Module 6: Enzymatic Function

Objective

The objectives of this module are:

1. To document the pathway or process in which the protein coded by the gene you are annotating functions.
2. To determine if an Enzyme Commission (EC) number should be assigned to the protein encoded by your gene, or, if one has already been assigned, to confirm that it is correct.

Materials

To perform this activity you will need:

- Access to the internet on a computer equipped with the most recent version of Firefox (preferred), Chrome or Safari.
- To have completed the sign up for GENI-ACT described in the Signing Up for GENI-ACT section of the manual.

Background

KEGG

KEGG (Kyoto Encyclopedia of Genes and Genomes) is an extremely diverse database of genomic information, contained in a number of sub-databases, including KEGG Pathways and Modules. These seek to define enzymatic pathways, subcellular structures, and a number of other modular or sequential functions and processes in terms of maps that visualize the pathway or module and the genes involved in them. A summary of KEGG in terms of its structure and history can be found at http://en.wikipedia.org/wiki/KEGG . Using this database you hope find a graphic describing the process or structure in which the protein you are annotating plays a roll.

MetaCyc

MetaCyc is a database of experimentally determined metabolic pathways. For each of these pathways, MetaCyc provides an abundance of information. MetaCyc can serve as a reference data set for computationally predicting the metabolic pathways of organisms from their sequenced genomes.

Expasy Enzyme

The Expasy Enzyme database is a repository of information relative to the nomenclature of enzymes. It is primarily based on the recommendations of the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (IUBMB), and it contains the following data for each type of characterized enzyme for which an EC (Enzyme Commission) number has been provided:

- EC number
- Recommended name
- Alternative names (if any)
- Catalytic activity
- Cofactors (if any)
- Pointers to the Swiss-Prot protein sequence entries that correspond to the enzyme (if any)
- Pointers to human disease(s) associated with a deficiency of the enzyme (if any)

Enzyme Commission (EC) Number

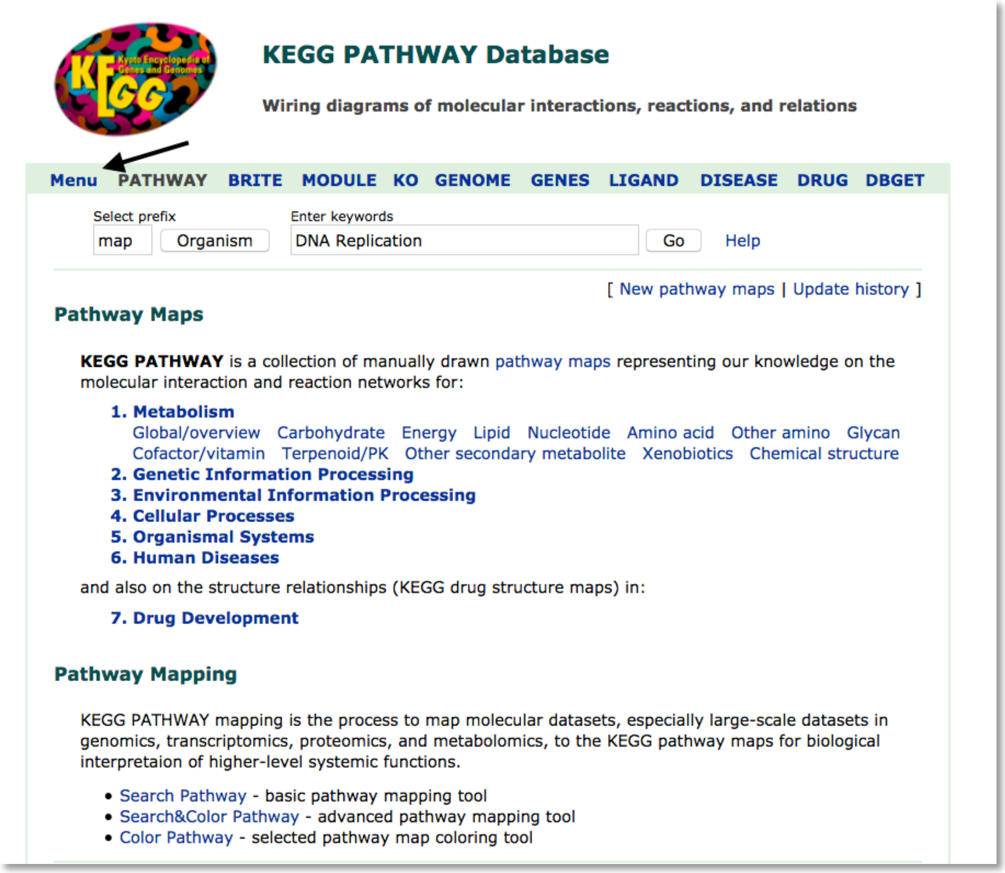
The Enzyme Commission number (EC number) is a numerical classification scheme for enzymes, based on the chemical reactions they catalyze. More detailed information on EC numbers can be found at

http://www.chem.qmul.ac.uk/iubmb/enzyme/ . If your protein is an enzyme, you may already know the EC number for it from your previous searches, but if you have not come across the number you will find it in this module. You may be the first to suggest the correct EC number if you are working on a hypothetical protein that you have found to have similarity to an enzyme.

Procedures

KEGG

1. Navigate to KEGG at http://www.genome.jp/kegg/pathway.html.
2. If you know the name of the pathway or structure in which your gene product participates, enter all or part of that name in the search box under "Pathway Entries and Pathway Modules" and click "Go." For the example we will use here, Ksed_00020, the gene product name is DNA polymerase III, beta subunit (as determined from the gene information page for this gene). One might deduce from this name that this protein functions in DNA replication. Figure 6.1 shows the KEGG start page with DNA replication entered in the search window. Hitting go after entering this term will result in in a page similar to Figure 6.2.



KEGG PATHWAY Database

Wiring diagrams of molecular interactions, reactions, and relations

Enter keywords: DNA Replication

[New pathway maps | Update history]

Pathway Maps

KEGG PATHWAY is a collection of manually drawn pathway maps representing our knowledge on the molecular interaction and reaction networks for:

1. **Metabolism**
   Global/overview Carbohydrate Energy Lipid Nucleotide Amino acid Other amino Glycan
   Cofactor/vitamin Terpenoid/PK Other secondary metabolite Xenobiotics Chemical structure
2. **Genetic Information Processing**
3. **Environmental Information Processing**
4. **Cellular Processes**
5. **Organismal Systems**
6. **Human Diseases**

and also on the structure relationships (KEGG drug structure maps) in:

7. **Drug Development**

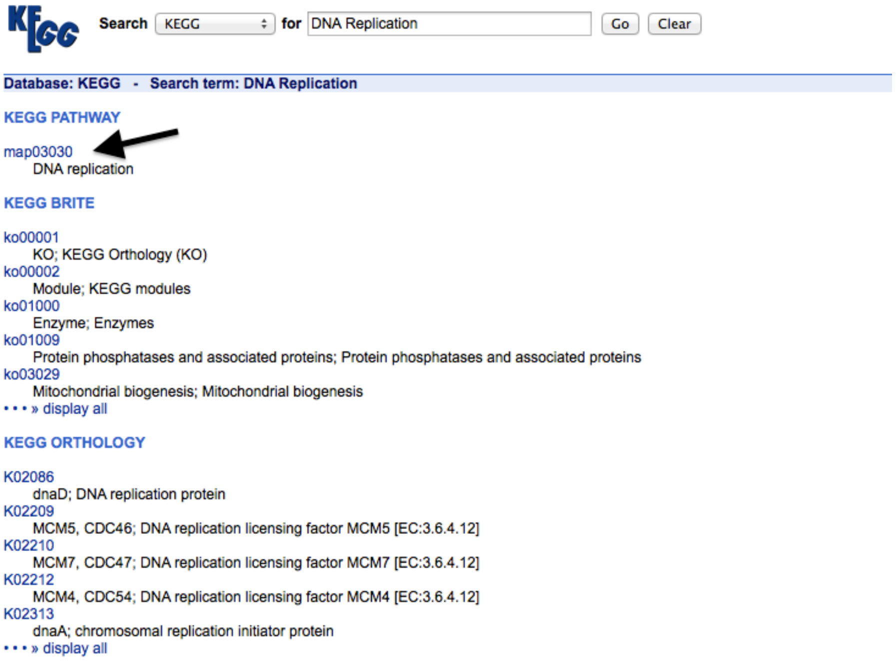
Pathway Mapping

KEGG PATHWAY mapping is the process to map molecular datasets, especially large-scale datasets in genomics, transcriptomics, proteomics, and metabolomics, to the KEGG pathway maps for biological interpretaion of higher-level systemic functions.

- Search Pathway - basic pathway mapping tool
- Search&Color Pathway - advanced pathway mapping tool
- Color Pathway - selected pathway map coloring tool

Figure 6.1. The KEGG start page, with DNA replication entered into the search box. The arrow points to the pull down menu to get to KEGG2, which is referred to later in this section.

3. On the resulting page, all pathways, structures or pathway linked to the search terms chosen are listed (Figure 6.2).
4. Click on the hyperlink to see the Pathway page for that pathway Figure 6.3).



Search KEGG for DNA Replication

Database: KEGG - Search term: DNA Replication

KEGG PATHWAY

map03030
DNA replication

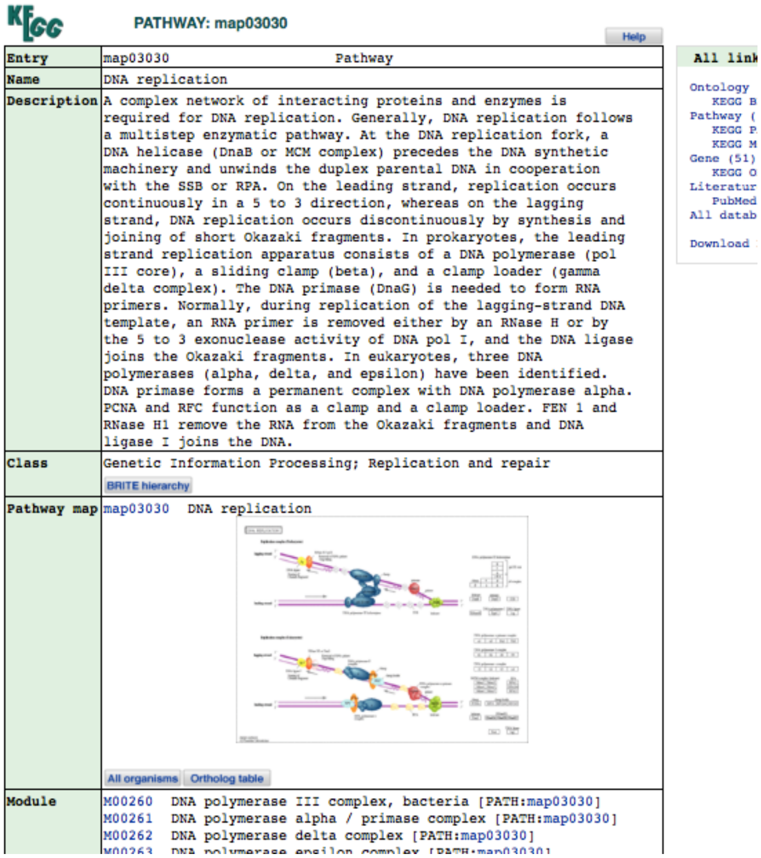
KEGG BRITE

ko00001
KO; KEGG Orthology (KO)
ko00002
Module; KEGG modules
ko01000
Enzyme; Enzymes
ko01009
Protein phosphatases and associated proteins; Protein phosphatases and associated proteins
ko03029
Mitochondrial biogenesis; Mitochondrial biogenesis
• • • » display all

KEGG ORTHOLOGY

K02086
dnaD; DNA replication protein
K02209
MCM5, CDC46; DNA replication licensing factor MCM5 [EC:3.6.4.12]
K02210
MCM7, CDC47; DNA replication licensing factor MCM7 [EC:3.6.4.12]
K02212
MCM4, CDC54; DNA replication licensing factor MCM4 [EC:3.6.4.12]
K02313
dnaA; chromosomal replication initiator protein
• • • » display all

Figure 6.2. The results of the KEGG t search for DNA Replication. Note the pathway hit is DNA replication. Clicking on the hyperlink (Arrow), reveals the full description of the KEGG process, as shown in Figure 6.3.



Entry	map03030 Pathway
Name	DNA replication
Description	A complex network of interacting proteins and enzymes is required for DNA replication. Generally, DNA replication follows a multistep enzymatic pathway. At the DNA replication fork, a DNA helicase (DnaB or MCM complex) precedes the DNA synthetic machinery and unwinds the duplex parental DNA in cooperation with the SSB or RPA. On the leading strand, replication occurs continuously in a 5 to 3 direction, whereas on the lagging strand, DNA replication occurs discontinuously by synthesis and joining of short Okazaki fragments. In prokaryotes, the leading strand replication apparatus consists of a DNA polymerase (pol III core), a sliding clamp (beta), and a clamp loader (gamma delta complex). The DNA primase (DnaG) is needed to form RNA primers. Normally, during replication of the lagging-strand DNA template, an RNA primer is removed either by an RNase H or by the 5 to 3 exonuclease activity of DNA pol I, and the DNA ligase joins the Okazaki fragments. In eukaryotes, three DNA polymerases (alpha, delta, and epsilon) have been identified. DNA primase forms a permanent complex with DNA polymerase alpha. PCNA and RFC function as a clamp and a clamp loader. FEN 1 and RNase H1 remove the RNA from the Okazaki fragments and DNA ligase I joins the DNA.
Class	Genetic Information Processing; Replication and repair
Pathway map	map03030 DNA replication
Module	M00260 DNA polymerase III complex, bacteria [PATH:map03030] M00261 DNA polymerase alpha / primase complex [PATH:map03030] M00262 DNA polymerase delta complex [PATH:map03030] M00263 DNA polymerase epsilon complex [PATH:map03030]

Figure 6.3. The KEGG Pathway Page for DNA Replication. See text for explanation.

5. Click on the pathway map link to view the map graphic (Figure 6.4).
6. The online instructions for this module ask you to simply record the pathway identification number and the reference pathway image in your notebook, but KEGG can offer much more information to help you with your annotation.
7. If you click on the reference pathway pull down menu at the top of the page you will see an image similar to that in figure 6.5, in which organisms having the genes in the pathway, process or structure are listed, but without any seeming order.

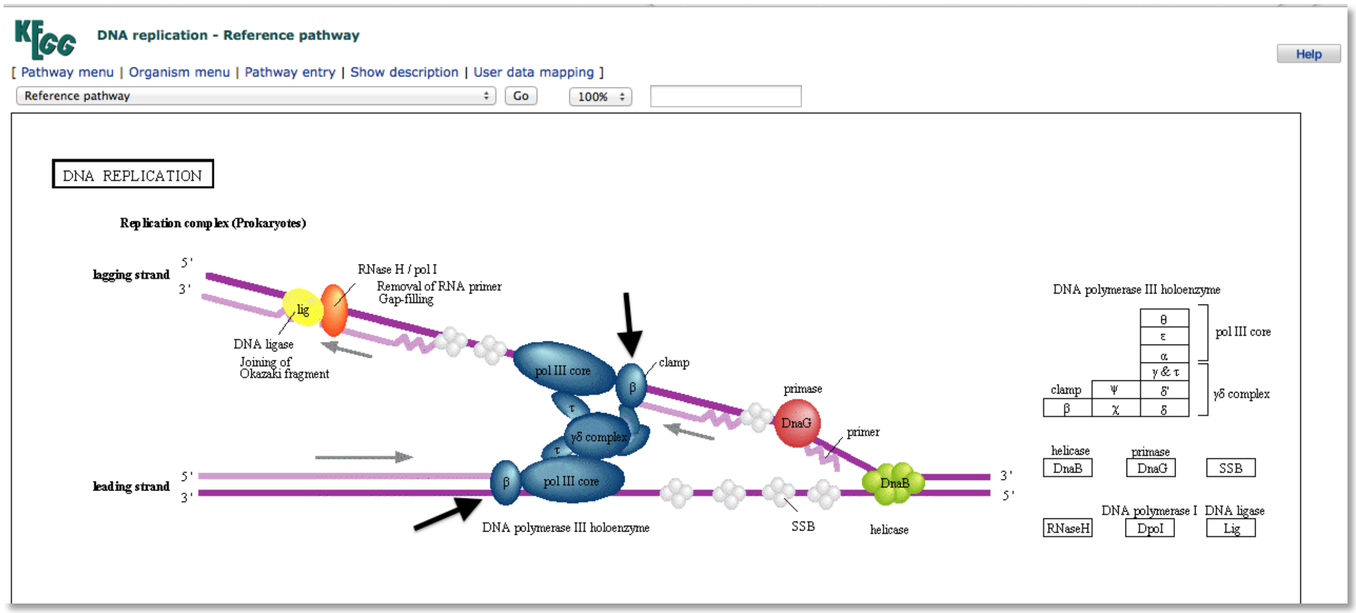


Figure 6.4. The reference pathway page for DNA replication (map 03030). The beta subunits of the DNA polymerase III holoenzyme (the name we suspect Ksed_00020 should have) are indicated by the arrows. This image shows a process rather than a true metabolic pathway, and not all organisms will have every gene product shown in a KEGG map for every pathway, process or structure. If the gene you are annotating is an enzyme in a multistep pathway, you will see a map showing all enzymes involved in the process and the products of each step.

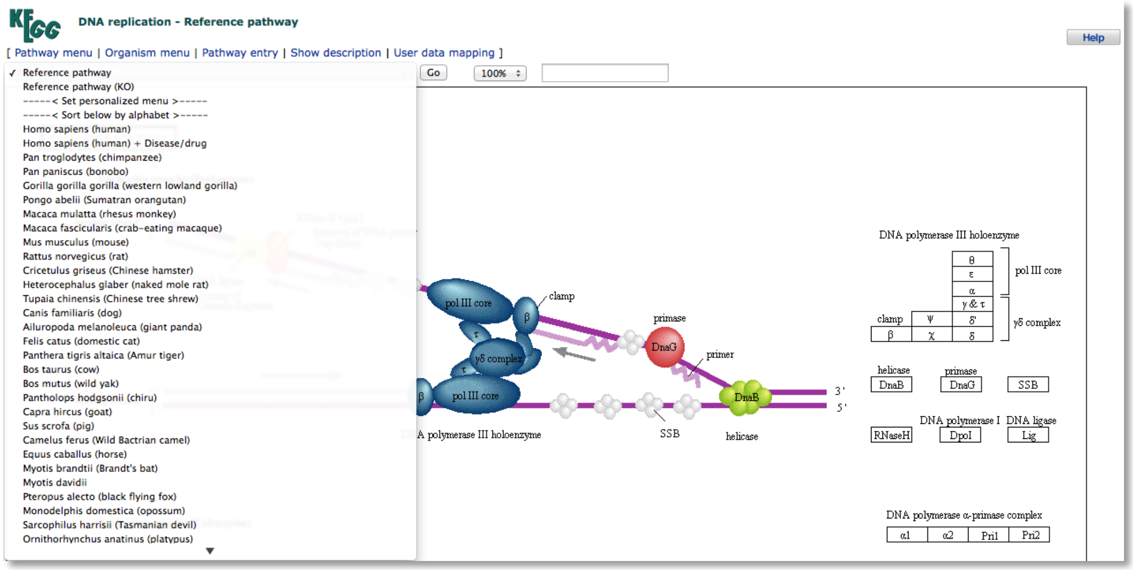


Figure 6.5. The Reference Pathway pull down menu showing some of the species having genes in the DNA replication pathway as well as options to customize the menu, one of which is the Sort Below By Alphabet option discussed in the text.

8. Click on the “sort below by alphabet” option and click on the go button as shown in figure 6.6. Now when you pull down the menu all of the organisms will be listed in alphabetical order by genus name.

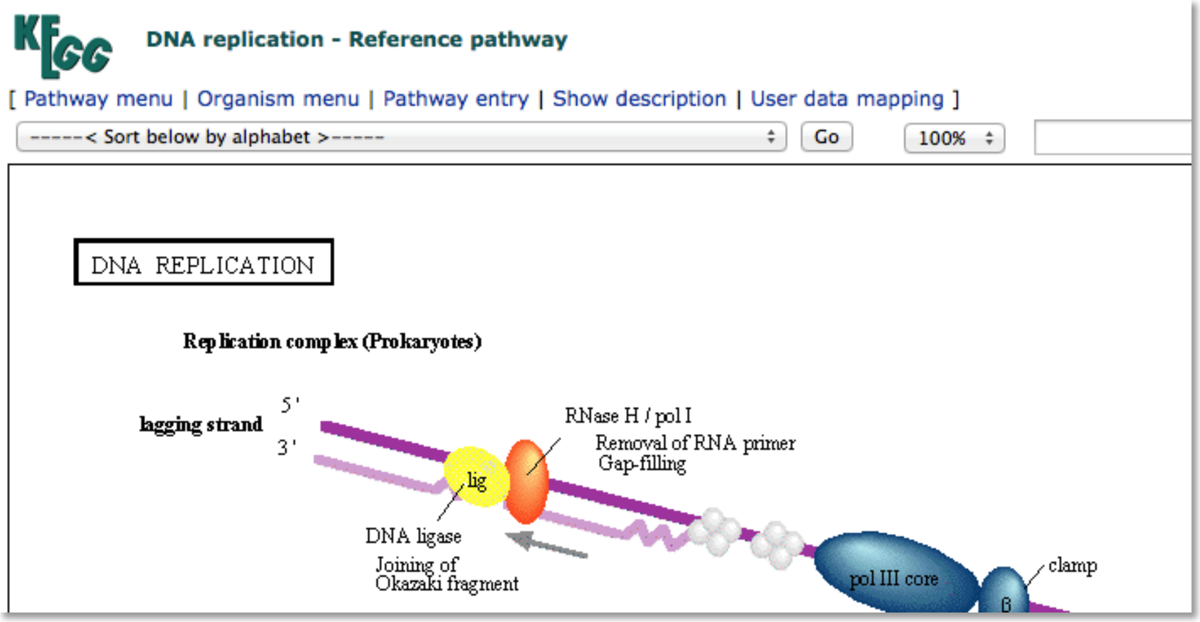


Figure 6.6. A portion of the KEGG pathway map with the Sort below by alphabet menu item selected. Hitting the Go button next to the selection will alphabetize the list of organisms.

9. Scroll down until you come to *Kytococcus sedentarius* in the list and select it…and then hit the go button a second time. You will now see a variation of the reference pathway image in which some of the items in the reference pathway are highlighted with color (Figure 6.7)

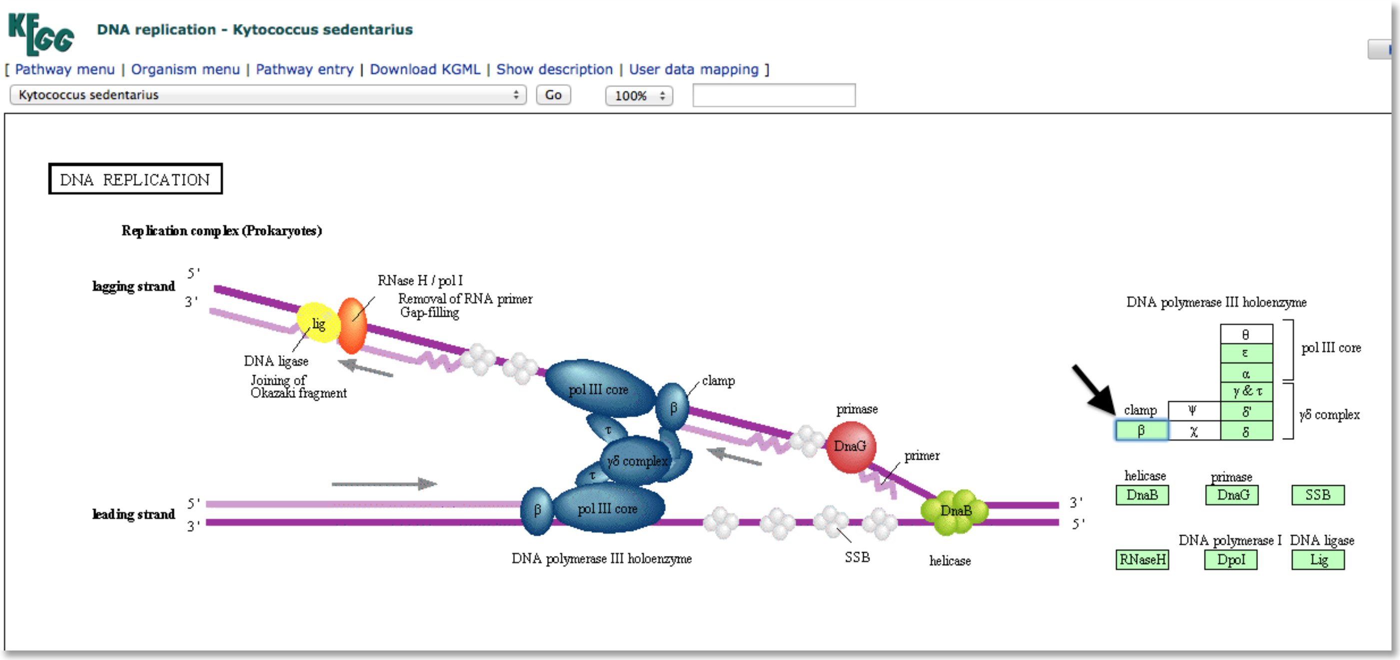
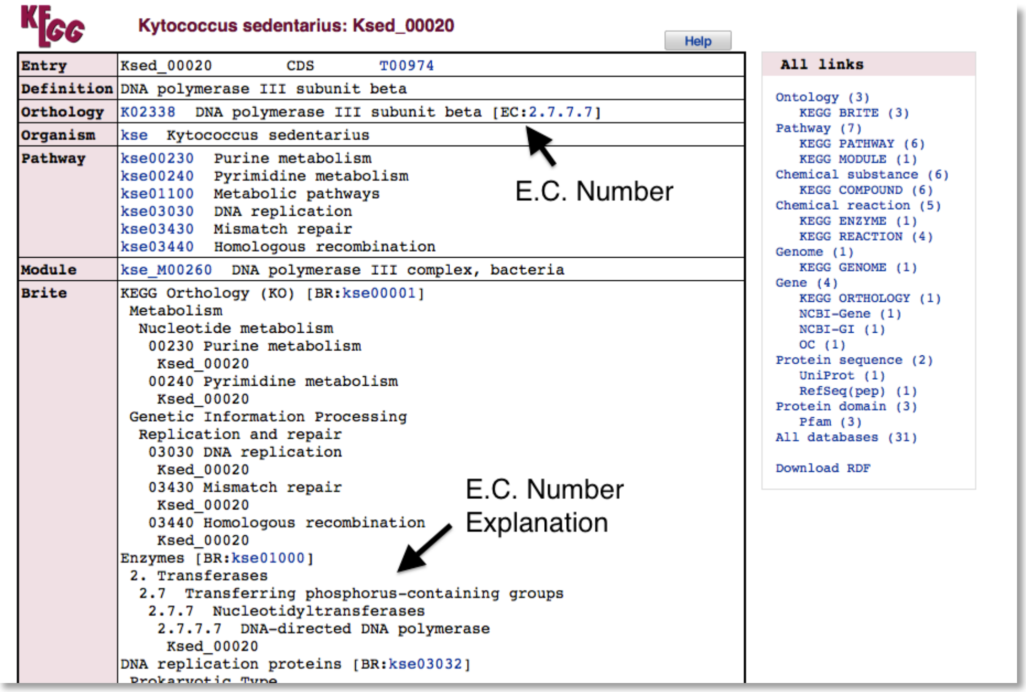


Figure 6.7. The *Kytococcus sedentarius* variation of the DNA Replication map. The gene boxes highlighted in green have been called in *Kytococcus* by the automated gene caller. One of the highlighted boxes indicated by the arrow is the beta subunit of DNA polymerase III. It is a hyperlink, and when clicked will take you to a KEGG version of a gene information page as shown in Figure 6.8.

10. Save the graphic by Snipping (PC) or Grab (Mac), and upload it to the Lab Notebook.

II. If you click on the β highlighted symbol (arrow in Figure 6.7 above) on the *Kytococcus sedentarius* version of the pathway map you will be taken to a page shown in Figure 6.8 (details in caption).



Kytococcus sedentarius: Ksed_00020

```
Entry       Ksed_00020          CDS        T00974
Definition  DNA polymerase III subunit beta
Orthology   K02338  DNA polymerase III subunit beta [EC:2.7.7.7]
Organism    kse  Kytococcus sedentarius
Pathway     kse00230  Purine metabolism
            kse00240  Pyrimidine metabolism
            kse01100  Metabolic pathways
            kse03030  DNA replication
            kse03430  Mismatch repair
            kse03440  Homologous recombination
Module      kse_M00260  DNA polymerase III complex, bacteria
Brite       KEGG Orthology (KO) [BR:kse00001]
             Metabolism
              Nucleotide metabolism
               00230 Purine metabolism
                Ksed_00020
               00240 Pyrimidine metabolism
                Ksed_00020
             Genetic Information Processing
              Replication and repair
               03030 DNA replication
                Ksed_00020
               03430 Mismatch repair
                Ksed_00020
               03440 Homologous recombination
                Ksed_00020
            Enzymes [BR:kse01000]
             2. Transferases
              2.7  Transferring phosphorus-containing groups
               2.7.7  Nucleotidyltransferases
                2.7.7.7  DNA-directed DNA polymerase
                 Ksed_00020
            DNA replication proteins [BR:kse03032]
             Prokaryotic Type
```

```
All links

Ontology (3)
   KEGG BRITE (3)
Pathway (7)
   KEGG PATHWAY (6)
   KEGG MODULE (1)
Chemical substance (6)
   KEGG COMPOUND (6)
Chemical reaction (5)
   KEGG ENZYME (1)
   KEGG REACTION (4)
Genome (1)
   KEGG GENOME (1)
Gene (4)
   KEGG ORTHOLOGY (1)
   NCBI-Gene (1)
   NCBI-GI (1)
   OC (1)
Protein sequence (2)
   UniProt (1)
   RefSeq(pep) (1)
Protein domain (3)
   Pfam (3)
All databases (31)

Download RDF
```

Figure 6.8. The KEGG gene information page resulting from clicking on the β hyperlink in figure 6.7. Of interest in this figure is that it identifies Ksed_00020 and provides additional information, including an E.C. number for the enzyme and an explanation of what the E.C. number means. The E.C. number will be recorded in a later portion of this module.

Alternative Approach if Searching KEGG Did Not Yield Useful Results

In the event you cannot determine the name of the pathway or structure that your gene is involved with after following the steps outlined in items 1-11 above, there is an alternative approach you can take.

1. Click on the Menu button at the top of the KEGG main page (see Figure 6.1 in this section), select KEGG2 and enter into the "Search KEGG" box all or part of the gene product name the previous modules have indicated belongs to your gene (Figure 6.9).

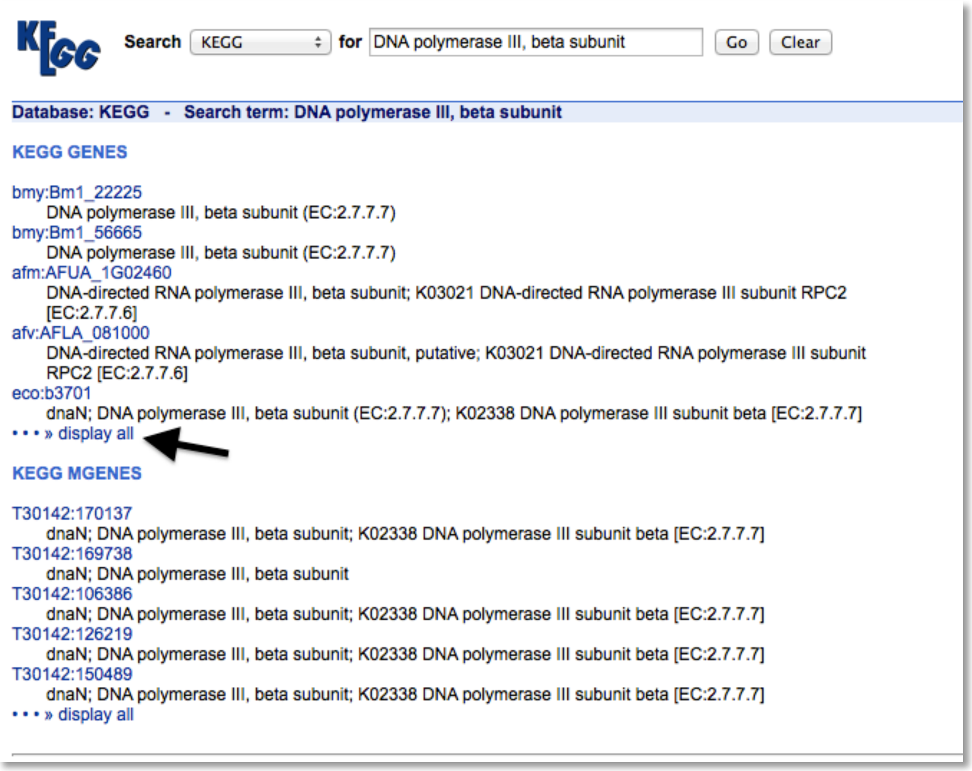
KEGG - Table of Contents

Search KEGG for DNA polymerase III, beta subunit

Category	Entry Point	Search & Compute	DBGET Search
Systems information	KEGG PATHWAY KEGG BRITE KEGG MODULE KEGG Mapper KEGG Atlas	Search Pathway Search Brite Reconstruct Module Map Taxonomy	PATHWAY BRITE MODULE
Genomic information	KEGG ORTHOLOGY KEGG Annotation *New!*	KO system	ORTHOLOGY
	KEGG GENOME KEGG GENES KEGG Organisms [Species | Genus] *New!*	SSDB search OC viewer† BLAST† / FASTA† KAAS†	GENOME GENES DGENES MGENOME† MGENES†
	KEGG LIGAND	SIMCOMP† / SUBCOMP† KCaM†	COMPOUND

Figure 6.9. The KEGG2 search page with the name of Ksed_00020 entered into the search box.

2. Click "Go" to search KEGG for that gene product name. If any of the results there correspond to the gene product name you searched, click on the entries one at a time until you come to one with an Orthology section listed. In figure 6.10, the first two hits do not have an orthology section (not shown) and the next two hits are RNA polymerases, not DNA polymerase. However, the 5th result, eco:b3701, does have one as shown in Figure 6.11.



DNA polymerase III, beta subunit

Database: KEGG - Search term: DNA polymerase III, beta subunit

KEGG GENES

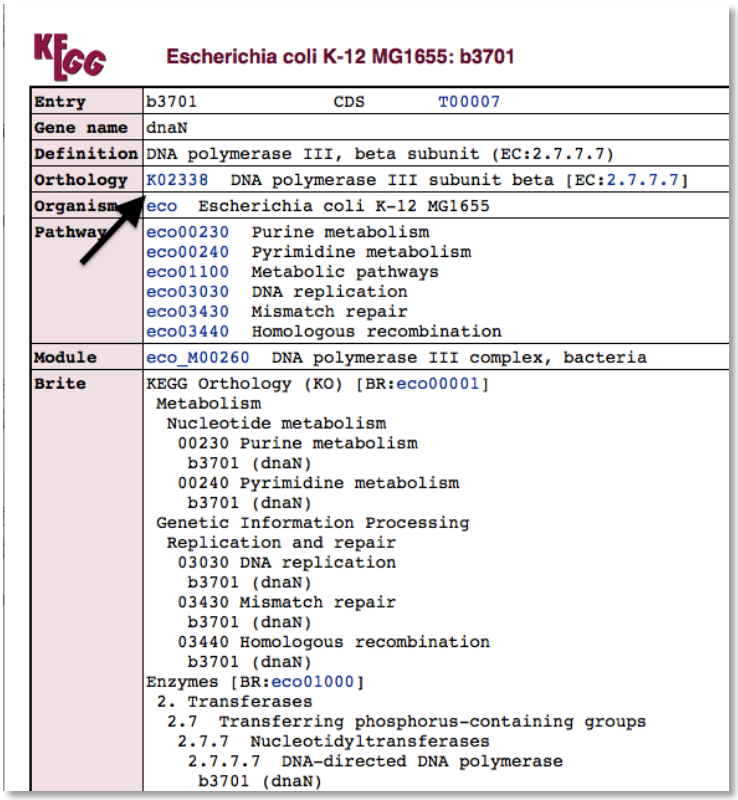
bmy:Bm1_22225
DNA polymerase III, beta subunit (EC:2.7.7.7)
bmy:Bm1_56665
DNA polymerase III, beta subunit (EC:2.7.7.7)
afm:AFUA_1G02460
DNA-directed RNA polymerase III, beta subunit; K03021 DNA-directed RNA polymerase III subunit RPC2 [EC:2.7.7.6]
afv:AFLA_081000
DNA-directed RNA polymerase III, beta subunit, putative; K03021 DNA-directed RNA polymerase III subunit RPC2 [EC:2.7.7.6]
eco:b3701
dnaN; DNA polymerase III, beta subunit (EC:2.7.7.7); K02338 DNA polymerase III subunit beta [EC:2.7.7.7]
• • • » display all

KEGG MGENES

T30142:170137
dnaN; DNA polymerase III, beta subunit; K02338 DNA polymerase III subunit beta [EC:2.7.7.7]
T30142:169738
dnaN; DNA polymerase III, beta subunit
T30142:106386
dnaN; DNA polymerase III, beta subunit; K02338 DNA polymerase III subunit beta [EC:2.7.7.7]
T30142:126219
dnaN; DNA polymerase III, beta subunit; K02338 DNA polymerase III subunit beta [EC:2.7.7.7]
T30142:150489
dnaN; DNA polymerase III, beta subunit; K02338 DNA polymerase III subunit beta [EC:2.7.7.7]
• • • » display all

Figure 6.10. The KEGG2 results page for the DNA Polymerase III, beta subunit search. The arrow points to a link to expand the results section if necessary. See text for an explanation.

3. eco:b3701 has *E. coli* specific pathway links (similar to the one generated above for *Kytococcus sedentarius*). No matter the organism you choose, if an orthology link is present, it will take you to links to general pathway pages (if one exists). As shown in Figure 6.11, there are 4 pathways to choose from. You would need to click on each one in succession to find the one that most fundamentally explains the role of your protein. In the case of the current example, only the DNA replication link clearly shows the DNA polymerase III, beta subunit. Once you get to the general pathway page you can follow instructions as described for a KEGG search beginning at step 4 on page 112.



Escherichia coli K-12 MG1655: b3701

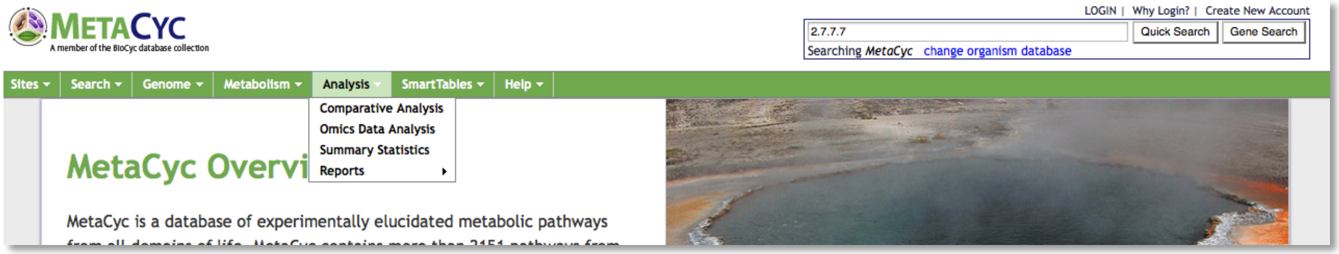
Entry	b3701 CDS T00007
Gene name	dnaN
Definition	DNA polymerase III, beta subunit (EC:2.7.7.7)
Orthology	K02338 DNA polymerase III subunit beta [EC:2.7.7.7]
Organism	eco Escherichia coli K-12 MG1655
Pathway	eco00230 Purine metabolism eco00240 Pyrimidine metabolism eco01100 Metabolic pathways eco03030 DNA replication eco03430 Mismatch repair eco03440 Homologous recombination
Module	eco_M00260 DNA polymerase III complex, bacteria
Brite	KEGG Orthology (KO) [BR:eco00001] Metabolism Nucleotide metabolism 00230 Purine metabolism b3701 (dnaN) 00240 Pyrimidine metabolism b3701 (dnaN) Genetic Information Processing Replication and repair 03030 DNA replication b3701 (dnaN) 03430 Mismatch repair b3701 (dnaN) 03440 Homologous recombination b3701 (dnaN) Enzymes [BR:eco01000] 2. Transferases 2.7 Transferring phosphorus-containing groups 2.7.7 Nucleotidyltransferases 2.7.7.7 DNA-directed DNA polymerase b3701 (dnaN)

Figure 6.11. The KEGG page for eco:b3701. This is the first relevant hit in the search results that has an Orthology section. Note also that it has *E. coli* specific list of pathways as well as an E.C. number and explanation. The arrow points to the KEGG orthology hyperlink.

4. If you do not get hits with the full name of your protein, trim the name (i.e., DNA polymerase III for the current example) and try again.
5. Record the pathway number and pathway image in your notebook to complete the module, but also take notes in your own notebook for other information you find in this module.

MetaCyc

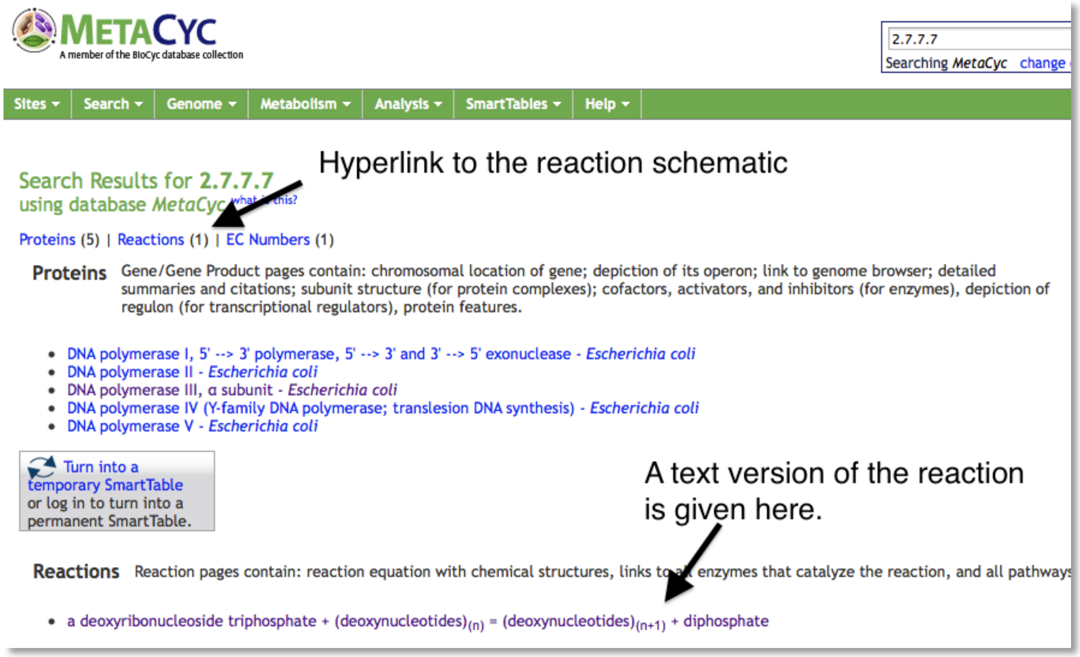
1. MetaCyc is a database of experimentally determined metabolic pathways. For each of these pathways, MetaCyc provides an abundance of information. Your protein will only participate in one of these pathways if it has an enzymatic function. **If you have determined that your protein is NOT an enzyme you can skip this module (state that fact in your notebook).**
2. Navigate to MetaCyc at http://metacyc.org
3. In the search box at the top right of the page, search MetaCyc for all or part of your gene product name or, ideally, the EC number if your gene product catalyzes a biochemical reaction. If in the previous modules, the EC number of the gene product was indicated by KEGG, or literature research, enter it in the search box to see the Reaction page for information about the corresponding biochemical reaction. In KEGG above, the E.C. Number for Ksed_00020 was determined to be 2.7.7.7, so this number could be used in the search (Figure 6.12). **If you do not have an E.C. number use the name or portions of the name you have determined from your work in previous modules.**



MetaCyc is a database of experimentally elucidated metabolic pathways

Figure 6.12. The MetaCyc start page with the E.C. number for Ksed_00020 (2.7.7.7) entered into the search box.

4. Figure 6.13 shows the results of searching with the E.C. number.



Search Results for 2.7.7.7
using database MetaCyc what's this?

Proteins (5) | Reactions (1) | EC Numbers (1)

Proteins Gene/Gene Product pages contain: chromosomal location of gene; depiction of its operon; link to genome browser; detailed summaries and citations; subunit structure (for protein complexes); cofactors, activators, and inhibitors (for enzymes), depiction of regulon (for transcriptional regulators), protein features.

- DNA polymerase I, 5' --> 3' polymerase, 5' --> 3' and 3' --> 5' exonuclease - *Escherichia coli*
- DNA polymerase II - *Escherichia coli*
- DNA polymerase III, α subunit - *Escherichia coli*
- DNA polymerase IV (Y-family DNA polymerase; translesion DNA synthesis) - *Escherichia coli*
- DNA polymerase V - *Escherichia coli*

Turn into a temporary SmartTable or log in to turn into a permanent SmartTable.

Reactions Reaction pages contain: reaction equation with chemical structures, links to all enzymes that catalyze the reaction, and all pathways

- a deoxyribonucleoside triphosphate + (deoxynucleotides)$_{(n)}$ = (deoxynucleotides)$_{(n+1)}$ + diphosphate

Figure 6.13. The MetaCyc search results for E.C.2.7.7.7. The link to the reaction is shown near the top of the page and the text version at the bottom of the image. Clicking on the text will open the graphical version of the reaction (see text).

5. When you click on the Reactions link, look for the "Pathway" heading near the top of the page. If this reaction is a part of a MetaCyc pathway, then one or more of those pathways will be listed in this section. Only one reaction will be present if you search by E.C. Number (as is the case for Ksed_00020), but if you perform search using a gene name, you may have more than one pathway. If more than one is present in a search results click determine the one that best fits the information you have learned about your protein from modules done thus far.
6. Clicking on the reaction will lead you to the pathway graphic (Figure 6.14). You should save the reaction graphic by using Snip on a PC or Grab on the Mac, and then upload it to the Lab Notebook.

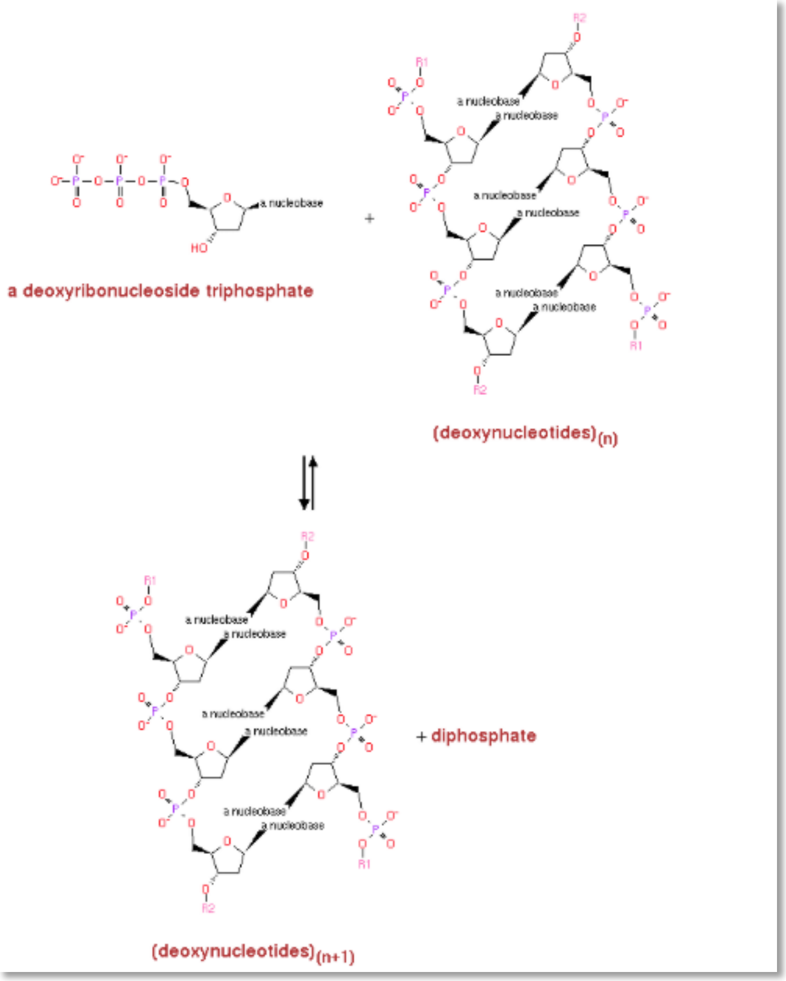
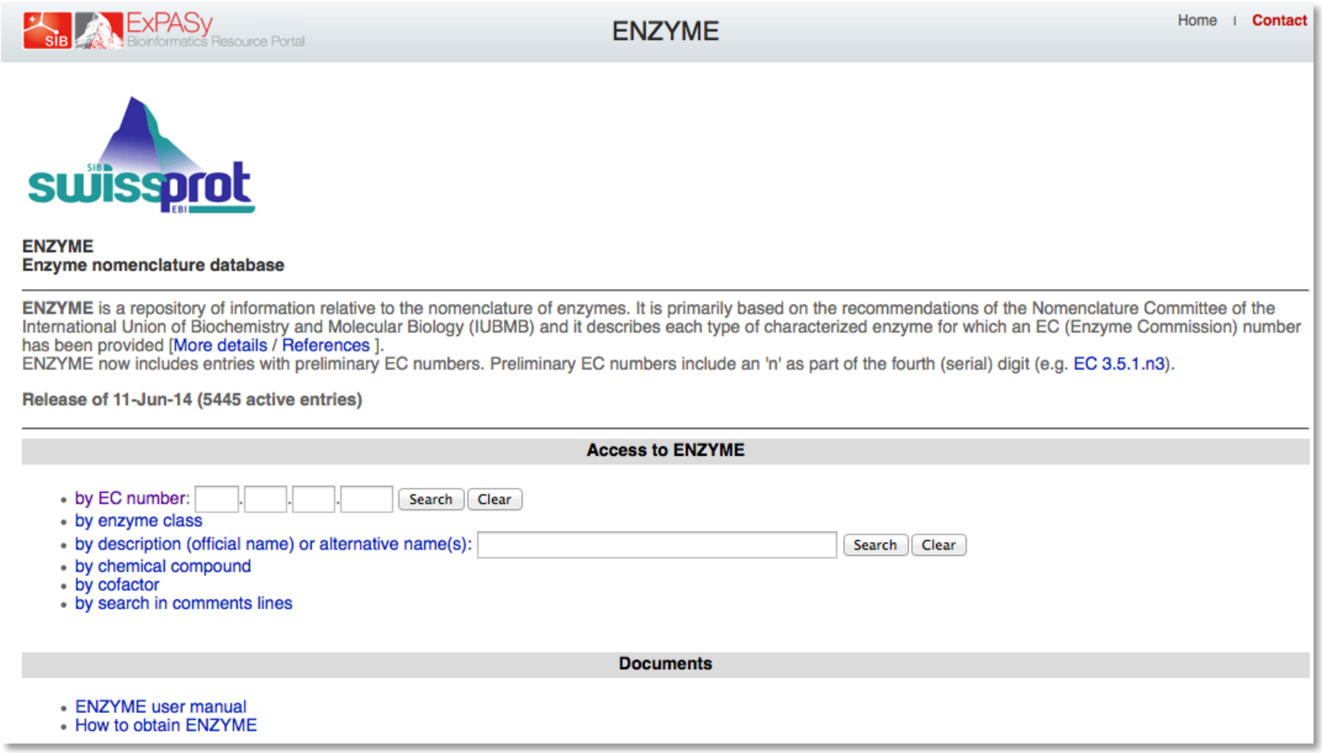


Figure 6.14. The reaction schematic for E.C. 2.7.7.7

E.C. Number - ExPASy ENZYME

1. ExPASy ENZYME is a database that contains a great deal of information pertaining to individual enzymes. Enzymes are classified by their Enzyme Commission (EC) numbers, where each subsequent digit in the number adds greater specificity about the reaction catalyzed by the enzyme (e.g. the four digits 2.3.3.8 for ATP citrate synthase indicate that the enzyme is a transferase, an acyltransferase, an acyl group converted into alkyl on transfer, and ATP citrate synthase, respectively.).

2. Go to http://enzyme.expasy.org/. The start page appears as in Figure 6.15.



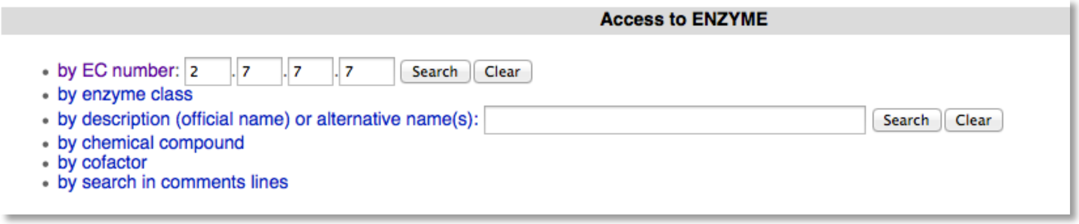
ENZYME
Enzyme nomenclature database

ENZYME is a repository of information relative to the nomenclature of enzymes. It is primarily based on the recommendations of the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (IUBMB) and it describes each type of characterized enzyme for which an EC (Enzyme Commission) number has been provided [More details / References].
ENZYME now includes entries with preliminary EC numbers. Preliminary EC numbers include an 'n' as part of the fourth (serial) digit (e.g. EC 3.5.1.n3).

Release of 11-Jun-14 (5445 active entries)

Figure 6.15. The ExPASy Enzyme Start Page showing the options for initiating searches.

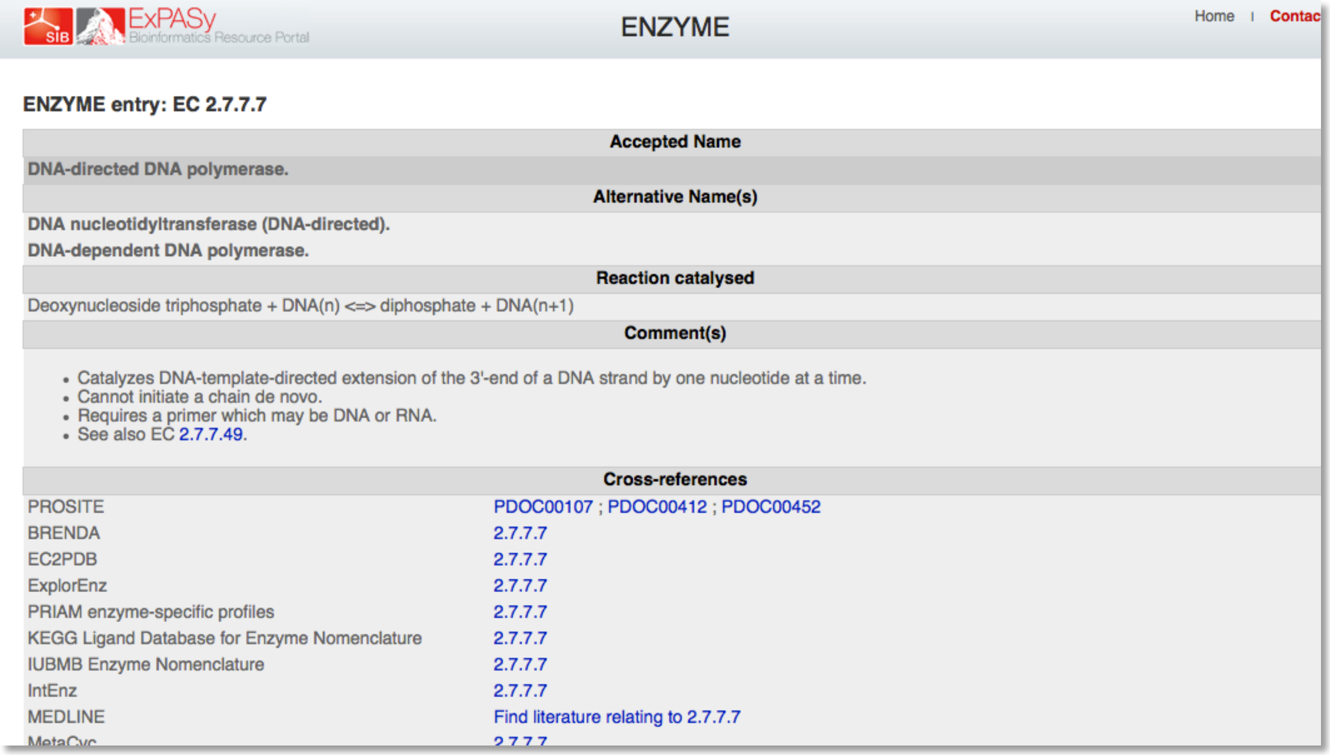
3. If you have an E.C. number (full or partial) from your previous searches you can enter it in the "by EC Number boxes). Figures 6.16 and 6.17 show the search and results pages respectively, using E.C. 2.7.7.7 as the search term.



Access to ENZYME

- by EC number: 2 . 7 . 7 . 7
- by enzyme class
- by description (official name) or alternative name(s):
- by chemical compound
- by cofactor
- by search in comments lines

Figure 6.16. Searching ExPASy Enzyme by EC number.



ENZYME entry: EC 2.7.7.7

Accepted Name

DNA-directed DNA polymerase.

Alternative Name(s)

DNA nucleotidyltransferase (DNA-directed).
DNA-dependent DNA polymerase.

Reaction catalysed

Deoxynucleoside triphosphate + DNA(n) <=> diphosphate + DNA(n+1)

Comment(s)

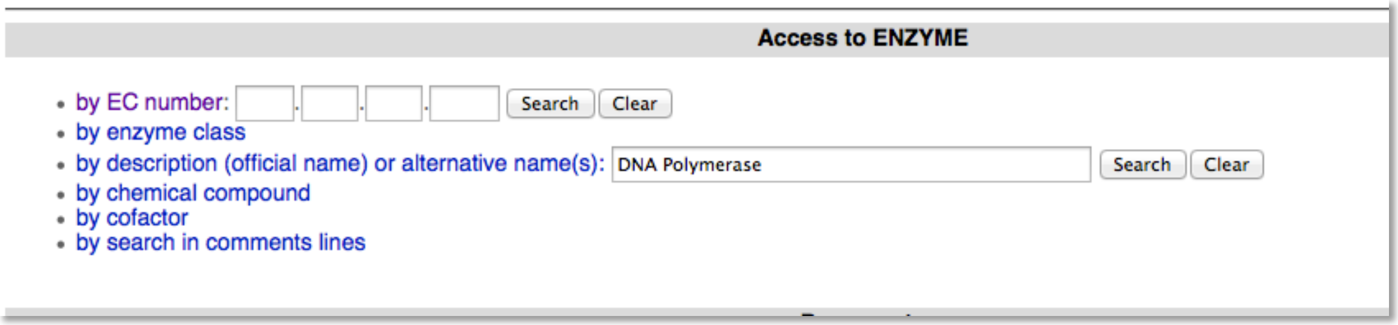
- Catalyzes DNA-template-directed extension of the 3'-end of a DNA strand by one nucleotide at a time.
- Cannot initiate a chain de novo.
- Requires a primer which may be DNA or RNA.
- See also EC 2.7.7.49.

Cross-references

PROSITE	PDOC00107 ; PDOC00412 ; PDOC00452
BRENDA	2.7.7.7
EC2PDB	2.7.7.7
ExplorEnz	2.7.7.7
PRIAM enzyme-specific profiles	2.7.7.7
KEGG Ligand Database for Enzyme Nomenclature	2.7.7.7
IUBMB Enzyme Nomenclature	2.7.7.7
IntEnz	2.7.7.7
MEDLINE	Find literature relating to 2.7.7.7
MetaCyc	2.7.7.7

Figure 6.17. The ExPASy Enzyme search results when searching by EC number. Basic information is given about the reaction that can facilitate understanding of function.

4. If you have not yet gotten any hint of an EC number in your previous modules you can also search by name or description as well (Figure 6.18).

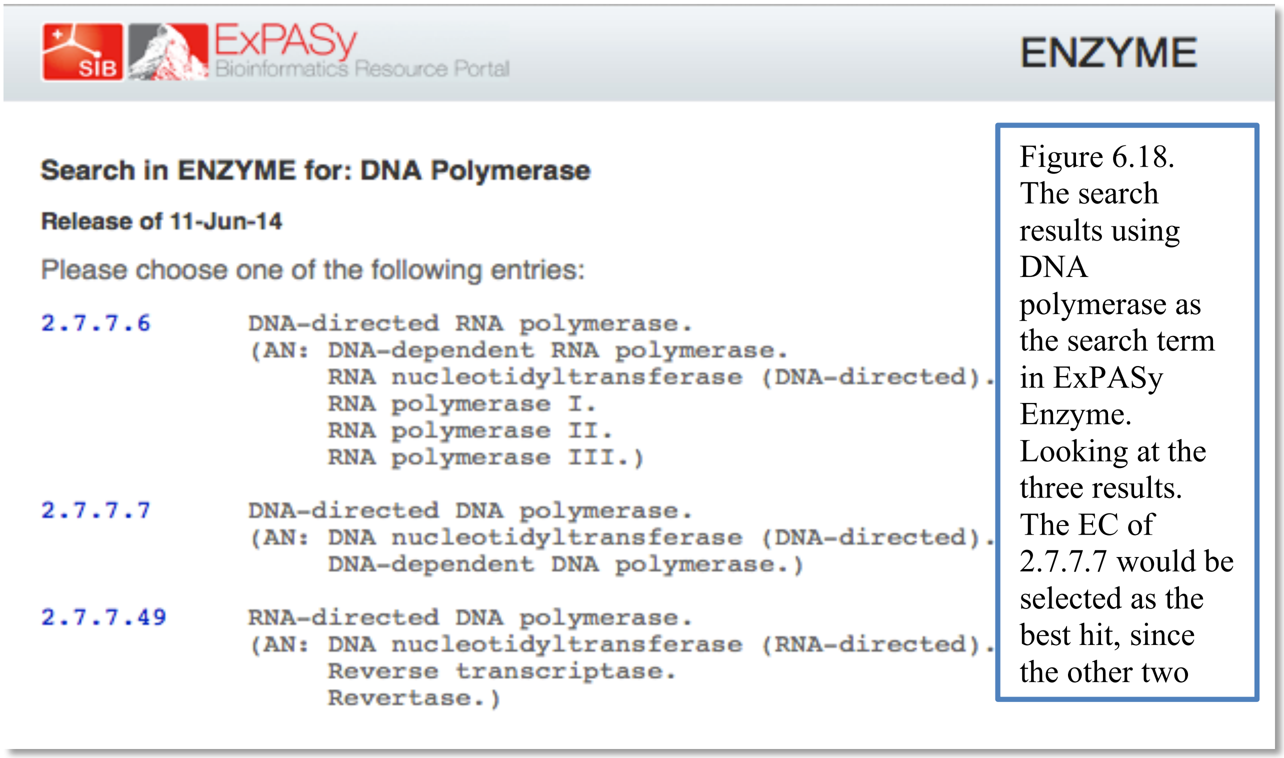


Access to ENZYME

- by EC number: ☐ . ☐ . ☐ . ☐ Search Clear
- by enzyme class
- by description (official name) or alternative name(s): DNA Polymerase Search Clear
- by chemical compound
- by cofactor
- by search in comments lines

Figure 6.18. The ExPASy Enzyme search page using a description or name as the search term (see text for why DNA polymerase was used instead of DNA polymerase III, beta subunit).

5. Searching for the name "DNA polymerase II, beta subunit" would result in no hits. In the event that searching with the full name of your protein doesn't give any hits, try trimming the name as had to be done for "DNA polymerase II, beta subunit". If the name is trimmed to "DNA polymerase", the results shown in Figure 6.19 are obtained. Results are thus likely to be less specific, and you may need to spend some time determining which is the best fit for your protein. In figure 6.19 the choice of "DNA-directed DNA polymerase" would be most appropriate since Ksed_00020 is not an "RNA-directed DNA polymerase" or a "DNA-directed RNA polymerase". In the event that you cannot determine the best fit by EC number and basic description, you can enter the EC numbers in the EC number search box one at a time and read the more detailed descriptions that will result before making a decision.



Search in ENZYME for: DNA Polymerase

Release of 11-Jun-14

Please choose one of the following entries:

```
2.7.7.6      DNA-directed RNA polymerase.
             (AN: DNA-dependent RNA polymerase.
                  RNA nucleotidyltransferase (DNA-directed).
                  RNA polymerase I.
                  RNA polymerase II.
                  RNA polymerase III.)

2.7.7.7      DNA-directed DNA polymerase.
             (AN: DNA nucleotidyltransferase (DNA-directed).
                  DNA-dependent DNA polymerase.)

2.7.7.49     RNA-directed DNA polymerase.
             (AN: DNA nucleotidyltransferase (RNA-directed).
                  Reverse transcriptase.
                  Revertase.)
```

Figure 6.18. The search results using DNA polymerase as the search term in ExPASy Enzyme. Looking at the three results. The EC of 2.7.7.7 would be selected as the best hit, since the other two