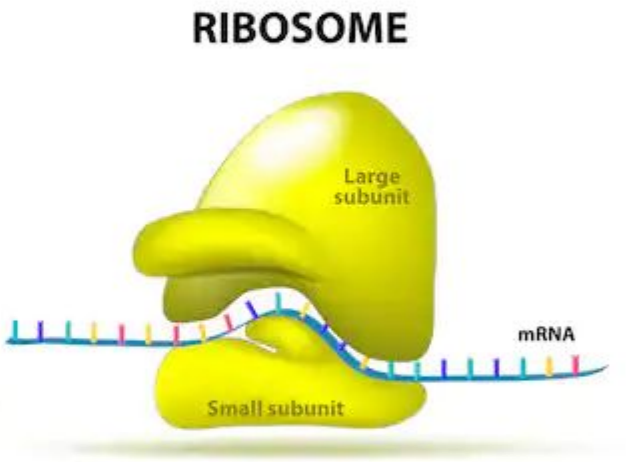
Cystic Fibrosis Patient

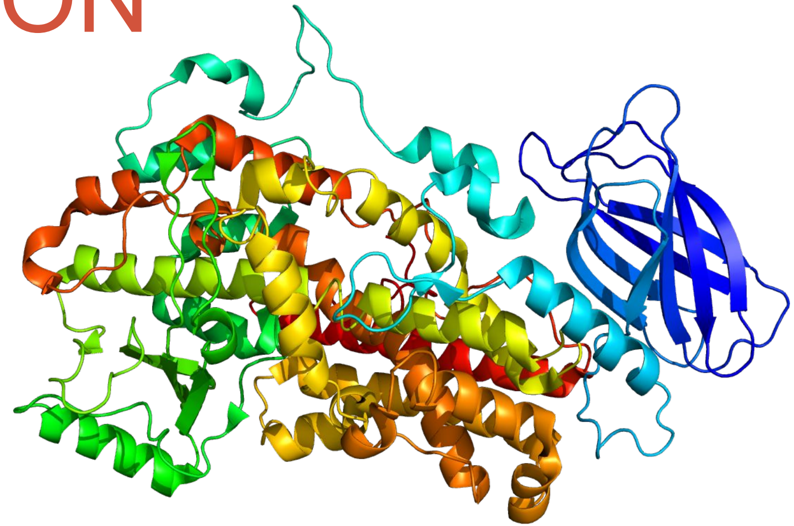
	The DNA has three bases **deleted** from it.
	How will this mRNA be different?
	The mutated transporter is missing a single amino acid within its protein structure. This changes the shape of the protein so much that it can no longer allow ions and water to escape out of the cell.

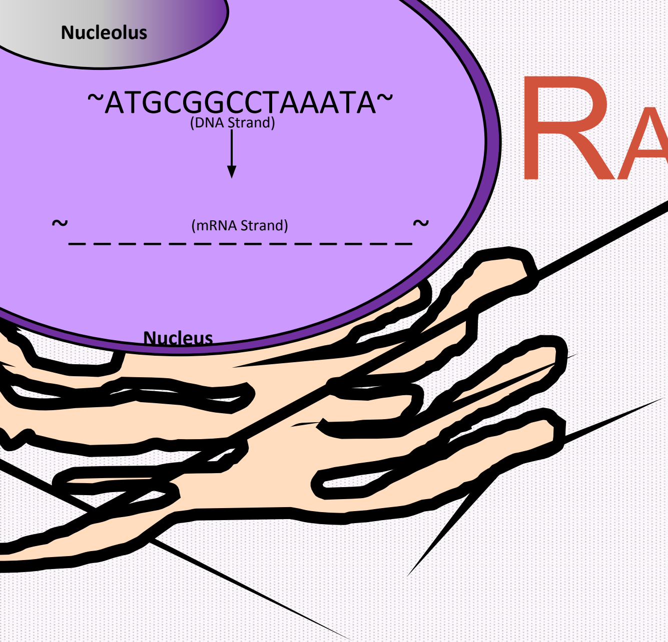
Predicted cystic fibrosis symptoms:

APPENDIX 3: ACCOMPANYING POWERPOINT PRESENTATION

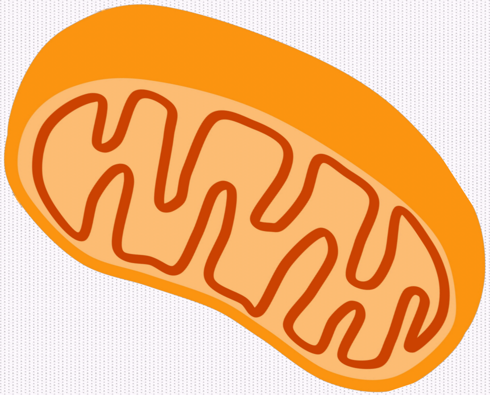
How to be a ribosome: protein translation

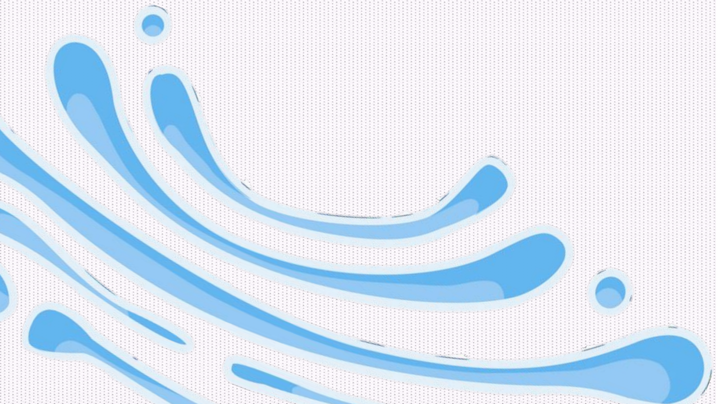


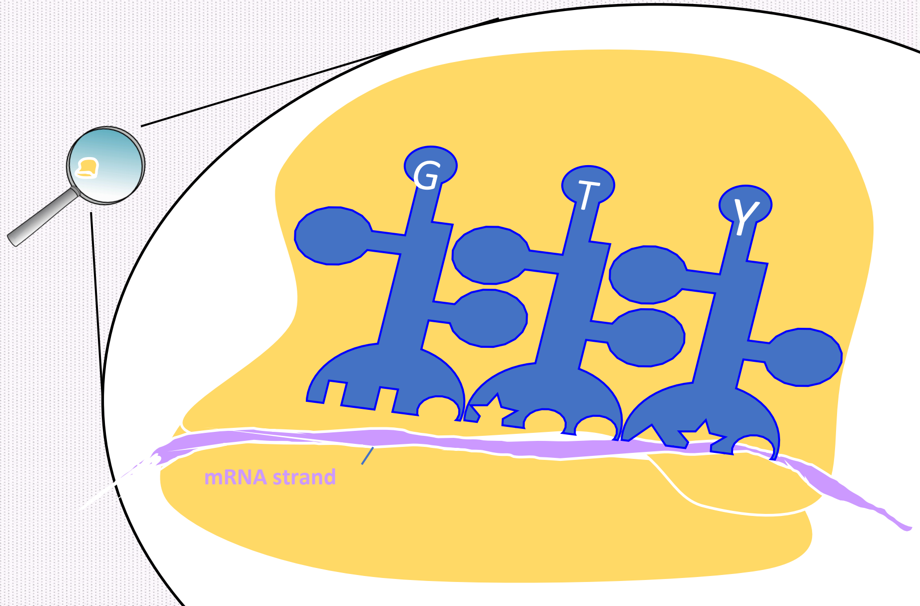


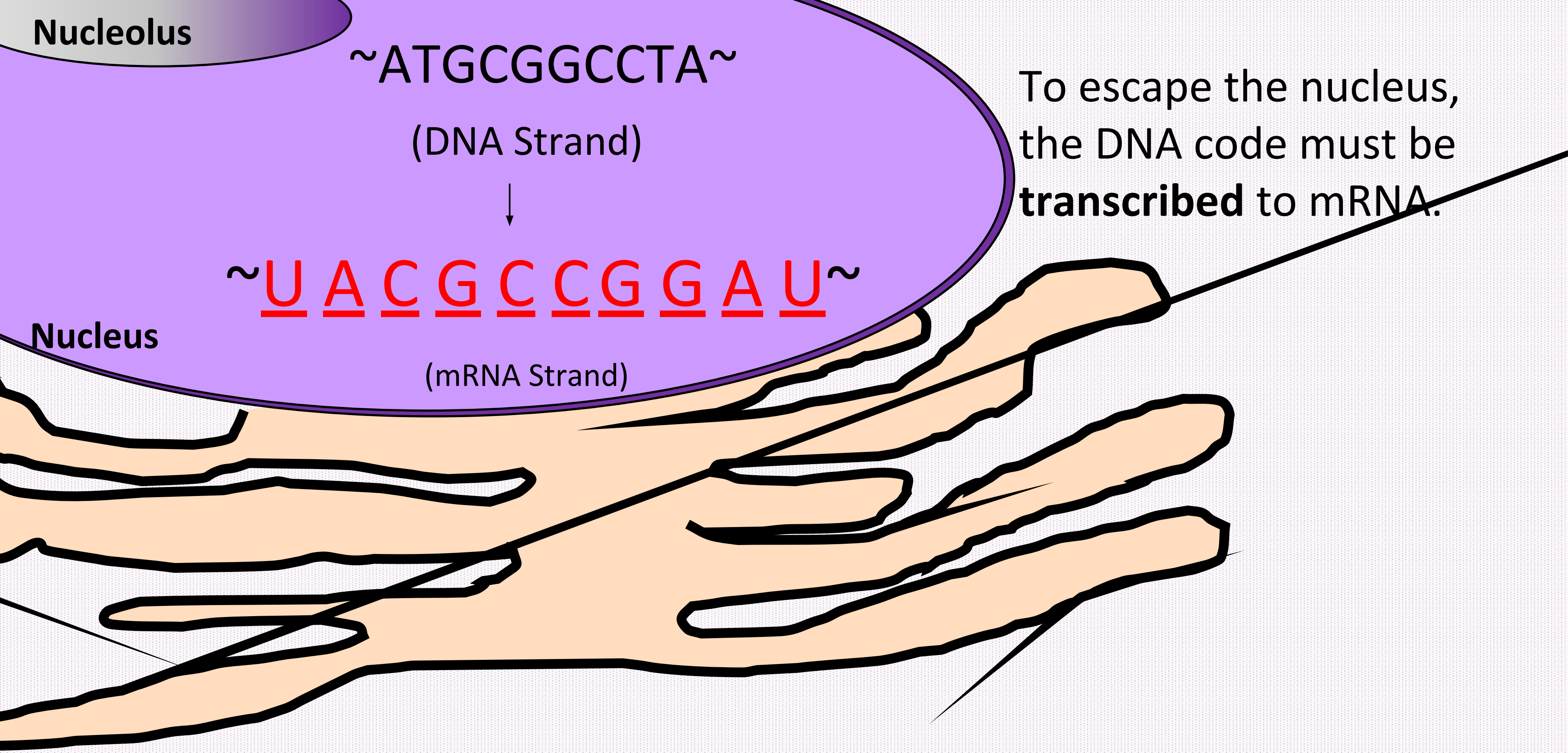


RACE THROUGH THE CELL



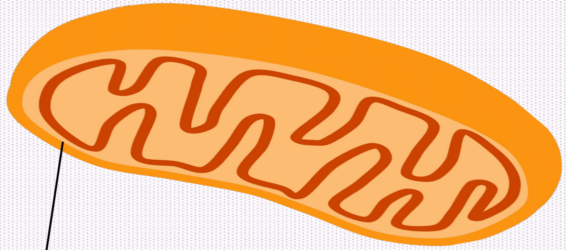






To escape the nucleus, the DNA code must be **transcribed** to mRNA.

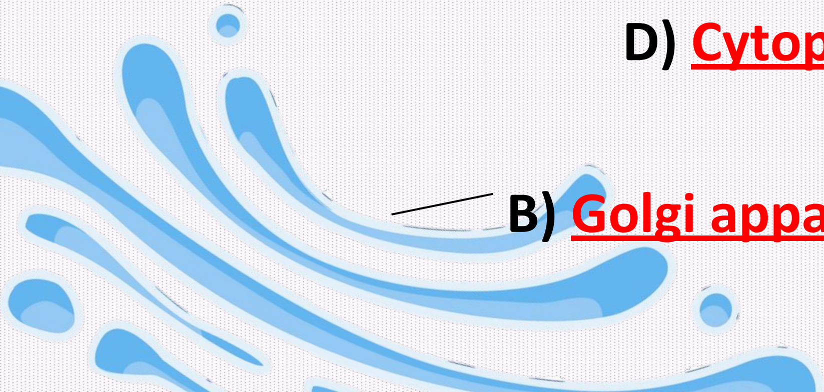
2. Label the four cell parts A B, C and D



A) Rough endoplasmic reticulum

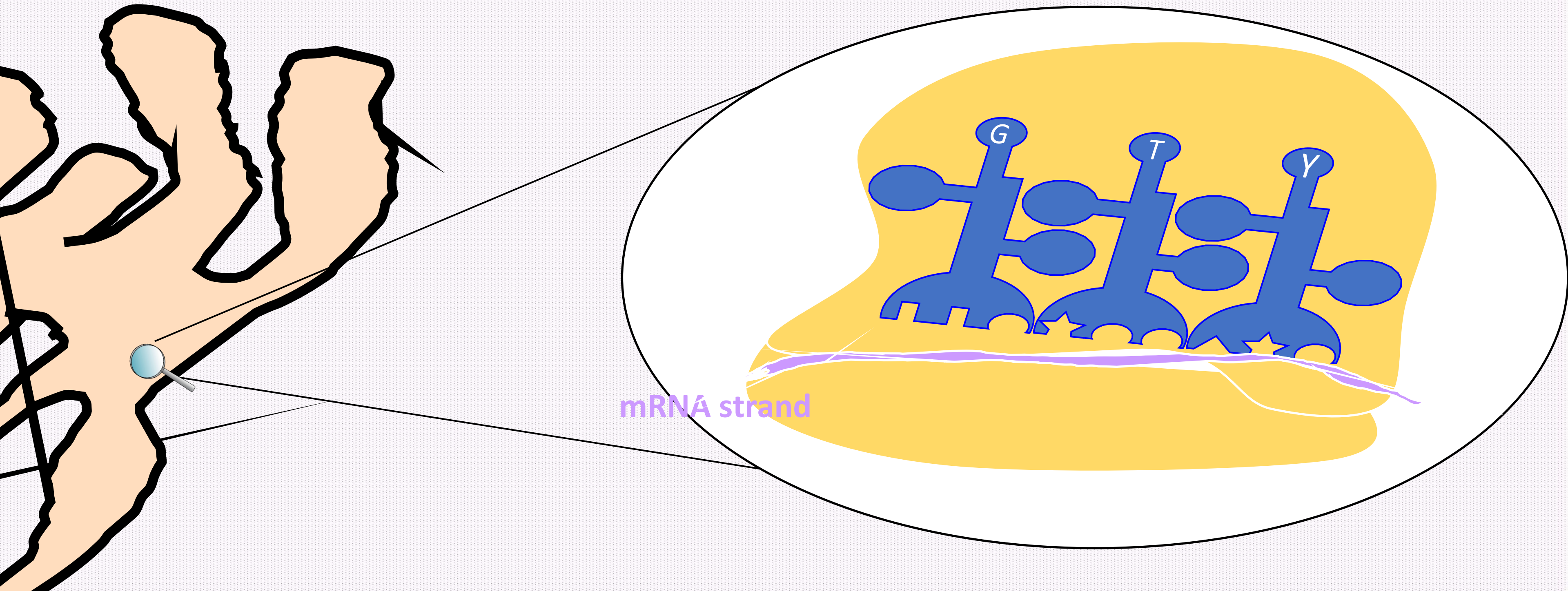
C) Mitochondrion

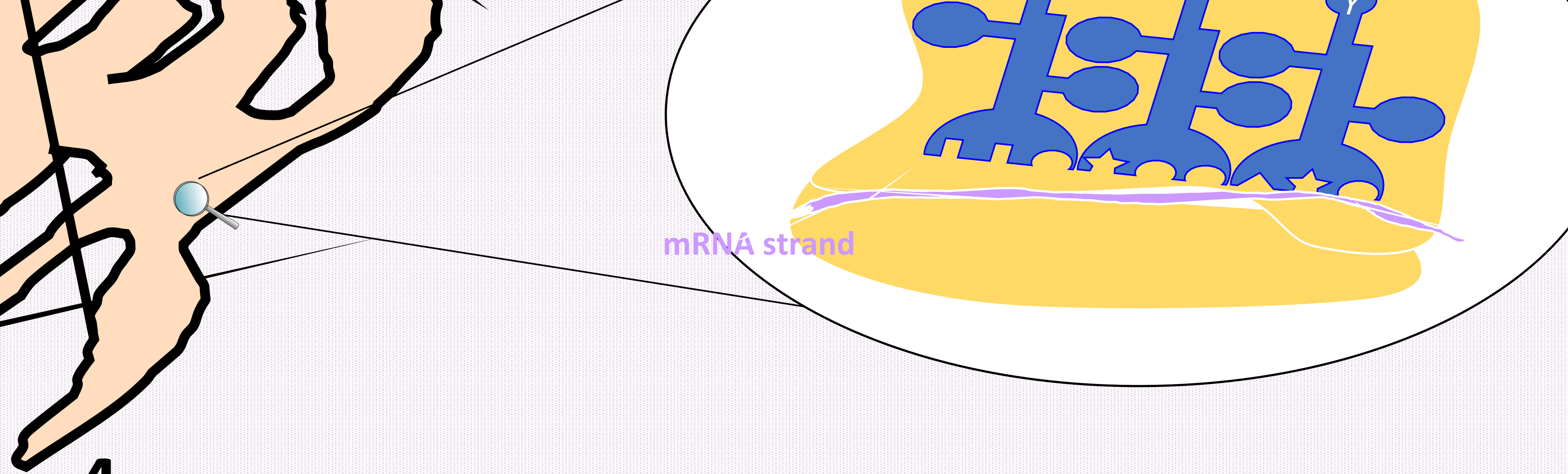
D) Cytoplasm



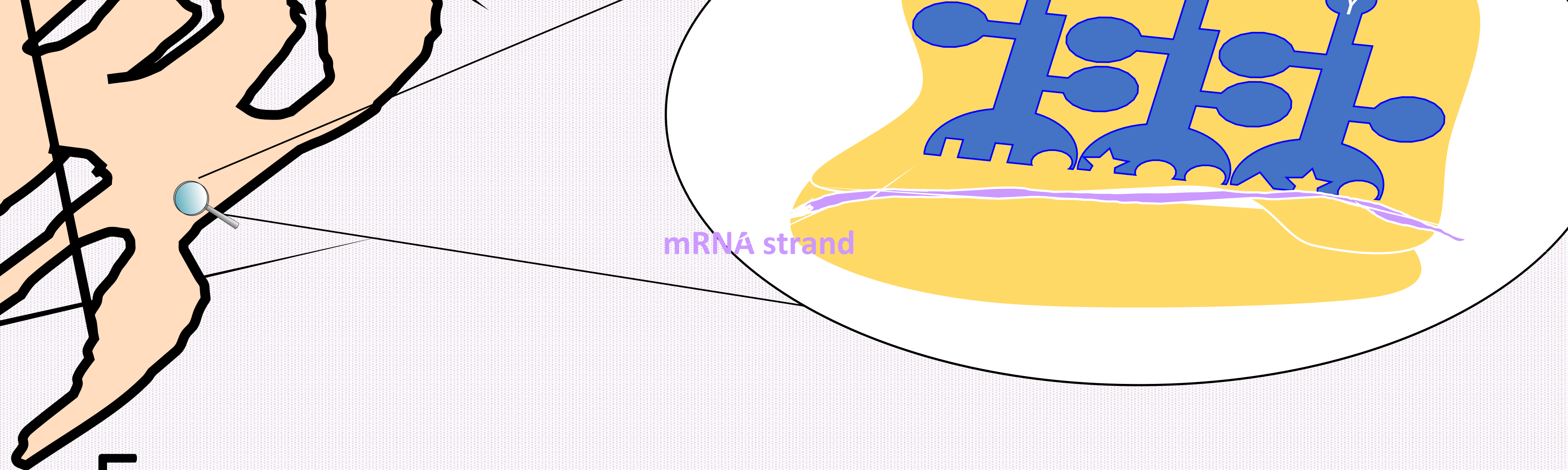
B) Golgi apparatus

3. Structures called **ribosomes** are required to attach to the mRNA to produce proteins. These are found either free in the **cytoplasm**, or attached to the **rough endoplasmic reticulum**.





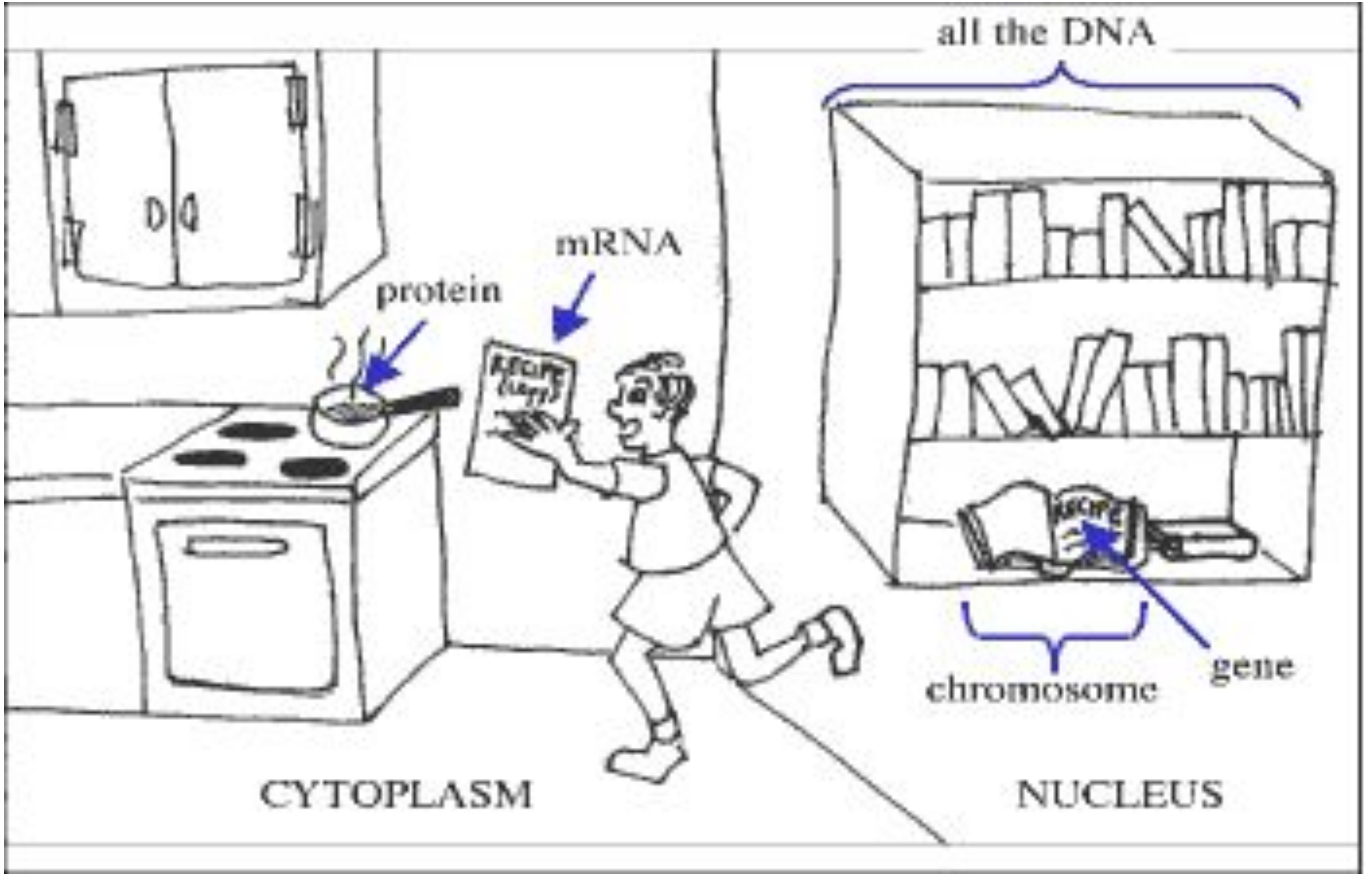
4. When the **ribosome** is attached to the mRNA, **tRNA** molecules can then recognize **codons** in the RNA. Then the process of **translation** transforms the mRNA code into a protein.

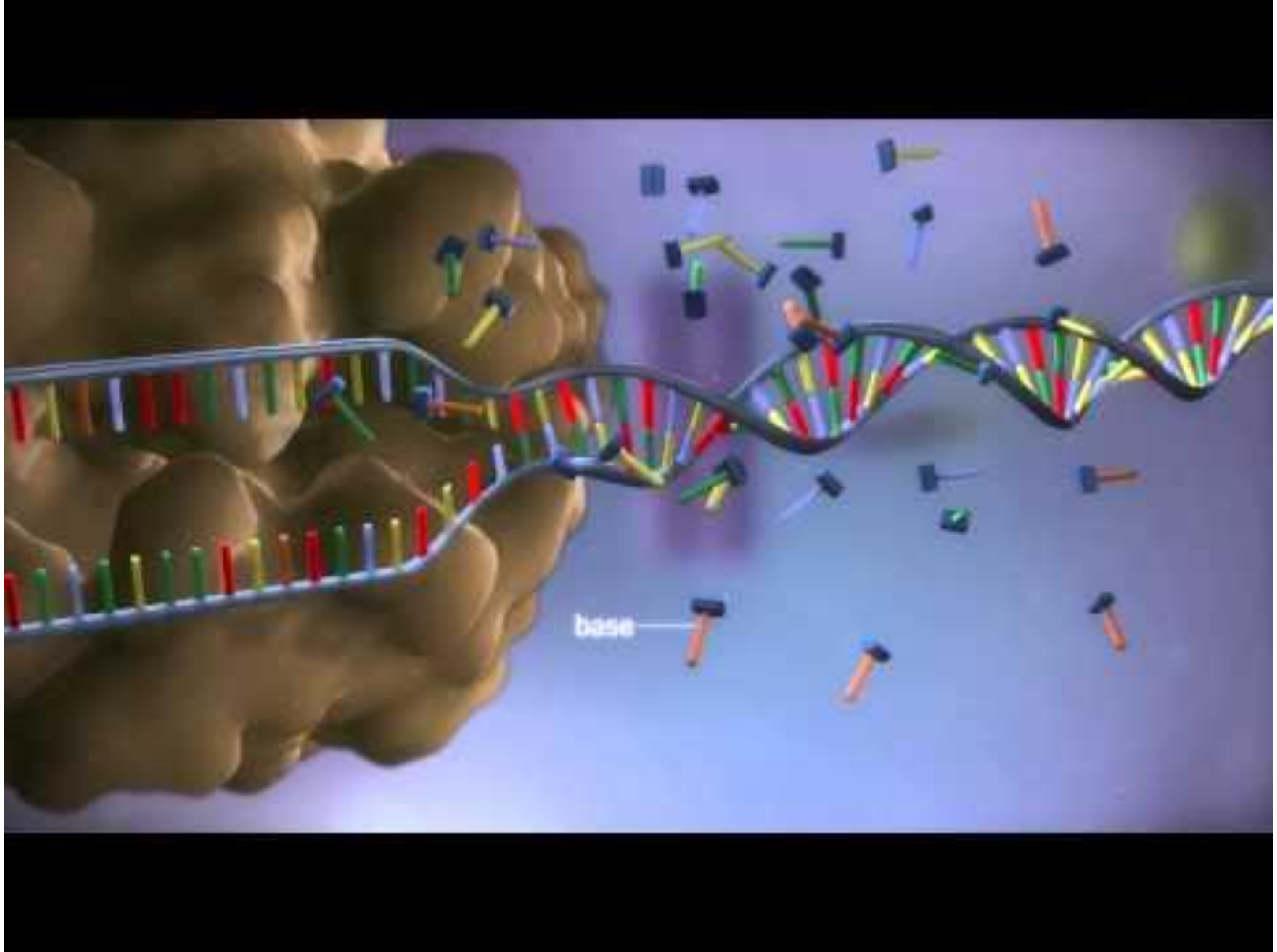


5. After a protein has been made, it is processed by two main organelles, the **endoplasmic reticulum**, and the **golgi apparatus**.

After processing, the finished protein is transported to the correct intracellular compartment or out of the cell to carry out its required function

Translation: from mRNA to Protein

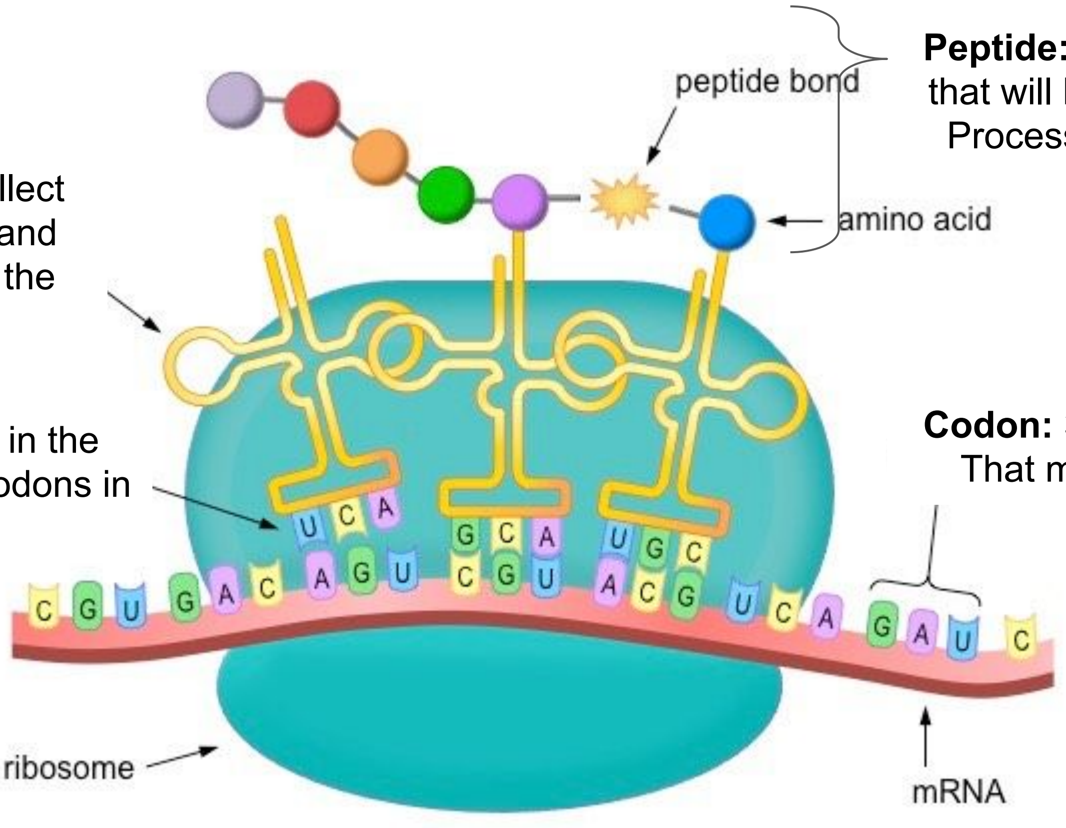



base

Translation: from mRNA to Protein

tRNA molecules: collect the right amino acid and recognise codons in the mRNA

Anti-codon: 3 bases in the tRNA which pair with codons in the mRNA

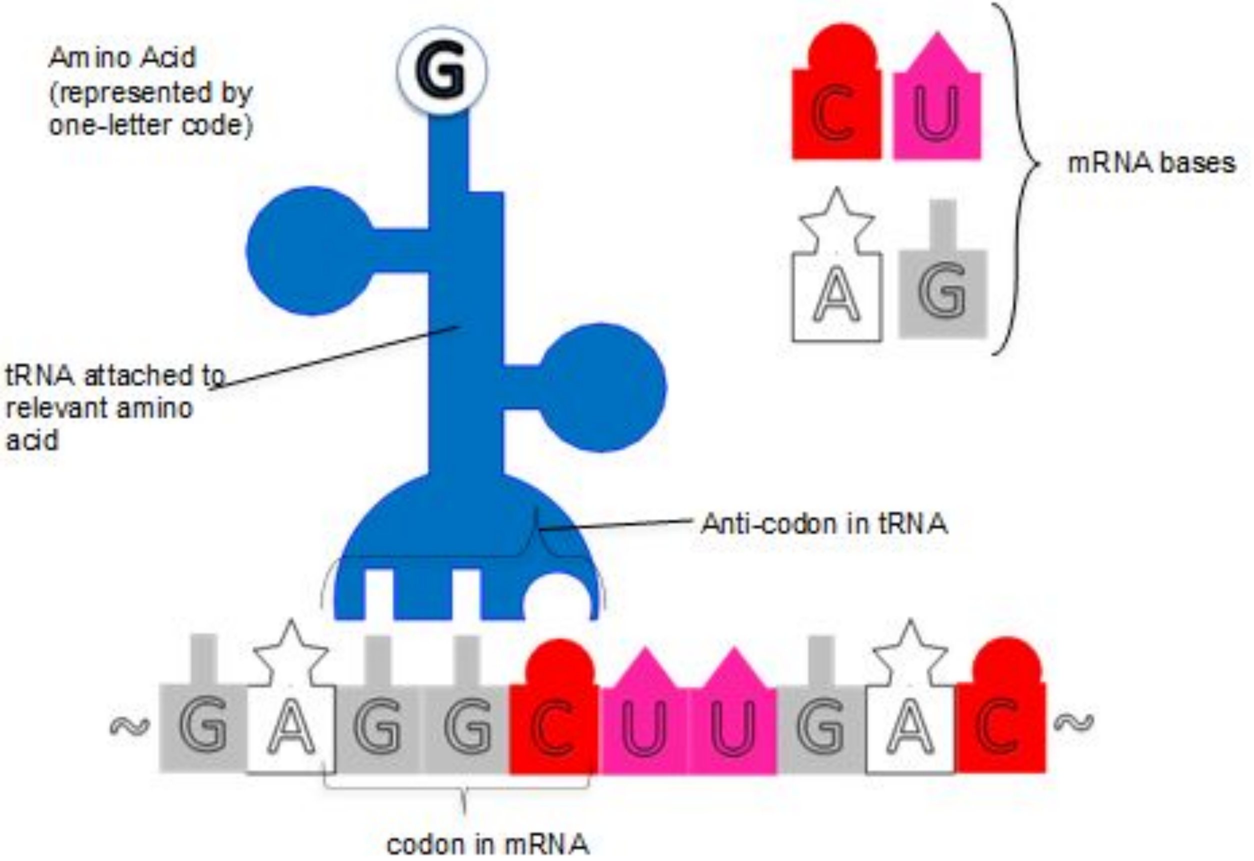


Peptide: chain of amino acids that will be lengthened and/or Processed to make the final protein.

Codon: 3 bases within mRNA That match an anti-codon

http://ib.bioninja.com.au

Using the kit pieces



Being a Ribosome: Translating

1) Use the mRNA bases to write out the following code;

CCUAUGGGCCAG

Now write down the amino acid sequence that this code **translates** to:

P-M-G-Q

2) Translate the following code; GGCCGUGAAGCUACC

Which amino acid sequence does it translate to?

G-R-E-A-T

3) Write your own word using the amino acids. What will the mRNA code for this word be?

Word______________ mRNA Code__________________________________

Being a Ribosome: Translating

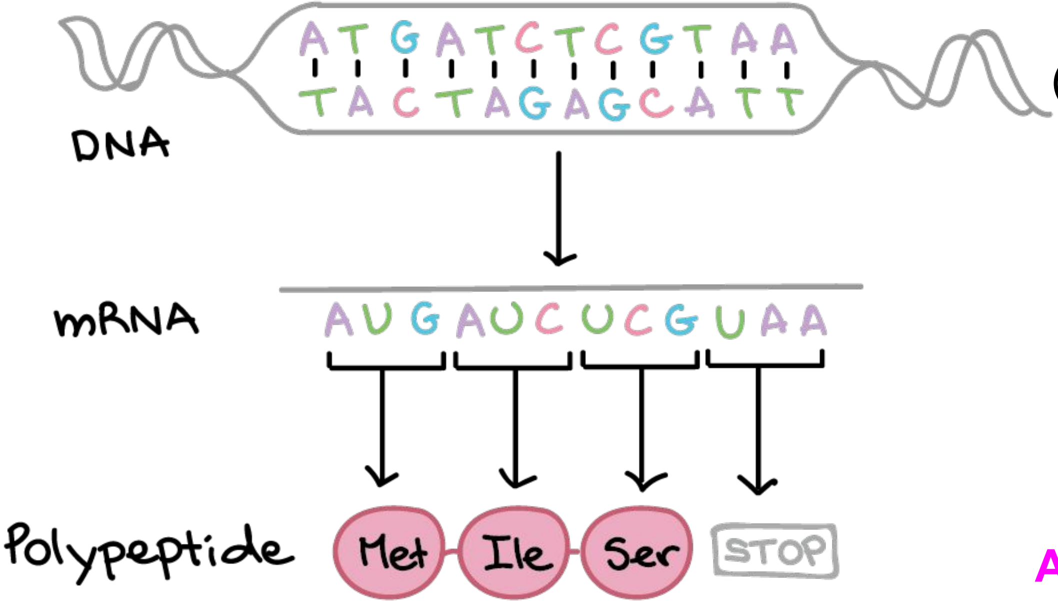
4) Which mRNA code gives the following amino acid sequence?
PSIFYQVNTA

CCU-AGU-AUA-UUU-UAC-CAG-GUU-AAU-ACC-GCU

5) Which mRNA code gives the following amino sequence?
KGWCLRMDCHE

AAC-GGC-UGG-UGC-UUG-CGU-AUG-GAU-UGC-CAU-GAA

MUTATIONS



When the DNA contains a **mutation** (accidental change in order of bases)

The transcribed mRNA will **also** be changed.

A different peptide sequence can be made

https://www.khanacademy.org/science/high-school-biology/hs-molecular-genetics/hs-rna-and-protein-synthesis/a/hs-rna-and-protein-synthesis-review

What Did Your Mutations Do?

1) Substituting one base in a codon can change the amino acid it codes for, which amino acids correspond to the following codons?

GCU: **A (Alanine)**
AUA: **I (Isoleucine)**
UAC: **Y (Tyrosine)**

CCU: **P (Proline)**
AUG: **M (Methionine)**
UGC: **C (Cysteine)**

2)a) which amino acid sequence results from translation of the following mRNA sequence?
AGUACAACC: **S-I-T**

b) now add just one C to the beginning of the mRNA sequence. What happens to your amino acid sequence?
The entire sequence changes- new peptide is **Q-Y-K**

What Did Your Mutations Do?

3) What **single change** do you have to make to the following mRNA sequence to change the amino acid sequence it makes from K-H-S to T-I-V?

AACCAUAGUU	K-H-S
ACCAUAGUU	T-I-V

Required change: **Deleting one A at the beginning of the sequence**

4) When only a **single** base in the DNA is **substituted, inserted or deleted**, it is called a **point mutation.** Using your answers to the questions above (and the kit pieces) to complete the following sentences.

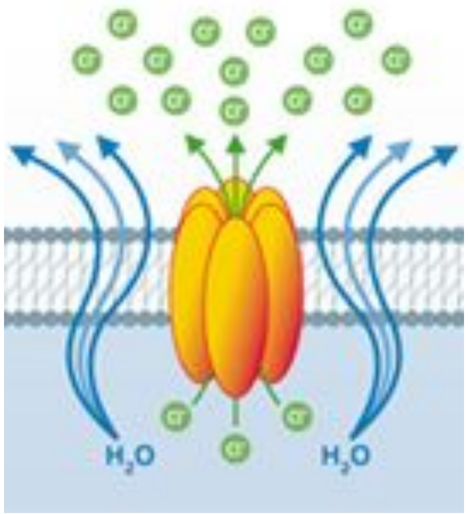
When a single DNA base is altered, **transcription**----- creates **mRNA** which also contains **a single** alteration.

When a base has been **substituted**, only one amino acid in the protein sequence is changed by the mutation.

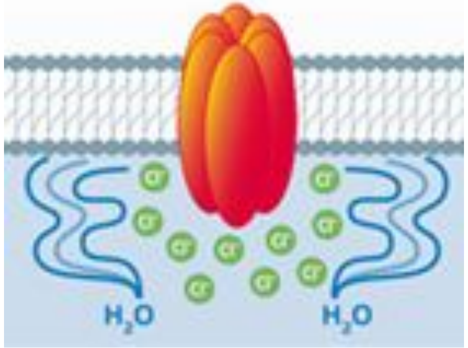
When a base has been **inserted** or **deleted**, every amino acid after the mutation is changed.

Mutations and Cystic Fibrosis

1) The mRNA from the healthy DNA is **normal**, so can produce the fully functional transporter protein



2) The mRNA in the cystic fibrosis contains a **deletion of three bases, just like the DNA.**



3) Because water can't escape the cells, the mucus in the lungs isn't thinned. Patients with CF might therefore suffer from **coughing, lung infections, difficulty breathing, chest pain....**