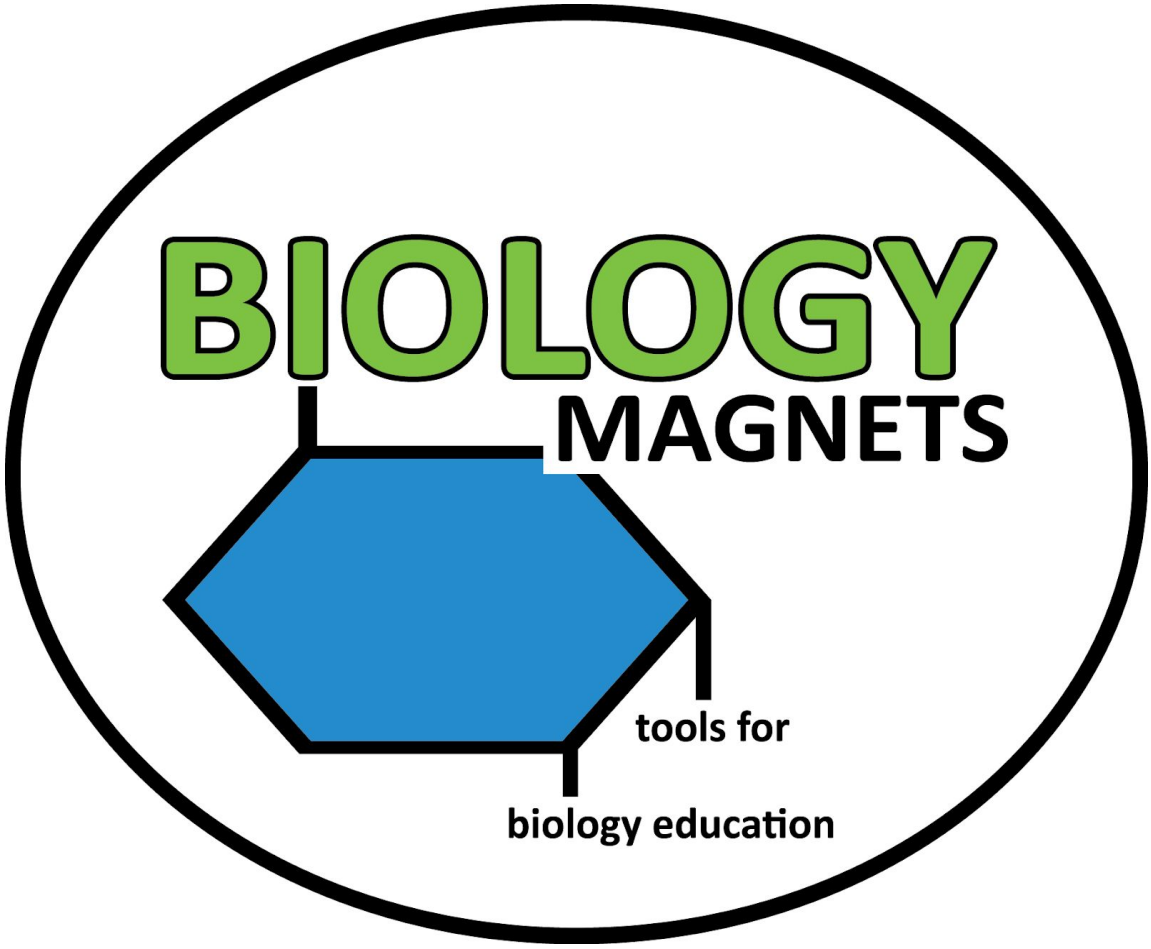
Biology Magnets Module 10: Cell Signaling - Teacher and Student Guides



Teacher Information

This module uses magnets designed for teacher and student interaction to guide learning about cell signaling. Contained in this guide are outlines for lessons that can last from 10 minutes to approximately 60 minutes depending upon teacher preference. The lessons have both teacher-centered and student-centered activities. The student-centered activities are most effective if students are in small groups. It may be necessary to have multiple magnet sets for large classes. Student handouts are provided which can be printed out and given to each student group to help guide their progress as they work with the magnets. If budget or board space is limited, groups can alternate between using a set of magnets and doing other activities. Teachers can refer to the videos posted at the Biology Magnet web site at Biologymagnets.com for further teaching instructions.

Magnet Care and Maintenance

Biology magnets are made to last for years. Periodically magnets will fall off or are knocked off the plastic. A piece of magnetic tape is included with each module, which should be able to replace around 10-12 magnets if necessary. Simply cut a new magnet and peel off the back to replace. Magnetic tape can be purchased from a hobby store to replace magnets lost over time. Laminate may peel off, especially on small pieces. Use transparent tape to re-attach laminate that comes loose, curling the tape over the back of the magnet. The machines used to cut Biology magnets are not perfectly accurate. Sometimes a bit of white or black outline on the edges occurs or a cut might be slightly off center. Use scissors to remove extra outline that is unnecessary if desired. Note that white outline virtually disappears from view when the magnets are on a white board. Store magnets in the clasp envelopes in which they arrived for easy organization.

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Epidermal Growth Factor Receptor (EGFR) – This image has been released into the public domain by its original copyright holder. By Emw - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=8814760. Modified to add background, outlines and label. Alpha helix added in center and part of protein repeated three times at base. The new work is released with the above license.

Growth Factor Receptor Bound Protein 2 (GRB2) – This file is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported. By Emw - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=8814578. Modified to add background, outlines and label. The new work is released with the above license.

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RAS GTPase Protein – This file is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license. By Emw - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=8821275. Modified to add background, outlines and label. The new work is released with the above license.

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Extracellular Signal-Regulated Kinases (ERK1/2) – This file is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license. By C31004 (talk) 18:37, 24 March 2008 (UTC) - self-made, CC BY-SA 3.0, https://en.wikipedia.org/w/index.php?curid=16547996. Modified to add background, outlines and label. The new work is released with the above license.

Fos-jun Transcription Factors – This file is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license. By Houq - pymol, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=44732872. Modified to add background, outlines and label, DNA strand removed. The new work is released with the above license.

Phosphorylase Kinase – This file is licensed under the Creative Commons Attribution 4.0 International license. By Deposition authors: Lowe, E.D., Noble, M.E.M., Skamnaki, V.T., Oikonomakos, N.G., Owen, D.J., Johnson, L.N.;visualization author: User:Astrojan - http://www.rcsb.org/pdb/explore/explore.do?structureId=2phk, CC BY 4.0, https://commons.wikimedia.org/w/index.php?curid=50051835. Modified to add background, outlines and label. The new work is released with the above license.

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GTPase Activating (GAP) Protein - This file is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license. By Emw - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=8821246. Modified to add background, outlines and label, DNA strand removed. The new work is released with the above license.

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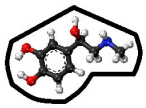
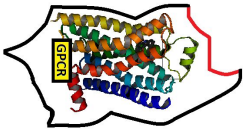
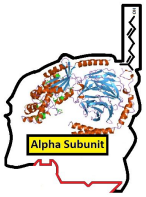
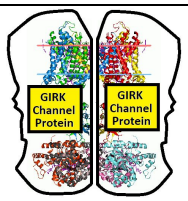
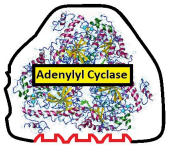
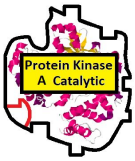
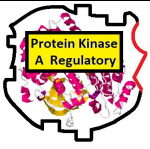
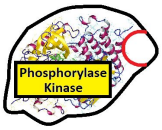
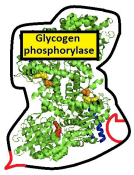
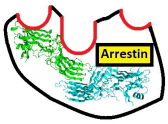
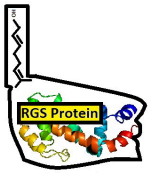
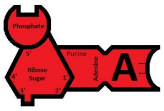
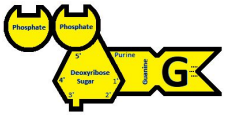
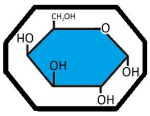
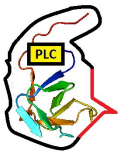
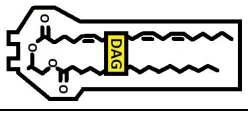
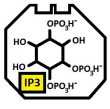
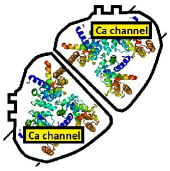
K+ ions, ATP, AMP, GTP, GDP, Phosphate groups, Calcium ions, Glucose, Estrogen – Copyright 2020 by Tom Willis, All Rights Reserved.

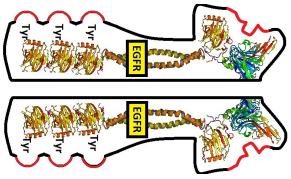
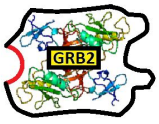
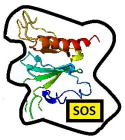
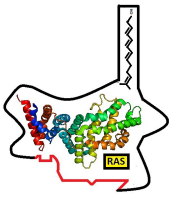
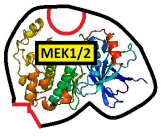
Module 10A – Cell Signaling – G Protein Signaling - Materials List

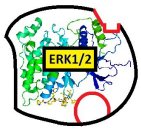
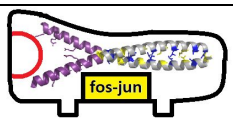
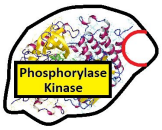
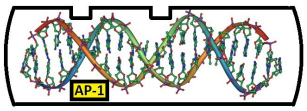
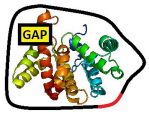
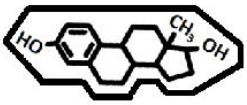
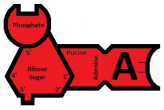
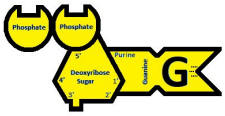
Magnet Name	Quantity	Picture	Function
Epinephrine	2		Binds to receptor protein in membrane
G Protein Coupled Receptor (GPCR)	1		Binds to epinephrine, activates G proteins in membrane
G Protein Alpha Subunit	1		Binds GDP, GTP, activates Adenylyl Cyclase
G Protein Beta Gamma Subunit	1		Activates GIRK channel
G Protein-coupled inwardly rectifying potassium channel (GIRK)	2		Binds to beta gamma subunit of G protein, allows K+ ions to enter cell
Adenylyl Cyclase	1		Binds to alpha subunit of G protein, changes ATP to cyclic AMP
Protein Kinase A Catalytic	2		Activates Glycogen phosphorylase, phosphorylated by ATP
Protein Kinase A Regulatory	2		Binds to cAMP, releases catalytic portion
Phosphorylase Kinase	1		Phosphorylates Glycogen Phosphorylase

Glycogen Phosphorylase	1		Phosphorylated by ATP, converts glycogen to glucose
G Protein Coupled Receptor Kinase (GPCRK)	1		Phosphorylates G protein receptor
Arrestin	1		Binds to G protein coupled receptor halting its activity
Regulator of G Protein Signaling (RGS Protein)	1		Binds to G protein and causes GTP to be replaced by GDP
Potassium Ions (K^+)	4		Move into cell through GIRK channel
Adenosine monophosphate (AMP)	4		Helps form ATP, binds to various proteins in activation
Phosphate	8		Forms ATP, ADP, used to phosphorylated proteins
Guanosine diphosphate	2		Binds to G proteins
Phosphate (GTP)	2		Binds to GDP to form GTP
Glucose	6		Forms glycogen, released by glycogen phosphorylase
Phospholipase C (PLC) Protein	1		Breaks PIP2 into DAG and IP3
Diacylglycerol (DAG)	1		Associates with IP3
Inositol Triphosphate (IP3)	1		Opens calcium channels in endoplasmic reticulum

Calcium Channel Proteins	2		Allow calcium to exit ER
Calcium	4		Stored in ER, released by IP3 activation
3" Magnetic Tape Strip	1		n/a
Total Pieces	53		

Module 10B – Cell Signaling – MAP-Kinase Signaling Pathway - Materials List

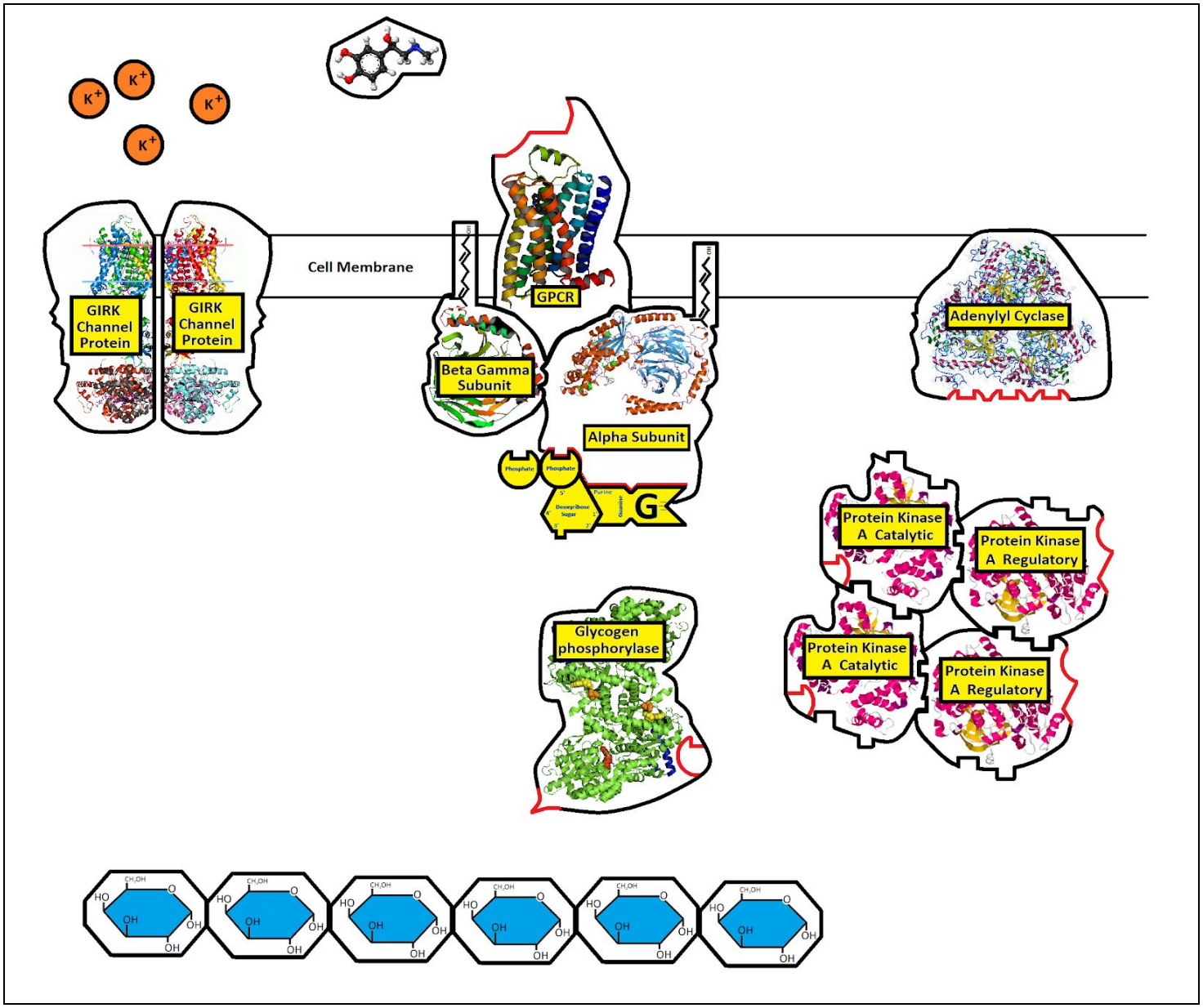
Magnet Name	Quantity	Picture	Function
Epidermal Growth Factor	2		Binds to receptor protein in membrane
Epidermal Growth Factor Receptor (EGFR)	2		Binds to EGR, activates phosphorylase activity within cell
Growth Factor Receptor Bound Protein 2 (GRB2)	1		Binds phosphorylated EGFR then binds to SOS
Son of Sevenless (SOS) protein	1		Binds GRB2 then Activates RAS
RAS GTPase Protein	1		Binds to GDP, which exchanges for GTP to activate RAS
Mitogen Activated Protein Kinase (MEK 1/2)	1		Signaled by RAS protein to phosphorylate ERK1/2

Extracellular Signal-Regulated Kinases (ERK1/2)	1		Phosphorylated by MEK1/2, phosphorylates fos-jun transcription factors
Fos-jun Transcription Factors	1		Bind DNA in the nucleus to start transcription
Phosphorylase Kinase	1		Phosphorylates Glycogen Phosphorylase
AP-1 Gene	1		Nuclear DNA coding for proteins which result in cell reproduction
GTPase Activating (GAP) Protein	1		Phosphorylates G protein receptor
Estrogen	1		Steroid hormone which moves through membrane to receptor
Estrogen Receptor Protein	1		Receives Estrogen and binds to DNA in the nucleus
Adenosine monophosphate (AMP)	4		Helps form ATP, binds to various proteins in activation
Phosphate	8		Forms ATP, ADP, used to phosphorylated proteins
Guanosine diphosphate	2		Binds to G proteins
Phosphate (GTP)	2		Binds to GDP to form GTP
3” Magnetic Tape Strip	1		n/a
Total Pieces	32		

Lesson 10A – G Protein Signaling (10-60 minutes)

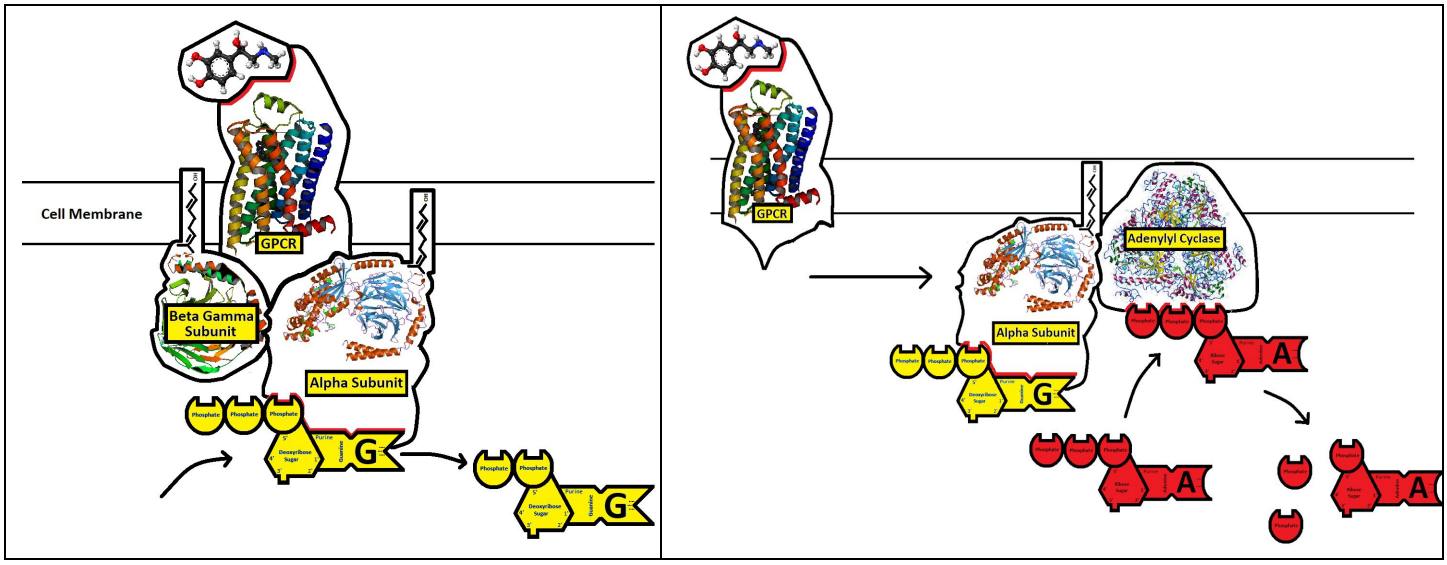
Teacher-Centered Activity (10-30 minutes): Epinephrine signaling pathway: This lesson reviews a common example of cell signaling using the Biology Magnets from Module 10 as shown in the table above. Start the lesson setting up the starting configuration of a cell membrane from a liver cell as shown (**Figure 10.A.1**). Draw the membrane with markers.

Figure 10.A.1 – Cell Signaling Initial Setup



First, reception of epinephrine occurs when epinephrine binds with the G-protein coupled receptor (GPCR), which causes a conformational change in the G protein within the membrane. This allows GTP to replace the GDP on the alpha subunit of the G protein (**Figure 10.A.2**) This leads to the dissociation of the alpha and beta/gamma subunits from the GPCR. The alpha subunit will move along the membrane until it binds adenylate cyclase. This activates the adenylate cyclase enzyme to break apart ATP into two phosphates and a cyclic AMP (cAMP) molecule. The cAMP molecule will then move through the cytoplasm where it acts as a second messenger to activate other enzymes (**Figure 10.A.3**).

Figure 10.A.2 – Epinephrine Reception	**Figure 10.A.3 – Adenylate Cyclase Activation and Activity**



Two cAMP molecules will attach to the regulatory subunits of the protein kinase A molecule **(figure 10.A.4)**, which causes the protein kinase A to break up into four pieces, releasing the catalytic subunits **(figure 10.A.5)**. The catalytic subunits are phosphorylated by ATP **(Figure 10.A.6)**, then catalyze the phosphorylation of the phosphorylase kinase enzyme **(Figure 10.A.7)**. Phosphoylase kinase in turn phosphorylates glycogen phosphorylase **(Figure 10.A.8)**. This causes the glycogen phosphorylase enzyme to be activated and become capable of breaking down glycogen into glucose. The glucose diffuses out of the cell and thus raises the blood glucose levels in the body **(Figure 10.A.9)**.

Figure 10.A.4 – Protein Kinase A Activation

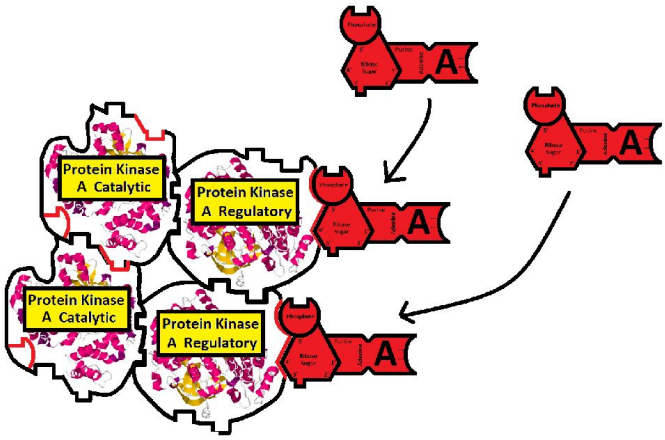


Figure 10.A.5 – Protein Kinase A Activation

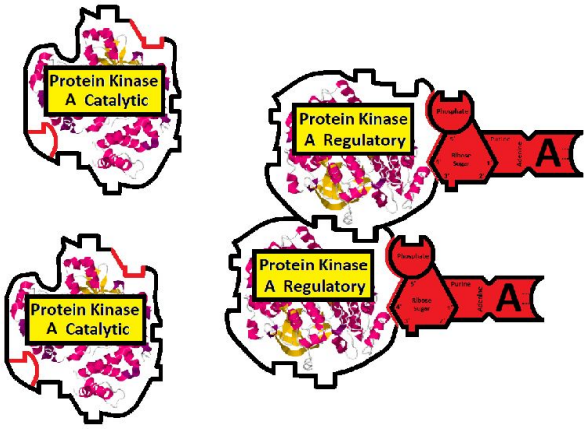


Figure 10.A.6 – Phosphorylation of Catalytic Subunits

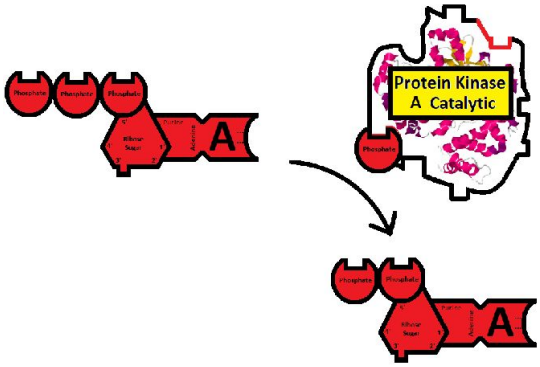


Figure 10.A.7 – Protein Kinase A/Phosphorylase Kinase

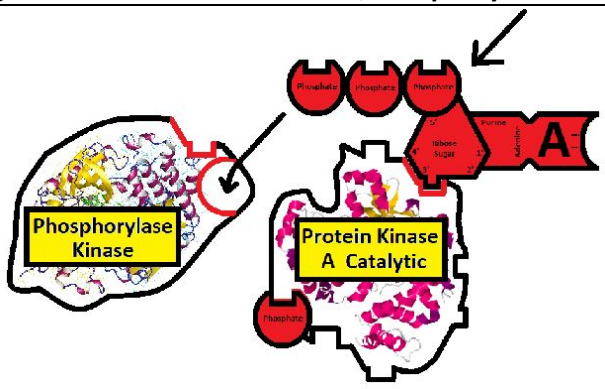
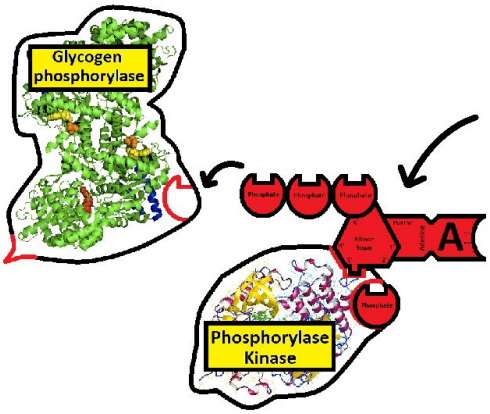
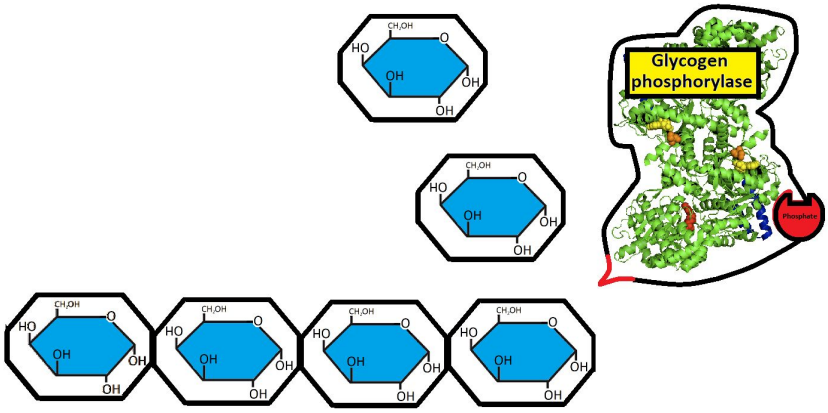
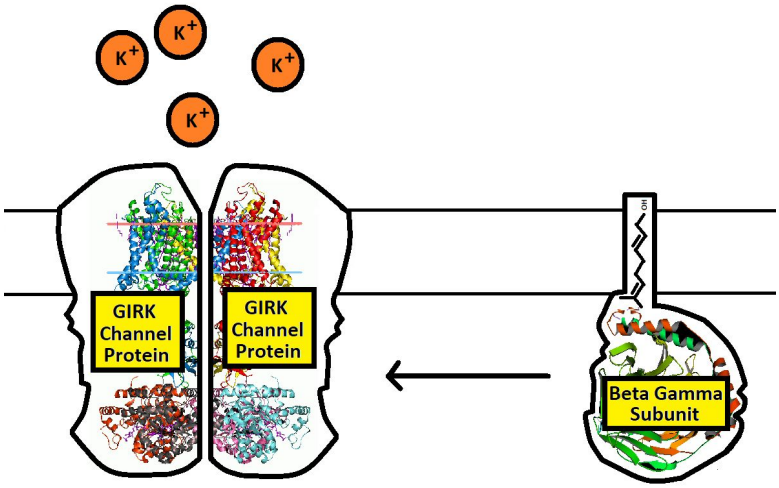
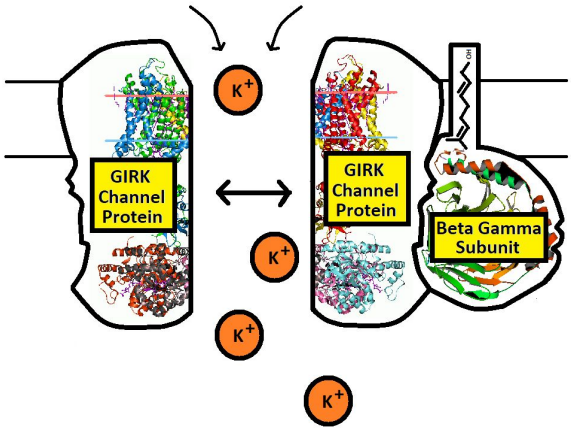


Figure 10.A.8 – Phosphorylase Kinase Activates Glycogen phosphorylase	Figure 10.A.9 – Glycogen Phosphorylase Breaks Down Glycogen to Glucose
	

Beta Gamma Subunit Activity: The beta gamma subunit of the G protein is also capable of activating other proteins. As an example of this, included is a GIRK channel protein, although it is not activated by epinephrine. After reception of the ligand, the beta gamma subunit separates from the receptor and alpha subunit and will move through the membrane and bind with G Protein-coupled inwardly rectifying potassium channel (GIRK) protein, causing the protein to open **(Figure 10.A.10)** and allow K+ ions into the cell **(Figure 10.A.11)**.

Figure 10.A.10 – Beta Gamma Binding	Figure 10.A.11 – GIRK Channel Opens
	

IP3 DAG Calcium Pathway: Upon receipt of the proper ligand, the IP3 DAG calcium pathway can also be activated by a G-protein. The Alpha Subunit with GTP attached is released from the beta gamma subunits and the receptor and travels along the membrane until contacting a phospholipase C (PLC) molecule **(Figure 10.A.12)**. This activates the phospholipase C and changes its shape so it can catalyze the breakdown of a PIP2 molecule, which consists of a DAG and IP3 molecule bound together in the membrane **(Figure 10.A.13)**. The two molecules are separated, with the DAG molecule remaining in the membrane and the IP3 molecule moving through the cytoplasm **(Figure 10.A.14).** The IP3 molecule interacts with calcium channels in the endoplasmic reticulum **(Figure 10.A.15)**. The calcium channels open and let calcium free, which can activate further proteins and cause various changes in the cell **(Figure 10.A.16)**.

Figure 10.A.12 – G Protein activates PLC

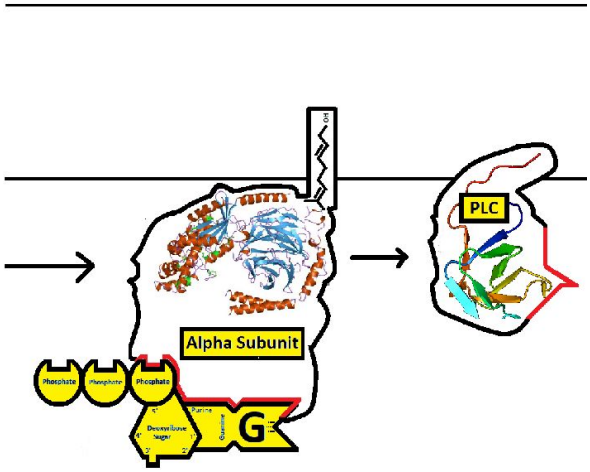


Figure 10.A.13 – PLC catalyzes breakdown of PIP2

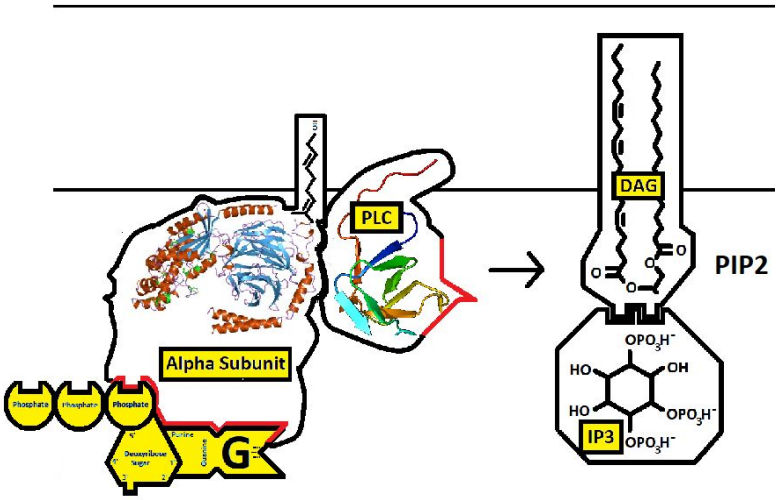


Figure 10.A.14 – PIP2 broken down to DAG and IP3

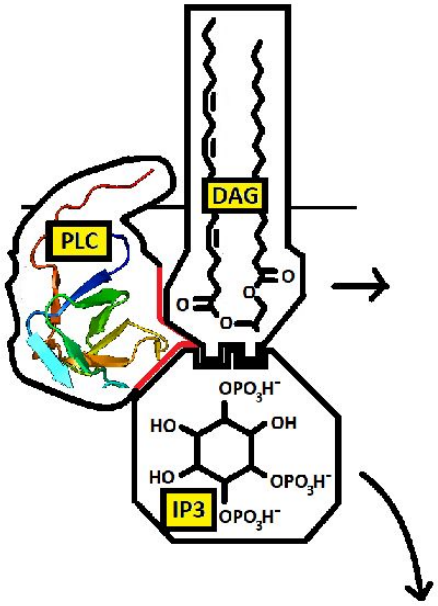


Figure 10.A.15 – PLC catalyzes breakdown of PIP2

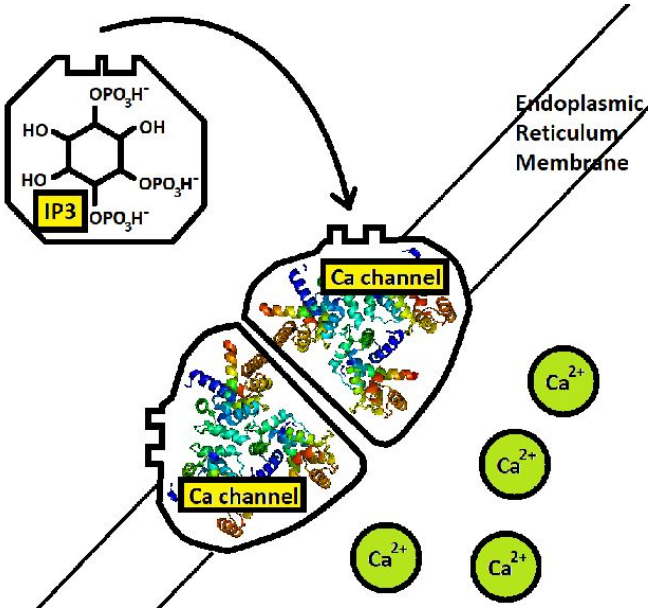
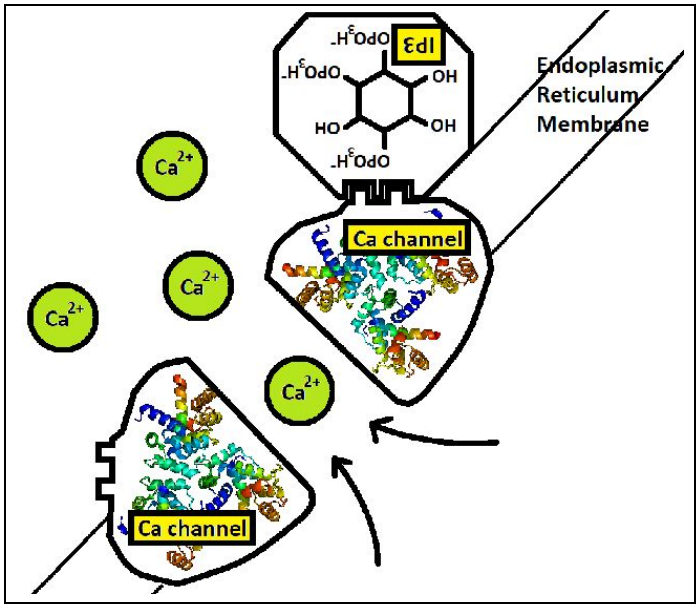


Figure 10.A.16 – PIP2 broken down to DAG and IP3

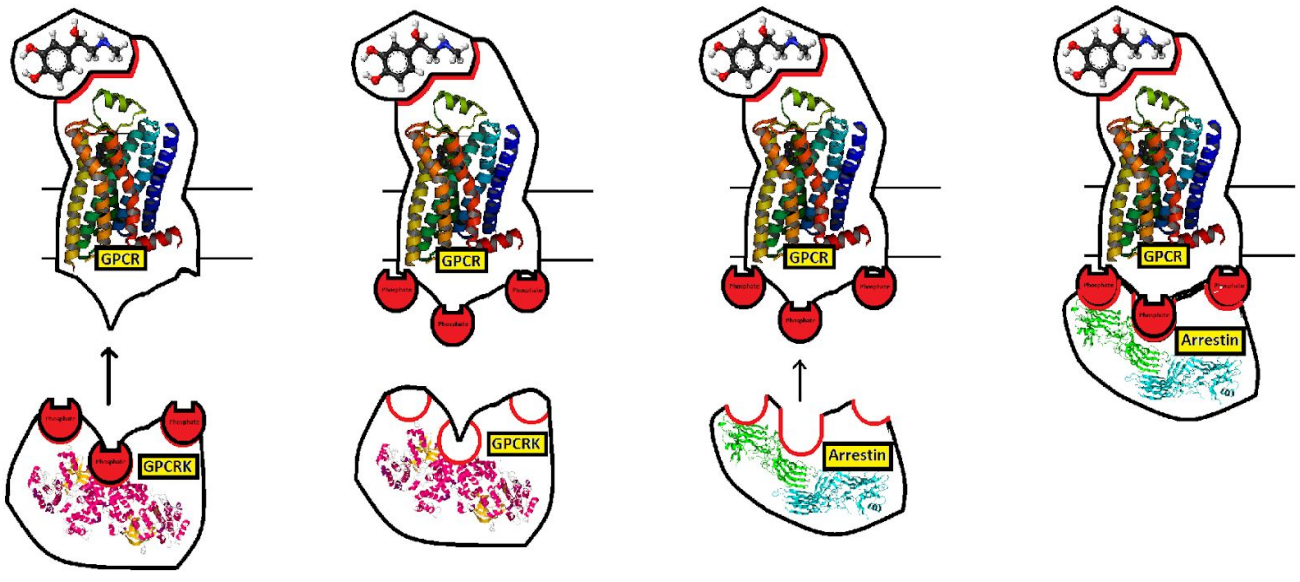


Student Centered Activity (20-50 minutes): After teaching G protein signaling, put students into small groups. A copy of the student guide for the lesson may be given to each group if necessary. Have the students take turns moving the magnets and modeling the cell signaling processes. Allow the students to correct and help one another. Continue to practice until each student can model G protein cell signaling accurately without looking at the guide.

Extra exercises:

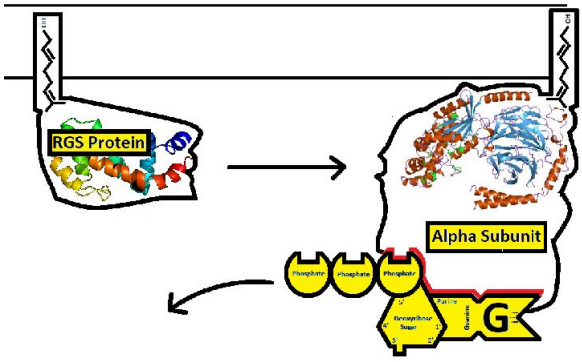
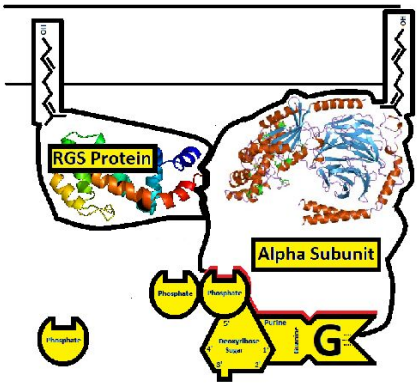
G-Protein Cellular Receptor Kinase Activity and Arrestin: The G protein signaling pathway can be shut down by the G-Protein cellular receptor kinase protein along with the arrestin protein. G protein cellular receptor kinase will cause phosphorylation of the GPCR**.** The arrestin protein will then bind to the phosphorylated receptor. This shuts down the ability of G proteins to be activated by receptors, even though they have received signals **(Figure 10.A.17).**

Figure 10.A.17– GPCRK and Arrestin shut down G Protein Receptor and stop signaling pathway



RGS Protein Activity: The regulator of G protein signaling (RGS) protein can further regulate G protein activity and slow down or shut down the signaling pathway. The RGS protein can bind to the activated G protein alpha unit **(Figure**

10.A.18), causing hydrolysis of the bound GTP into GDP + P, changing the shape of the alpha subunit and stopping its activity **(Figure 10.A.19)**.

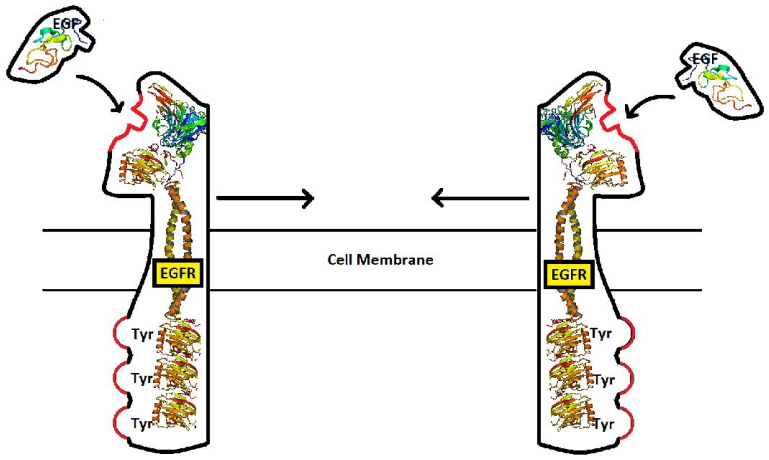
Figure 10.A.18 – RGS Protein binds alpha subunit	Figure 10.A.19 – G Protein inactivated
	

Internet research and making magnets: There are numerous examples of G protein cell signaling. Have the students do some internet or YouTube research to find a cell-signaling pathway that differs from the one shown in this activity. The students can use index cards, colored pencils, and magnetic tape to make their own magnets and present their pathway to other groups or to the teacher. For example, students could go to YouTube and watch *G protein signaling pathway-underlying photo-transduction* and make magnets to demonstrate that process.

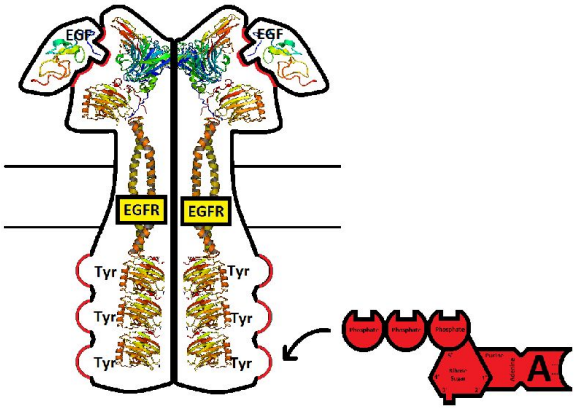
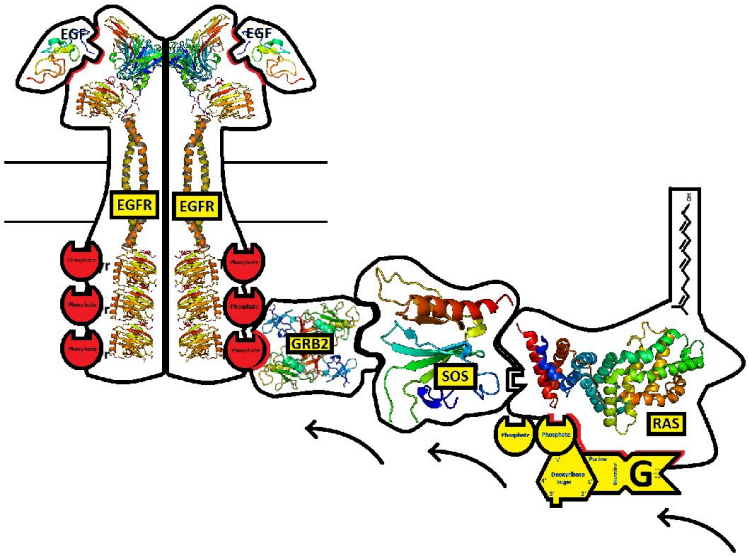
Lesson 10B – MAPK Signaling Pathway and Steroids – (10-50 Minutes)

Teacher-Centered Activity (10-30 minutes): MAPK signaling pathway: This lesson reviews another common example of cell signaling using the Biology Magnets from Module 10. Start the lesson setting up the starting configuration of a cell membrane with two EGF receptors. EGF is a *mitogen*, a molecule that leads to mitosis, thus the name of the signaling pathway, *mitogen activated protein kinase (MAPK)*. Draw the membrane with markers. The signaling pathway begins with EGF binding to the receptors, and the receptors coming together, forming a dimer (**Figure 10.B.1**).

Figure (**Figure 10.B.1**) – **Reception of Epidermal Growth Factor**



The reception of EGF prompts phosphorylation of the tyrosine residues by kinases on both receptors **(Figure 10.B.2).** . ATP becomes ADP and the phosphate is added to the tyrosine. The phosphorylation allows the GRB2 protein to attaches to the receptor, which then allows attachment of SOS followed by an inactive RAS protein with GDP attached **(Figure 10.B.3).**

Figure 10.B.2 – RGS Protein binds alpha subunit	Figure 10.B.3 – G Protein inactivated
	

The RAS protein will be activated upon binding with the SOS protein. GDP will break free and be replaced by a GTP molecule **(Figure 10.B.4)**. The activated RAS will then bind and phosphorylate B-RAF, which starts a phosphorylation cascade within the cytoplasm of the cell, The B-RAF binds an ATP molecule **(Figure 10.B.5)**, which will then be used to phosphorylate MEK1/2 **(Figure 10.B.6).** The MEK 1/2 then phosphorylates ERK ½ **(Figure 10.B.7).** Finally, the ERK1/2 phosphorylates the fos-jun transcription factor **(Figure 10.8.8),** which enters the nucleus and binds to the DNA at the AP-1 gene to start transcription **(Figure 10.8.9)**. The gene codes for several proteins which, when translated, initiate cell division.

Figure 10.B.4 – Activation of RAS	Figure 10.B.5 – Activation of B-RAF

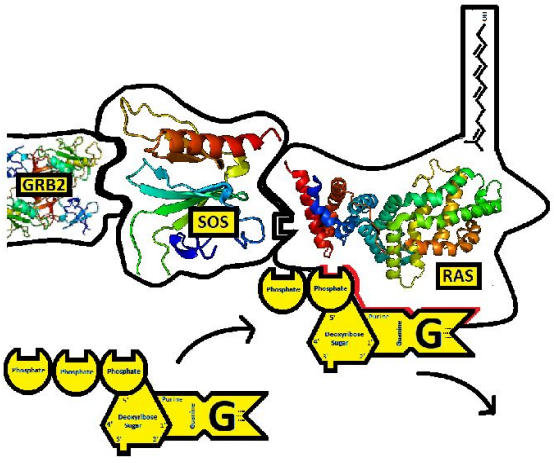
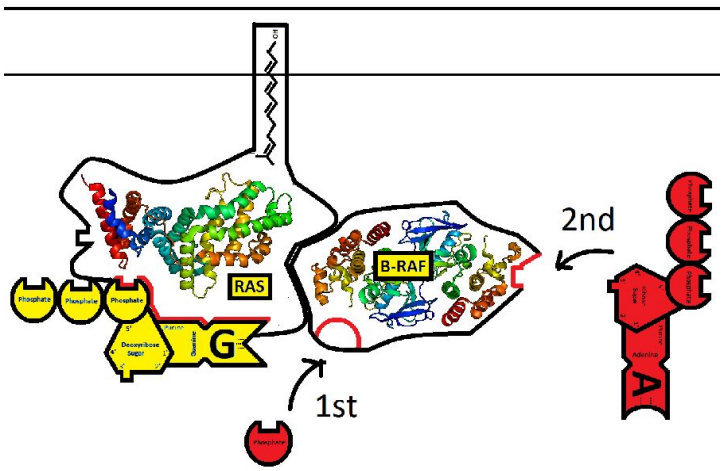

	

Figure 10.B.6 – Phosphorylation of MEK1/2	**Figure 10.B.7 – Activation of B-RAF**

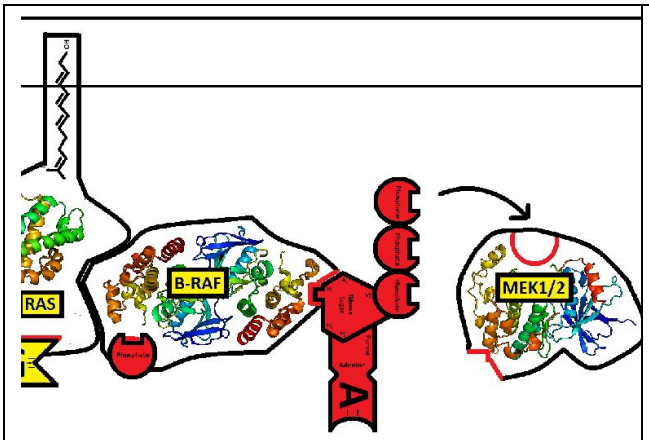


Figure 10.B.8 – Phosphorylation of fos-jun

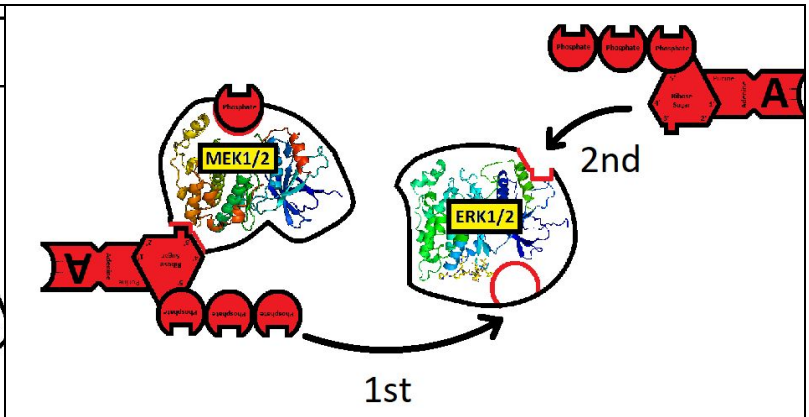
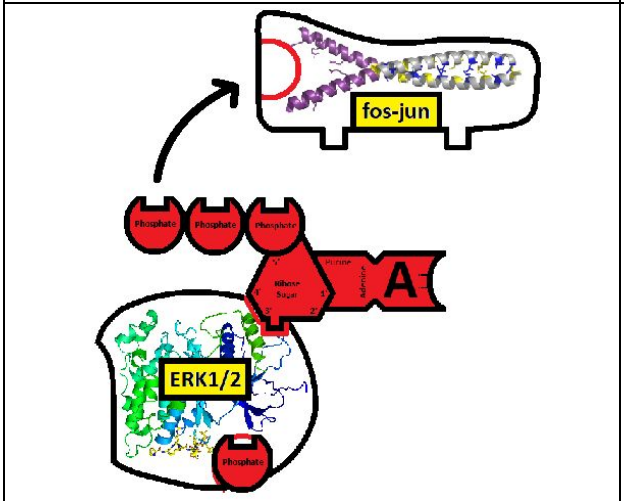
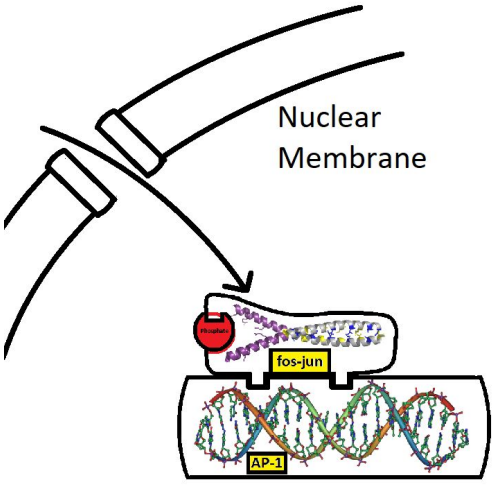


Figure 10.B.9 – G Protein inactivated





Student Centered Activity (10-40 minutes): After teaching the MAPK signaling pathway, put students into small groups. A copy of the student guide for the lesson may be given to each group if necessary. Have the students take turns moving the magnets and modeling the cell signaling processes. Allow the students to correct and help one another. Continue to practice until each student can model MAPK cell signaling accurately without looking at the guide.

Extra Exercises:

MAPK Regulation Using GAP Protein: The GTPase Activating Protein (GAP) is used by the cell to turn off or slow down the MAPK signal pathway. GTPase attaches to the RAS protein and hydrolyzes the GTP bound to RAS to GDP, inactivating the RAS protein **(Figure 10.B.10).** The B-RAF protein then detaches from RAS and becomes inactive, stopping the MAPK signaling pathway **(Figure 10.B.11)**.

Figure 10.B.10 – GAP Protein Inactivates RAS

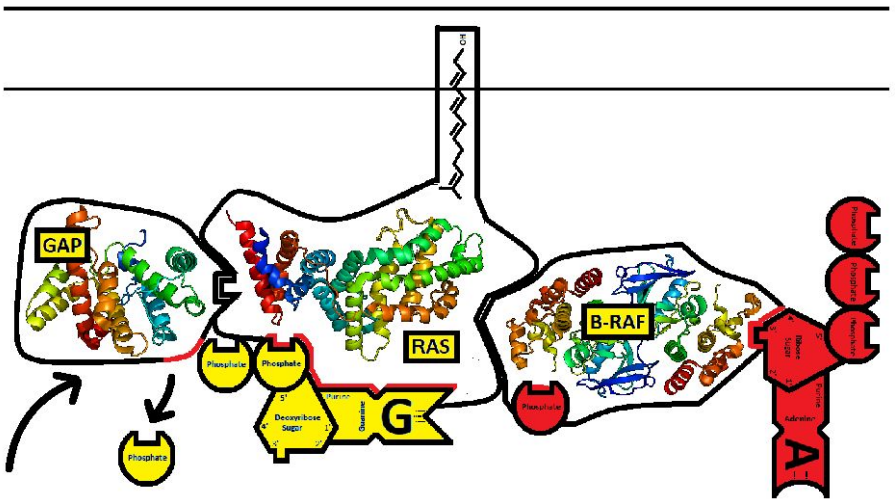
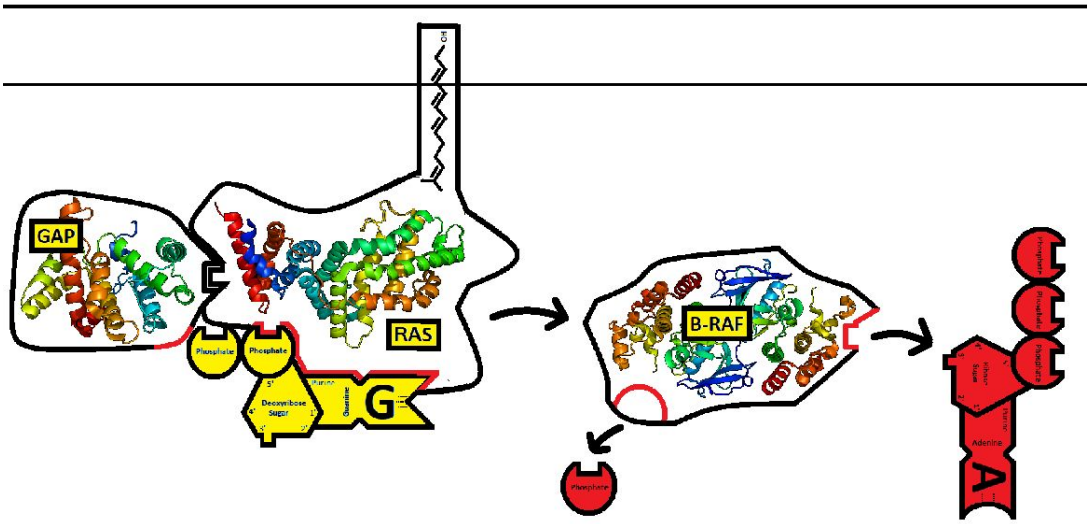
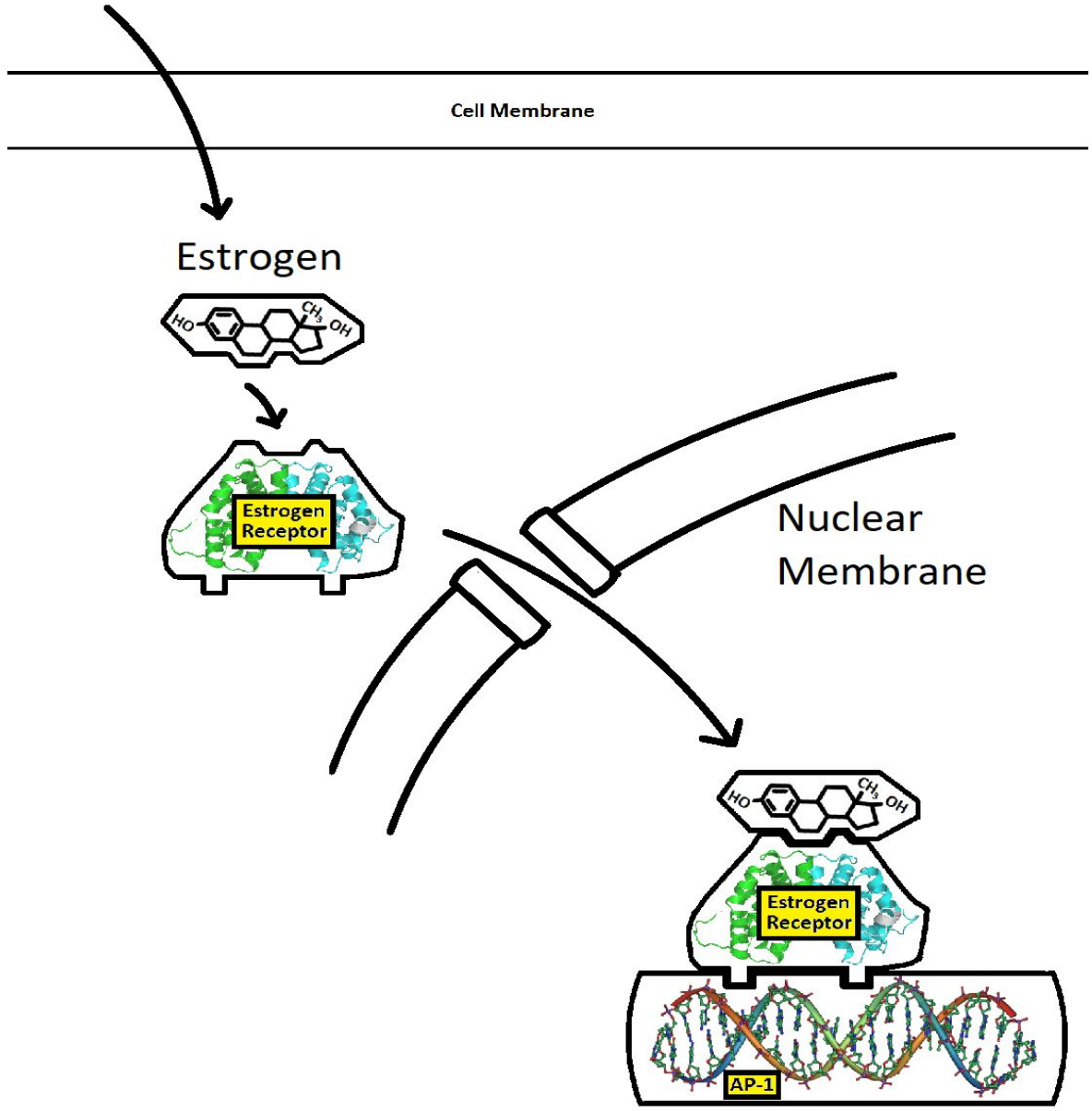


Figure 10.B.11 – B-RAF Detaches and Inactivates



Steroid Hormone Action: Steroid hormones such as estrogen and testosterone can enter the cell directly through the membrane. Because they are lipid soluble, they move through the lipid bilayer and bind with receptors in the cytoplasm or in the nucleus. Demonstrate this with the estrogen and estrogen receptor magnets **(Figure 10.B.12)**.

Figure (Figure 10.B.12) – Steroid Hormone Action

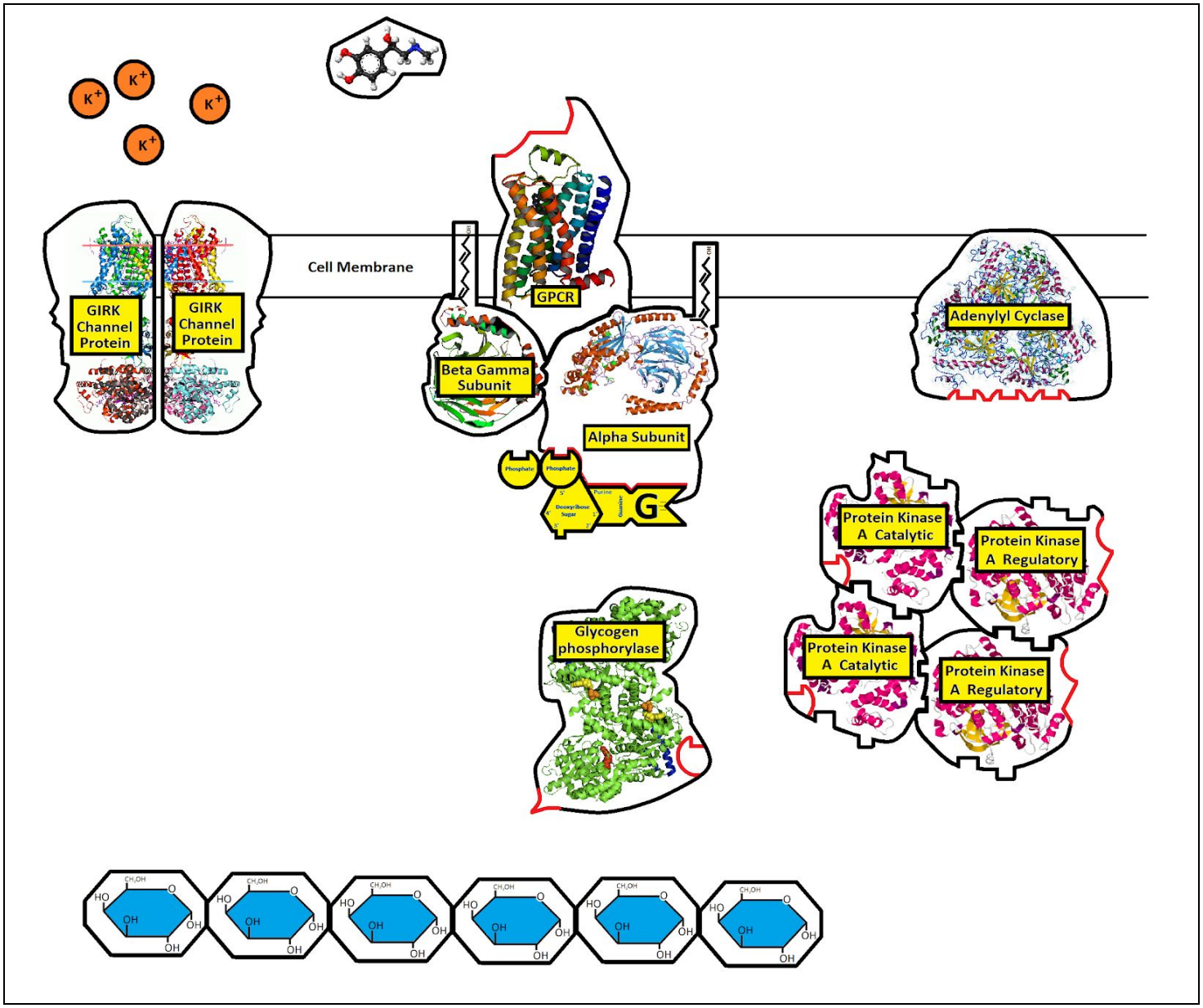


Internet research and making magnets: The MAPK pathway is actually more complicated than shown with the magnets in this module. Have the students do some internet research to find greater detail regarding the MAPK pathway and its effects. Similarly, students can research other types of steroid hormones and their methods of action. The students can use index cards, colored pencils, and magnetic tape to make their own magnets and present the pathways to other groups or to the teacher.

Lesson 10A – G Protein Signaling – Student Handout

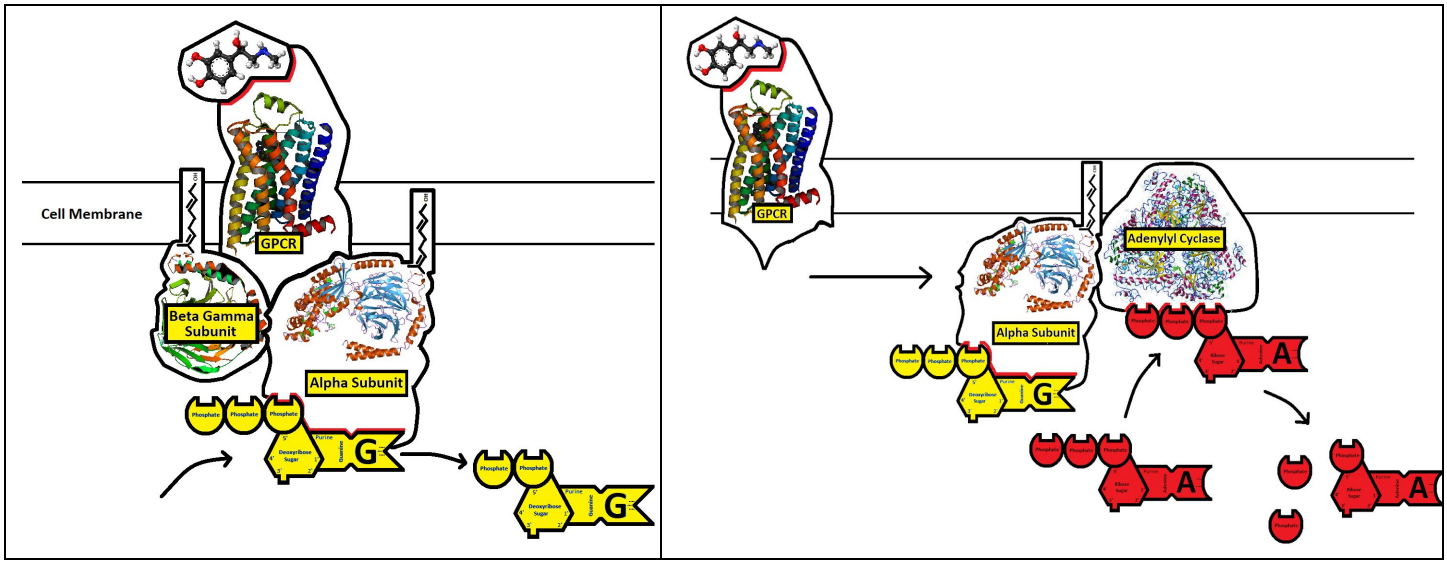
Epinephrine signaling pathway: Start the lesson setting up the starting configuration of a cell membrane from a liver cell as shown (**Figure 10.A.1**). Draw the membrane with markers.

Figure 10.A.1 – Cell Signaling Initial Setup



First, reception of epinephrine occurs when epinephrine binds with the G-protein coupled receptor (GPCR), which causes a conformational change in the G protein within the membrane. This allows GTP to replace the GDP on the alpha subunit of the G protein (**Figure 10.A.2**) This leads to the dissociation of the alpha and beta/gamma subunits from the GPCR. The alpha subunit will move along the membrane until it binds adenylate cyclase. This activates the adenylate cyclase enzyme to break apart ATP into two phosphates and a cyclic AMP (cAMP) molecule. The cAMP molecule will then move through the cytoplasm where it acts as a second messenger to activate other enzymes (**Figure 10.A.3**).

Figure 10.A.2 – Epinephrine Reception	**Figure 10.A.3 – Adenylate Cyclase Activation and Activity**



Two cAMP molecules will attach to the regulatory subunits of the protein kinase A molecule **(figure 10.A.4)**, which causes the protein kinase A to break up into four pieces, releasing the catalytic subunits **(figure 10.A.5)**. The catalytic subunits are phosphorylated by ATP **(Figure 10.A.6)**, then catalyze the phosphorylation of the phosphorylase kinase enzyme **(Figure 10.A.7)**. Phosphoylase kinase in turn phosphorylates glycogen phosphorylase **(Figure 10.A.8)**. This causes the glycogen phosphorylase enzyme to be activated and become capable of breaking down glycogen into glucose. The glucose diffuses out of the cell and thus raises the blood glucose levels in the body **(Figure 10.A.9)**.

Figure 10.A.4 – Protein Kinase A Activation

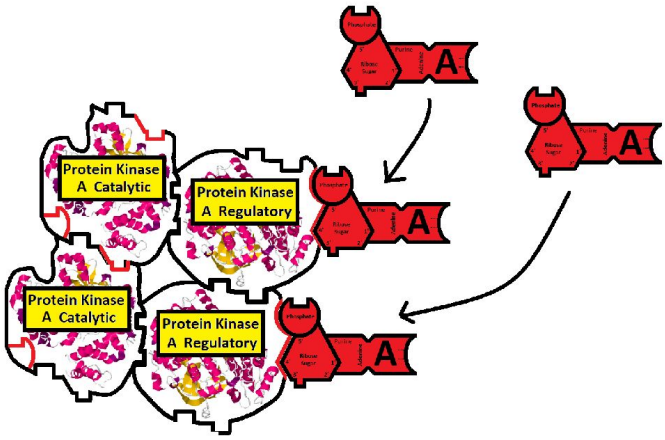


Figure 10.A.5 – Protein Kinase A Activation

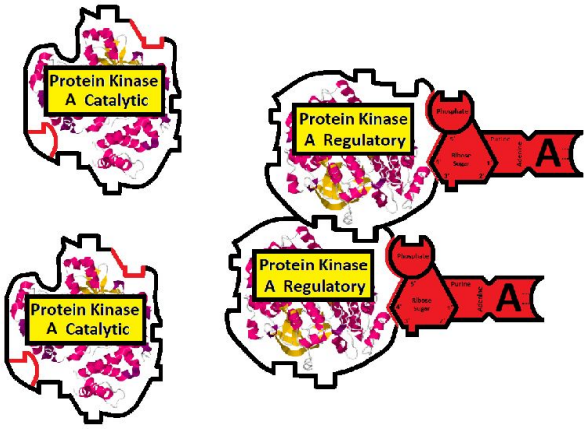


Figure 10.A.6 – Phosphorylation of Catalytic Subunits

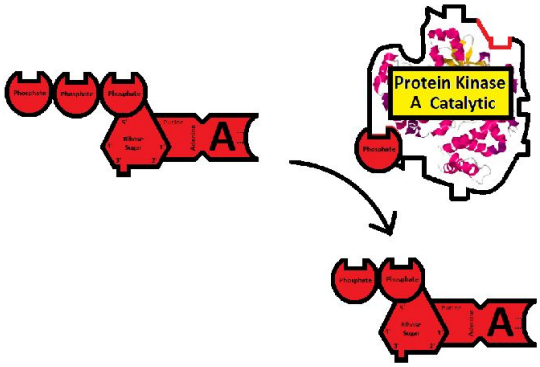


Figure 10.A.7 – Protein Kinase A/Phosphorylase Kinase

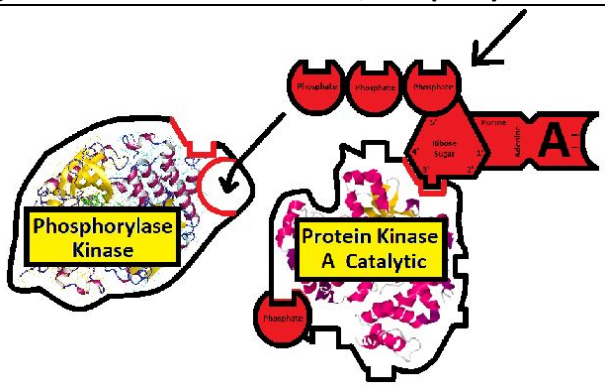


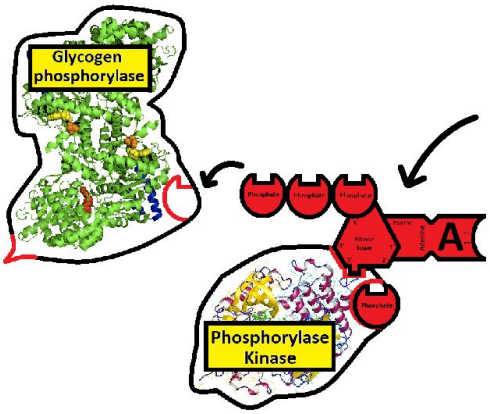
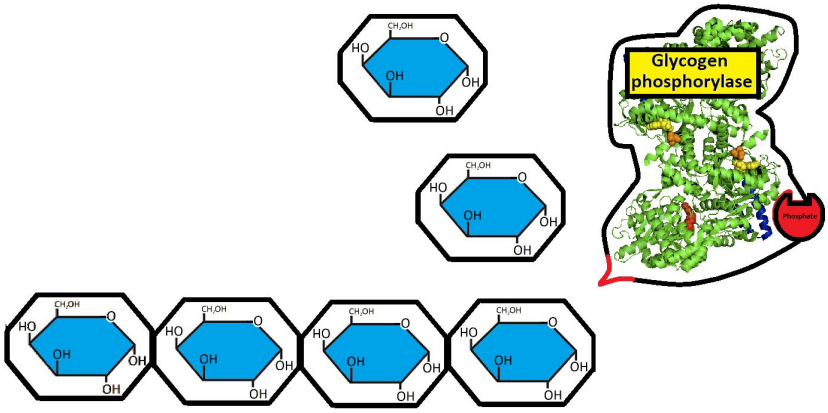
Figure 10.A.8 – Phosphorylase Kinase Activates Glycogen phosphorylase	Figure 10.A.9 – Glycogen Phosphorylase Breaks Down Glycogen to Glucose
	

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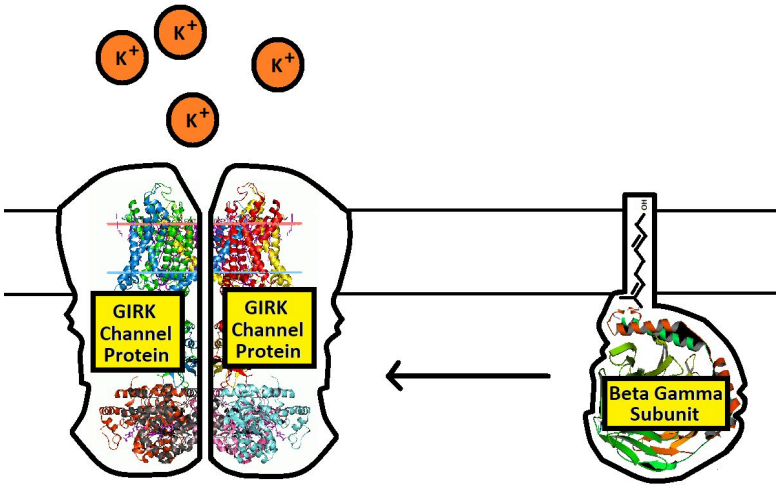
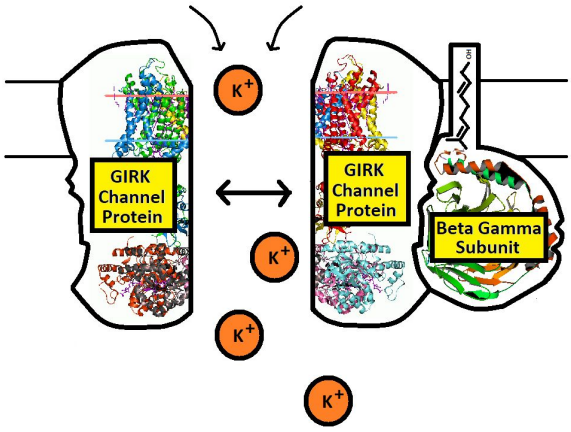
Figure 10.A.10 – Beta Gamma Binding	Figure 10.A.11 – GIRK Channel Opens
	

IP3 DAG Calcium Pathway: Upon receipt of the proper ligand, the IP3 DAG calcium pathway can also be activated by a G-protein. The Alpha Subunit with GTP attached is released from the beta gamma subunits and the receptor and travels along the membrane until contacting a phospholipase C (PLC) molecule **(Figure 10.A.12)**. This activates the phospholipase C and changes its shape so it can catalyze the breakdown of a PIP2 molecule, which consists of a DAG and IP3 molecule bound together in the membrane **(Figure 10.A.13)**. The two molecules are separated, with the DAG molecule remaining in the membrane and the IP3 molecule moving through the cytoplasm **(Figure 10.A.14).** The IP3 molecule interacts with calcium channels in the endoplasmic reticulum **(Figure 10.A.15)**. The calcium channels open and let calcium free, which can activate further proteins and cause various changes in the cell **(Figure 10.A.16)**.

Figure 10.A.12 – G Protein activates PLC

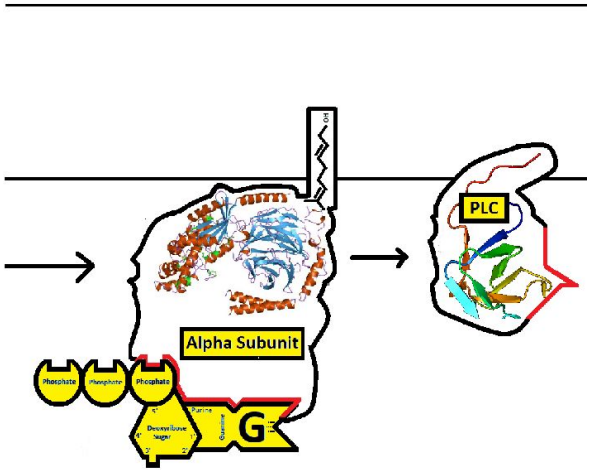


Figure 10.A.13 – PLC catalyzes breakdown of PIP2

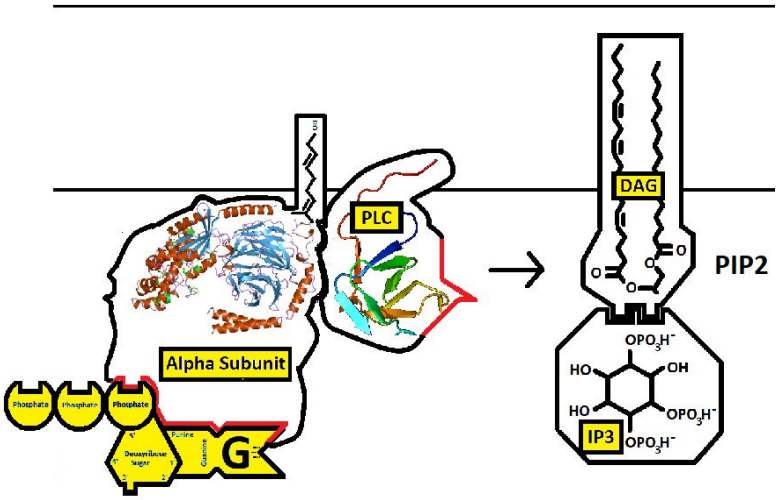


Figure 10.A.14 – PIP2 broken down to DAG and IP3

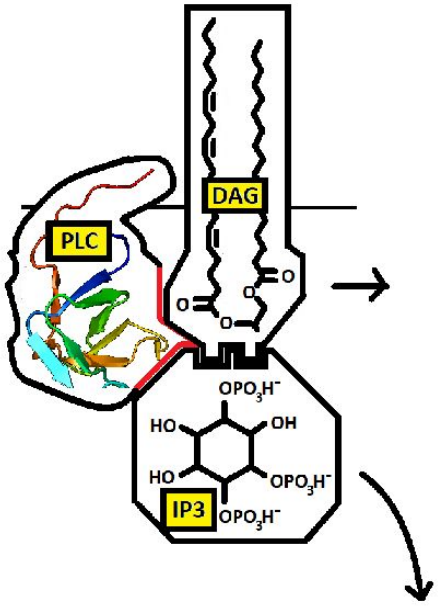


Figure 10.A.15 – PLC catalyzes breakdown of PIP2

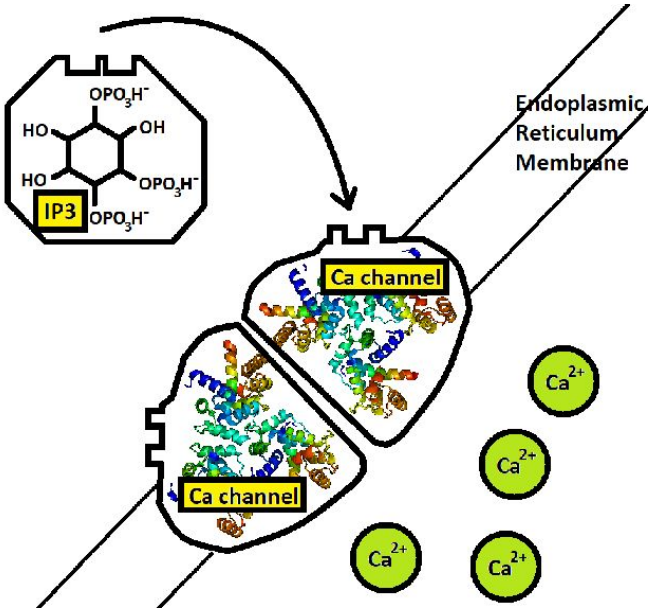
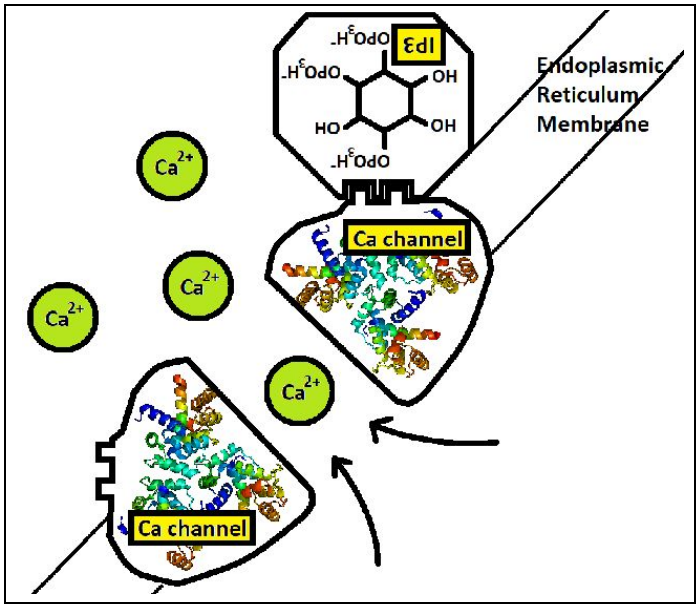


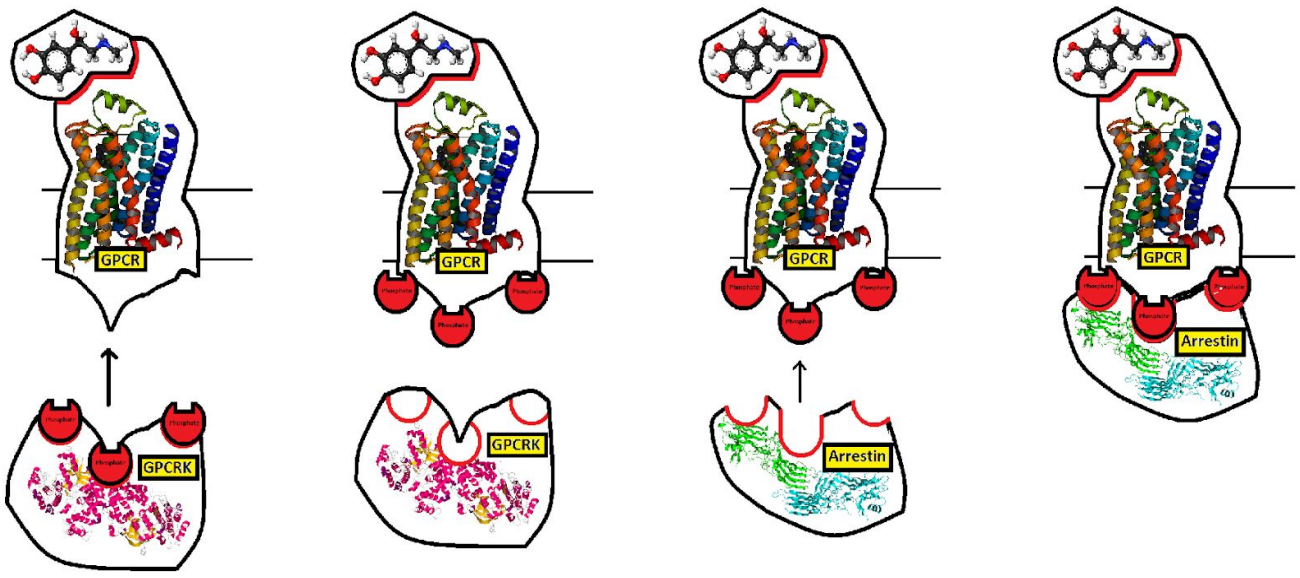
Figure 10.A.16 – PIP2 broken down to DAG and IP3



Extra Exercises:

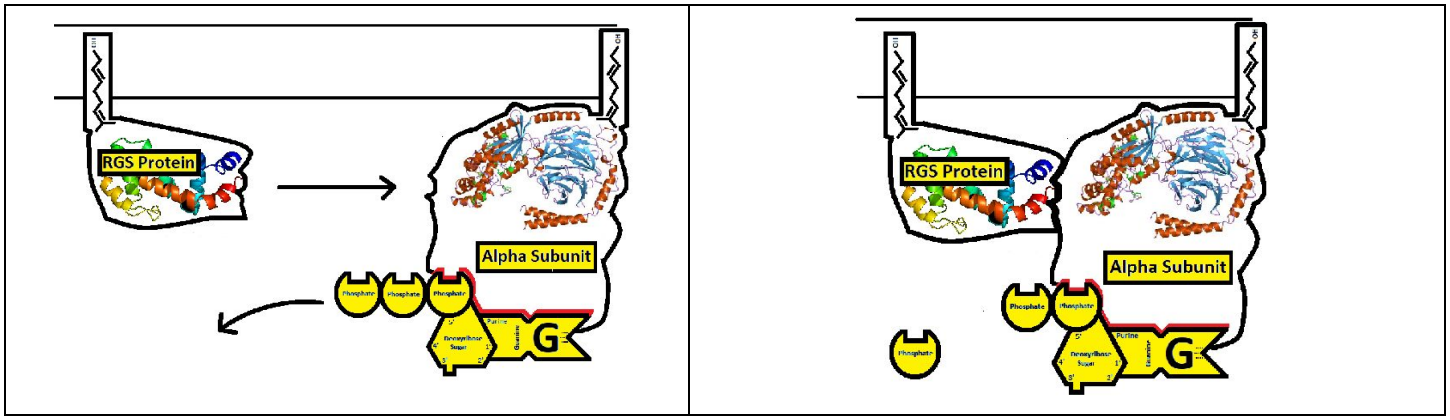
G-Protein Cellular Receptor Kinase Activity and Arrestin: The G protein signaling pathway can be shut down by the G-Protein cellular receptor kinase protein along with the arrestin protein. G protein cellular receptor kinase will cause phosphorylation of the GPCR**.** The arrestin protein will then bind to the phosphorylated receptor. This shuts down the ability of G proteins to be activated by receptors, even though they have received signals **(Figure 10.A.17).**

Figure 10.A.17 – GPCRK and Arrestin shut down G Protein Receptor and stop signaling pathway



RGS Protein Activity: The regulator of G protein signaling (RGS) protein can further regulate G protein activity and slow down or shut down the signaling pathway. The RGS protein can bind to the activated G protein alpha unit **(Figure 10.A.18)**, causing hydrolysis of the bound GTP into GDP + P, changing the shape of the alpha subunit and stopping its activity **(Figure 10.A.19)**.

Figure 10.A.18 – RGS Protein binds alpha subunit	Figure 10.A.19 – G Protein inactivated

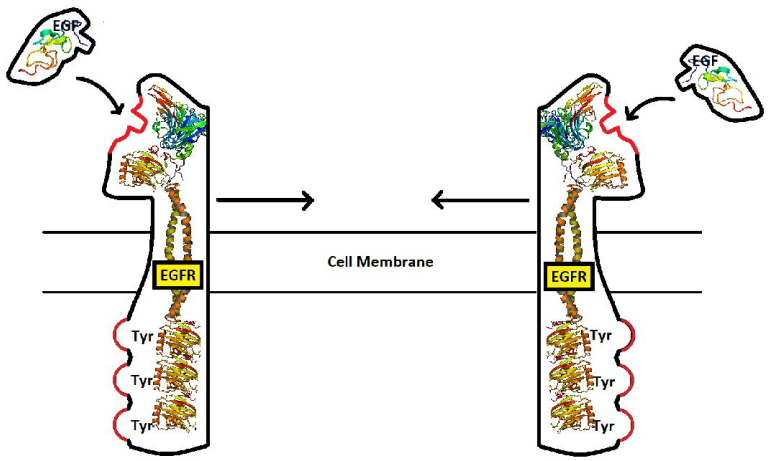


Internet research and making magnets: There are numerous examples of G protein cell signaling. Do some internet or YouTube research to find a cell-signaling pathway that differs from the one shown in this activity. Use index cards, colored pencils, and magnetic tape to make magnets and present the pathways to other groups or to the teacher. For example, go to YouTube and watch *G protein signaling pathway-underlying photo-transduction* and make magnets to demonstrate that process.

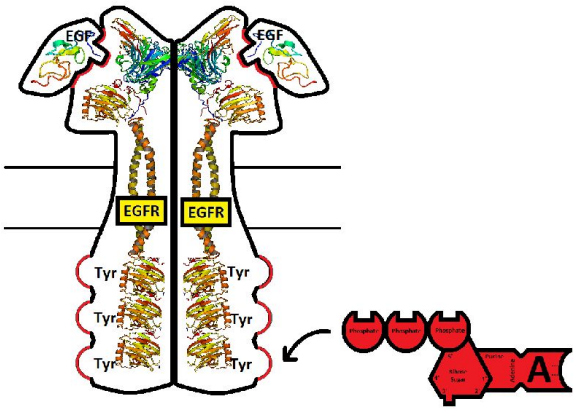
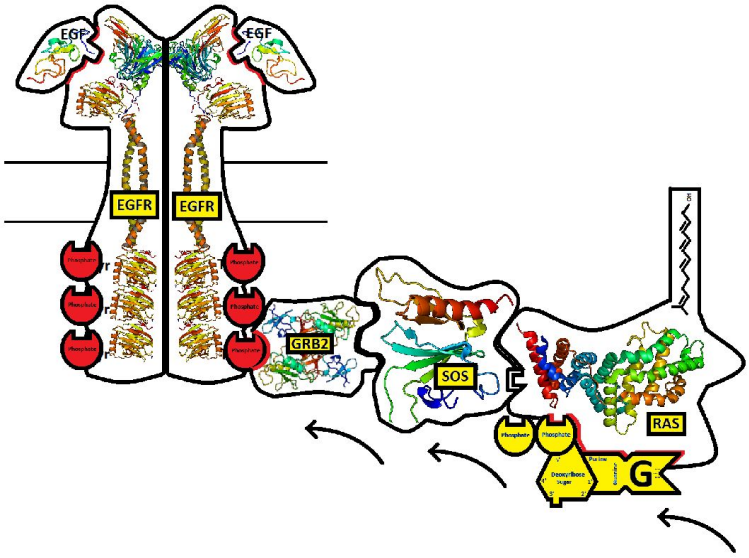
Lesson 10B – MAPK Signaling Pathway – Student Handout (10-40 Minutes)

MAPK signaling pathway: This lesson reviews another common example of cell signaling using the Biology Magnets from Module 10. Start the lesson setting up the starting configuration of a cell membrane with two EGF receptors. EGF is a *mitogen*, a molecule that leads to mitosis, thus the name of the signaling pathway, *mitogen activated protein kinase (MAPK)*. Draw the membrane with markers. The signaling pathway begins with EGF binding to the receptors, and the receptors coming together, forming a dimer (**Figure 10.B.1**).

Figure (Figure 10.B.1) – Reception of Epidermal Growth Factor



The reception of EGF prompts phosphorylation of the tyrosine residues by kinases on both receptors **(Figure 10.B.2).** . ATP becomes ADP and the phosphate is added to the tyrosine. The phosphorylation allows the GRB2 protein to attaches to the receptor, which then allows attachment of SOS followed by an inactive RAS protein with GDP attached **(Figure 10.B.3).**

Figure 10.B.2 – RGS Protein binds alpha subunit	Figure 10.B.3 – G Protein inactivated
	

The RAS protein will be activated upon binding with the SOS protein. GDP will break free and be replaced by a GTP molecule **(Figure 10.B.4)**. The activated RAS will then bind and phosphorylate B-RAF, which starts a phosphorylation cascade within the cytoplasm of the cell, The B-RAF binds an ATP molecule **(Figure 10.B.5)**, which will then be used to phosphorylate MEK1/2 **(Figure 10.B.6).** The MEK 1/2 then phosphorylates ERK ½ **(Figure 10.B.7).** Finally, the ERK1/2 phosphorylates the fos-jun transcription factor **(Figure 10.8.8),** which enters the nucleus and binds to the DNA at the AP-1 gene to start transcription **(Figure 10.8.9)**. The gene codes for several proteins which, when translated, initiate cell division.

Figure 10.B.4 – Activation of RAS	Figure 10.B.5 – Activation of B-RAF

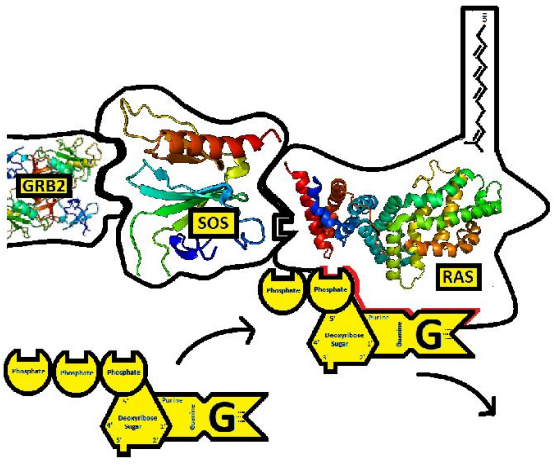
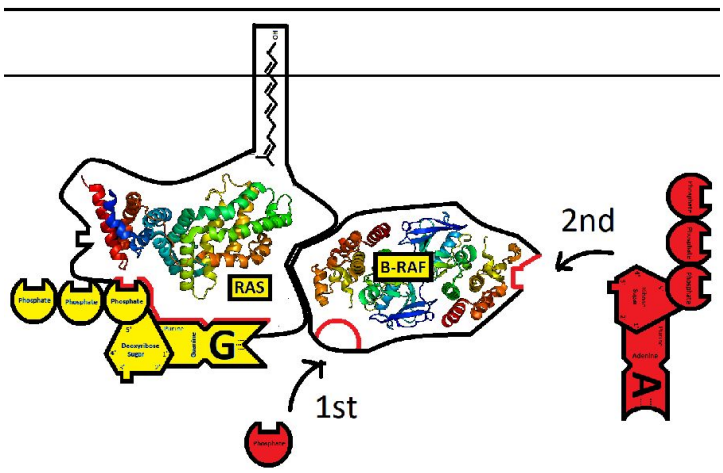

	

Figure 10.B.6 – Phosphorylation of MEK1/2	**Figure 10.B.7 – Activation of B-RAF**

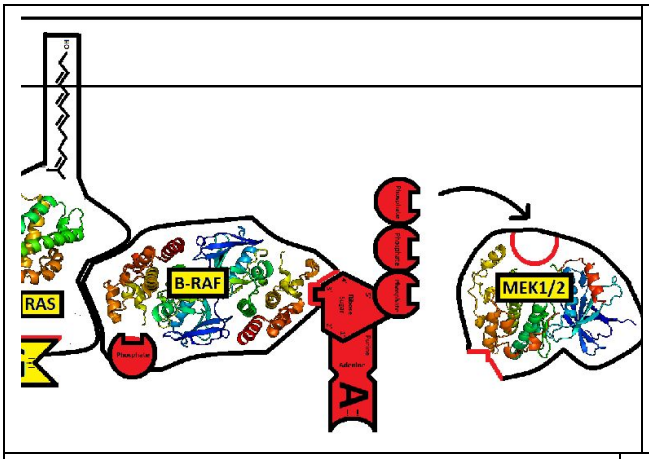


Figure 10.B.8 – Phosphorylation of fos-jun

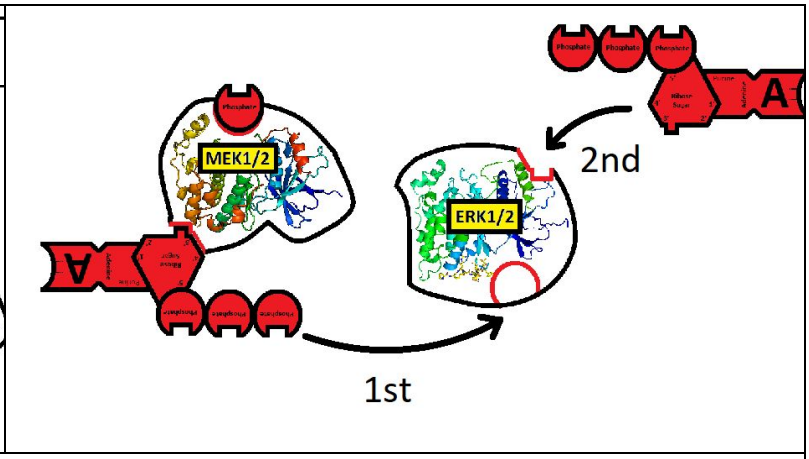
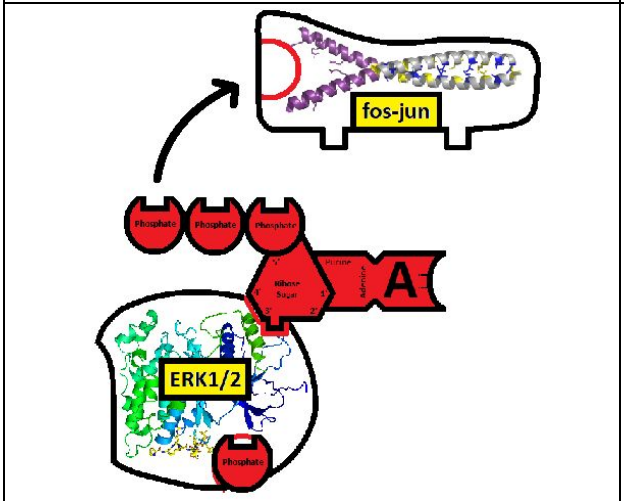
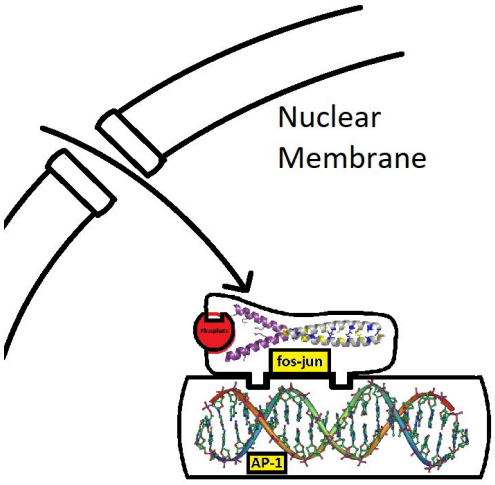


Figure 10.B.9 – G Protein inactivated





Extra Exercises:

MAPK Regulation Using GAP Protein: The GTPase Activating Protein (GAP) is used by the cell to turn off or slow down the MAPK signal pathway. GTPase attaches to the RAS protein and hydrolyzes the GTP bound to RAS to GDP, inactivating the RAS protein **(Figure 10.B.10).** The B-RAF protein then detaches from RAS and becomes inactive, stopping the MAPK signaling pathway **(Figure 10.B.11)**.

Figure 10.B.10 – GAP Protein Inactivates RAS

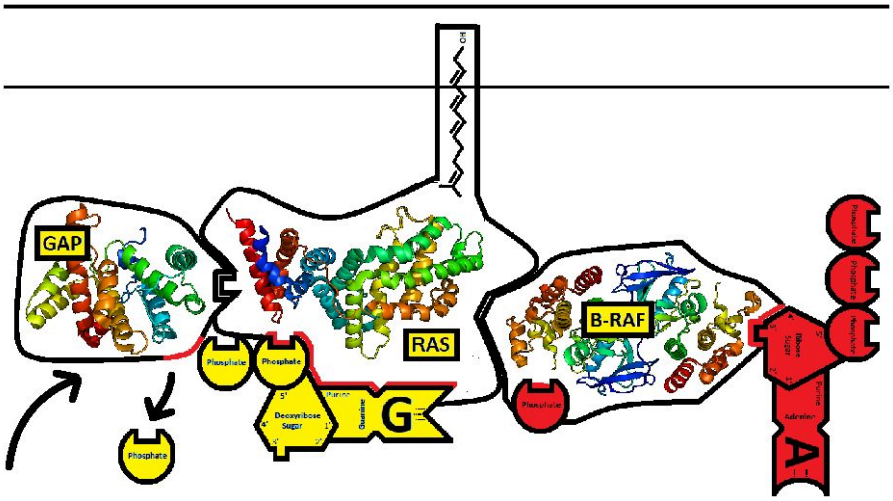
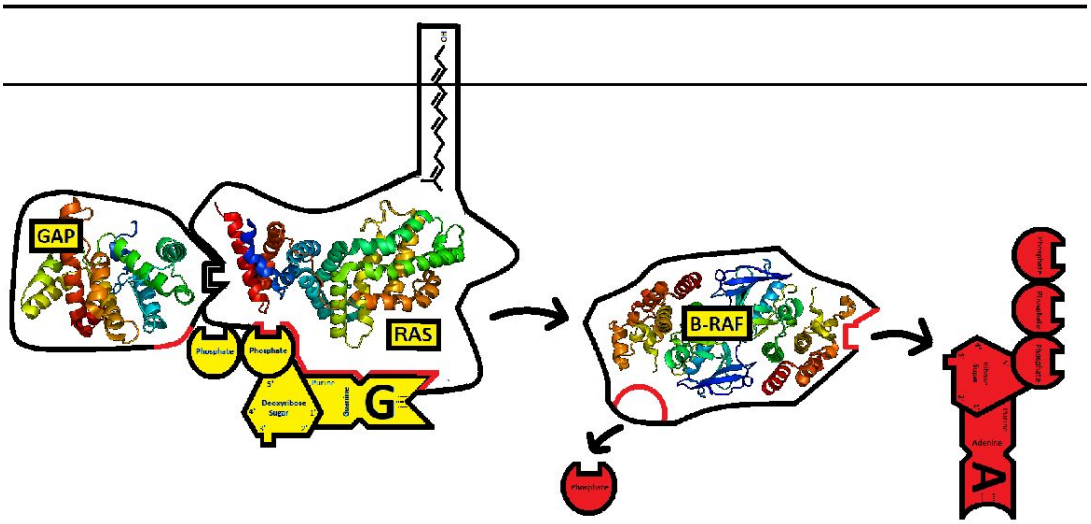
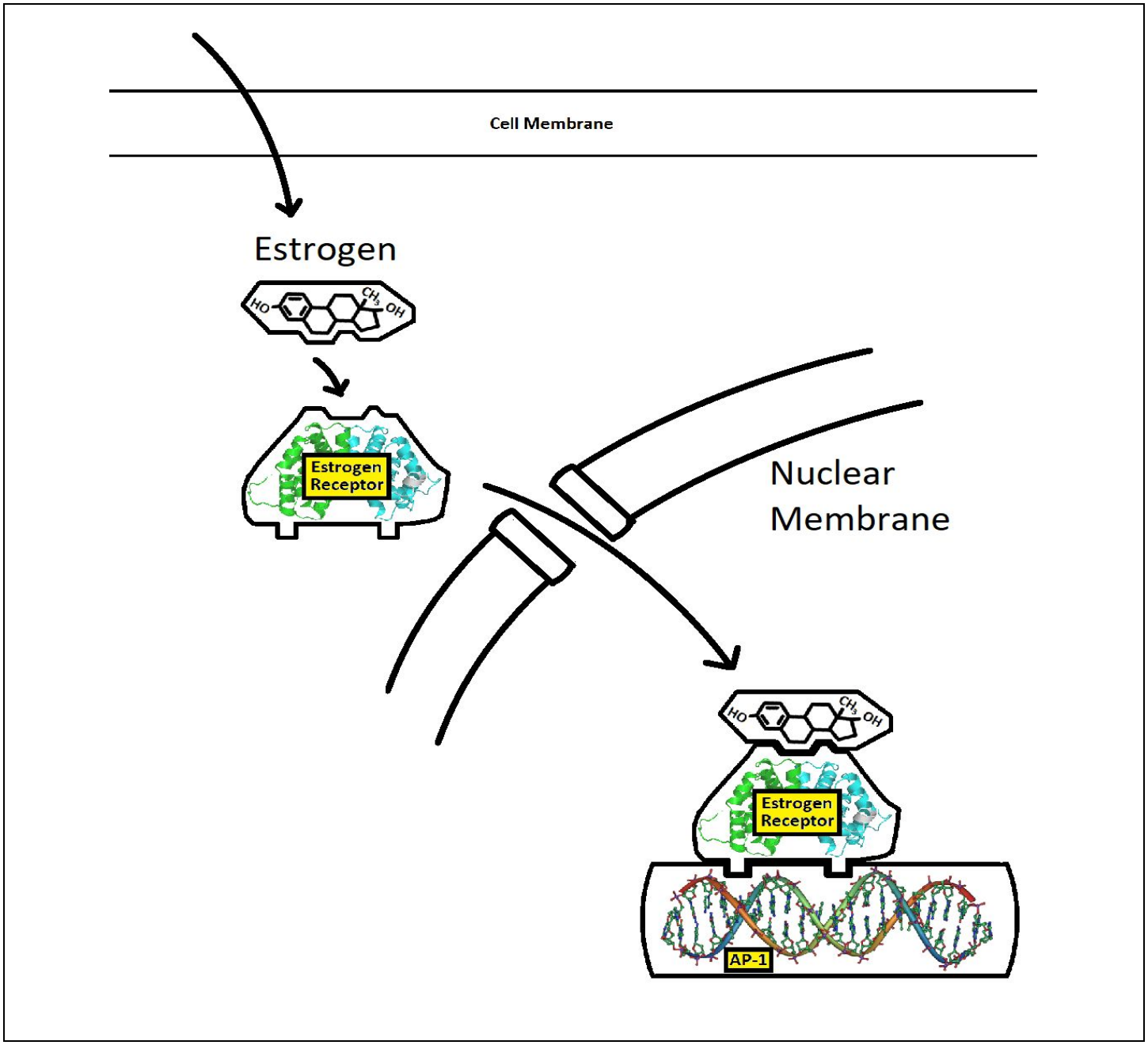


Figure 10.B.11 – B-RAF Detaches and Inactivates



Steroid Hormone Action: Steroid hormones such as estrogen and testosterone can enter the cell directly through the membrane. Because they are lipid soluble, they move through the lipid bilayer and bind with receptors in the cytoplasm or in the nucleus. Demonstrate this with the estrogen and estrogen receptor magnets **(Figure 10.B.12)**.

Figure (Figure 10.B.12) – Steroid Hormone Action



Internet research and making magnets: The MAPK pathway is actually more complicated than shown with the magnets in this module. Do some internet research to find greater detail regarding the MAPK pathway and its effects. Similarly, research other types of steroid hormones and their methods of action. Use index cards, colored pencils, and magnetic tape to make magnets and present the pathways to other groups or to the teacher.