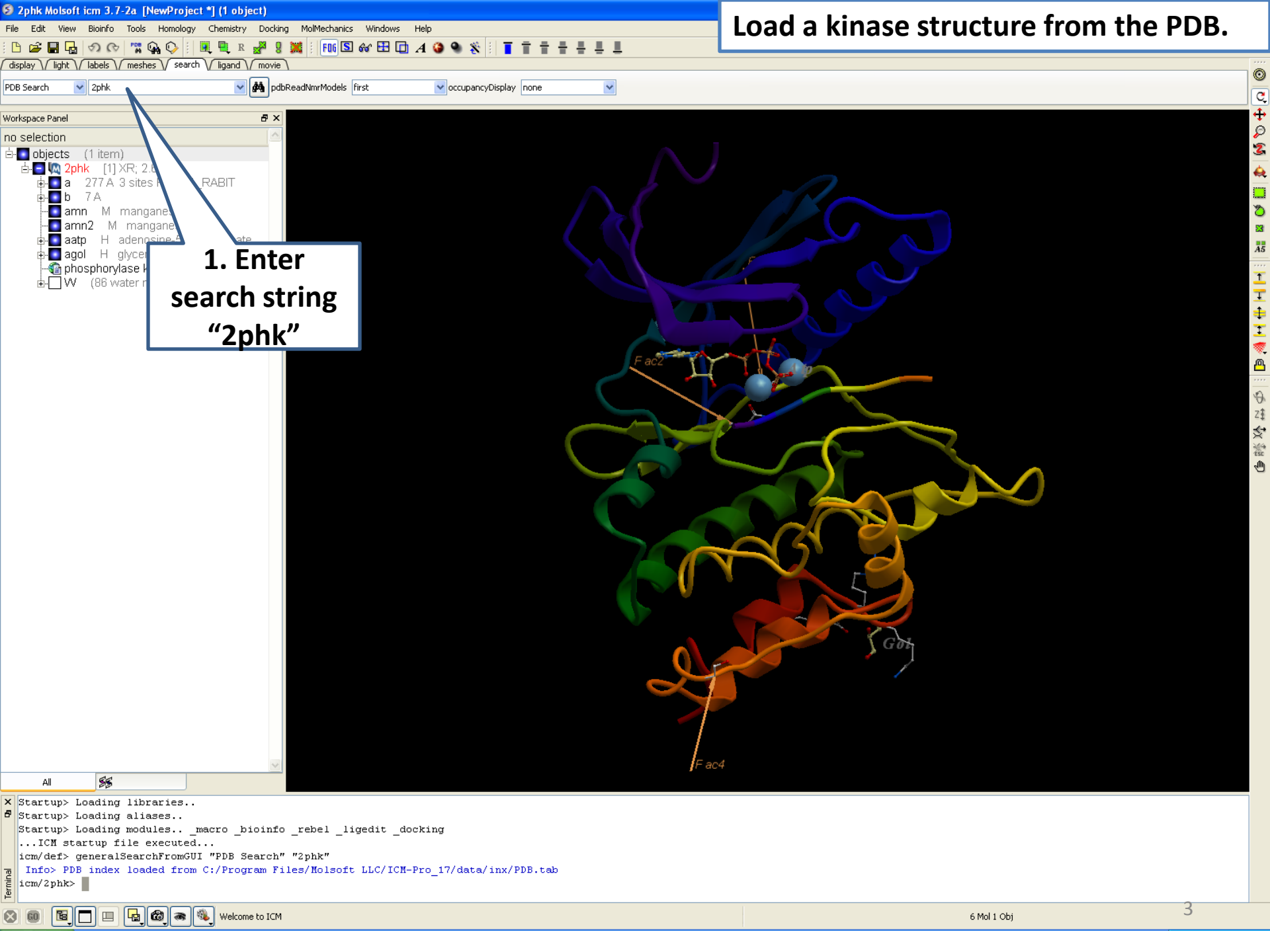
Working with sequences, alignments, and linking to 3D structure.

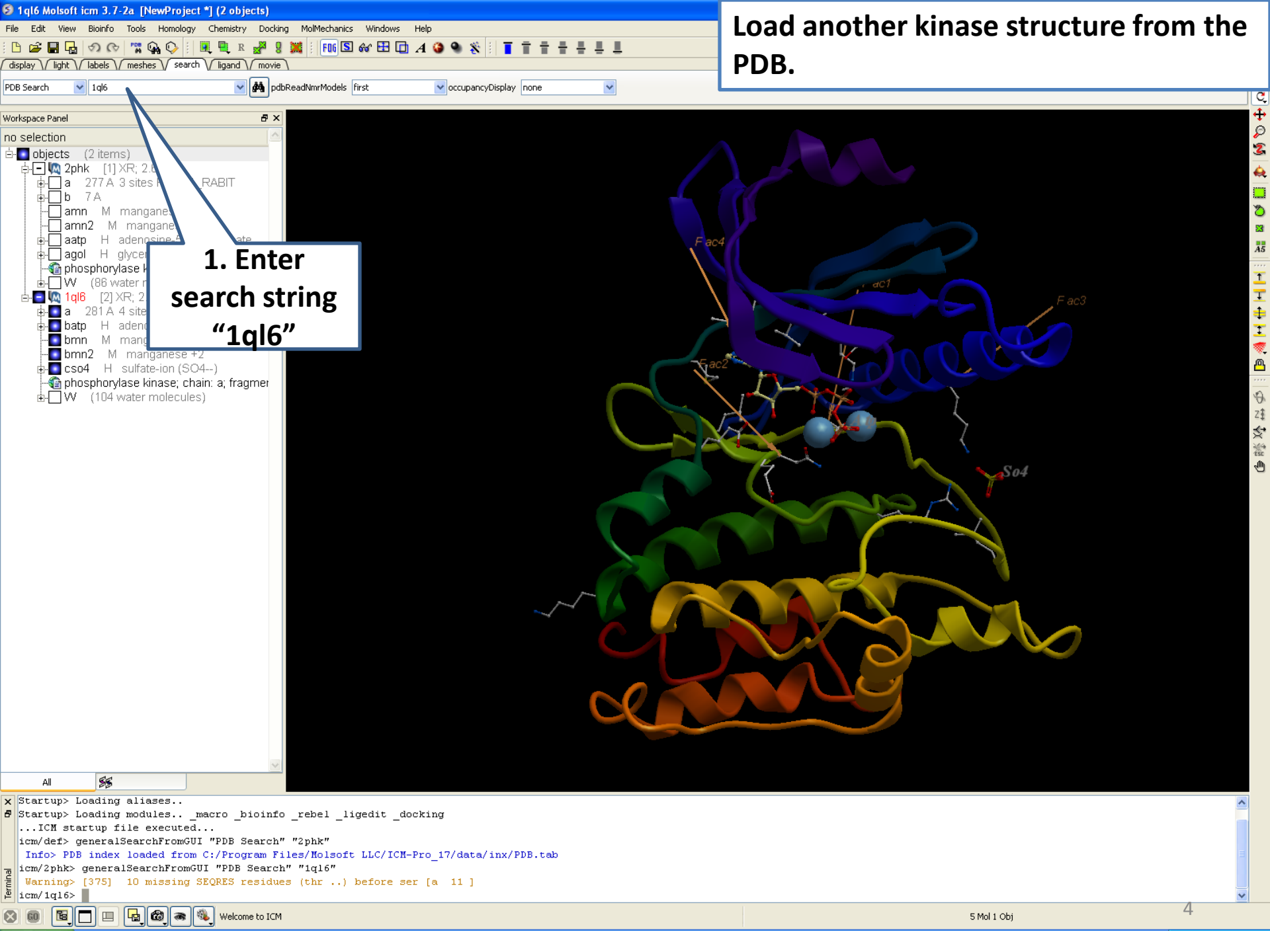
ICM-Pro

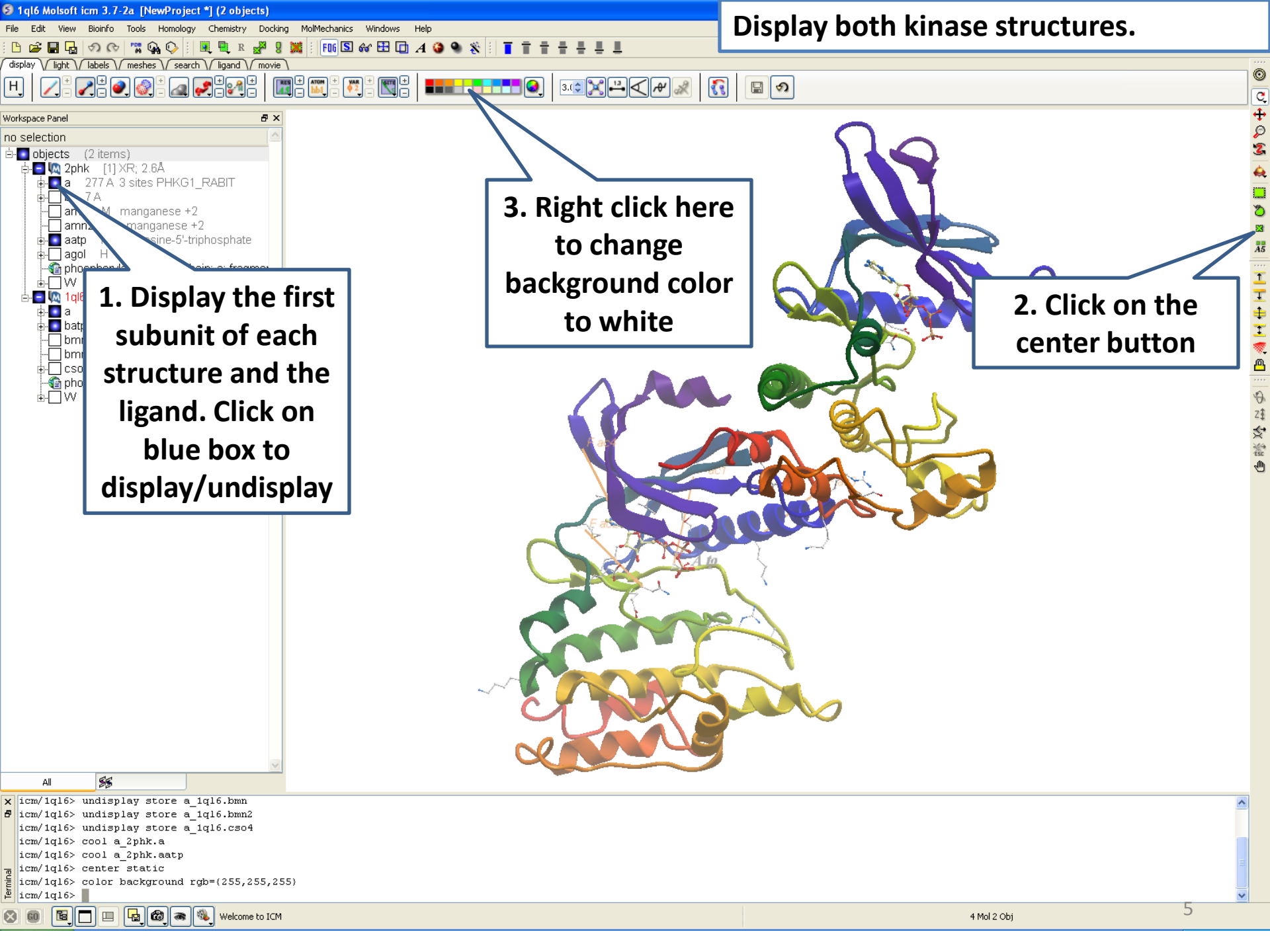
LOAD AND DISPLAY PROTEIN KINASE STRUCTURES

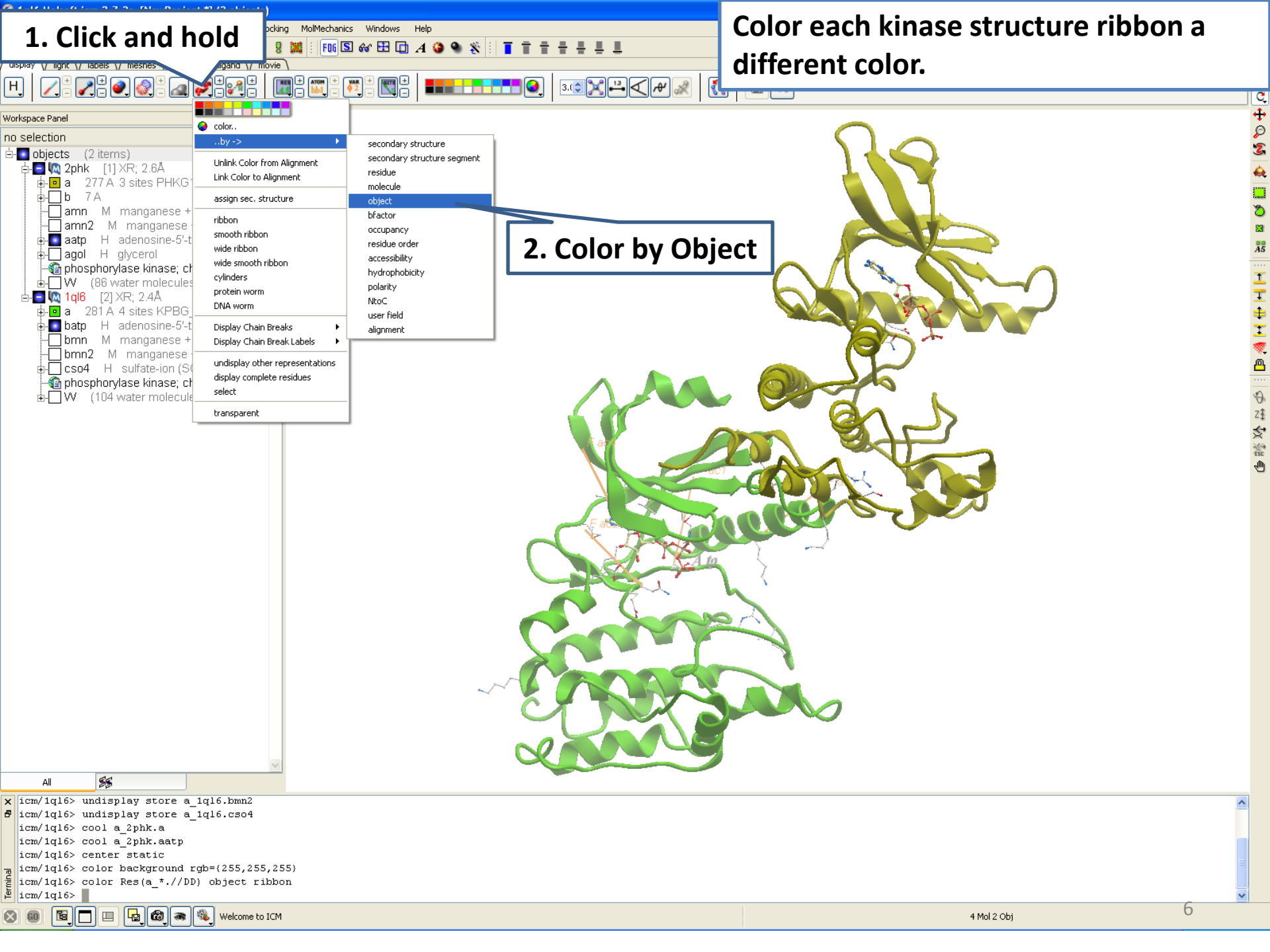
Load a kinase structure from the PDB.



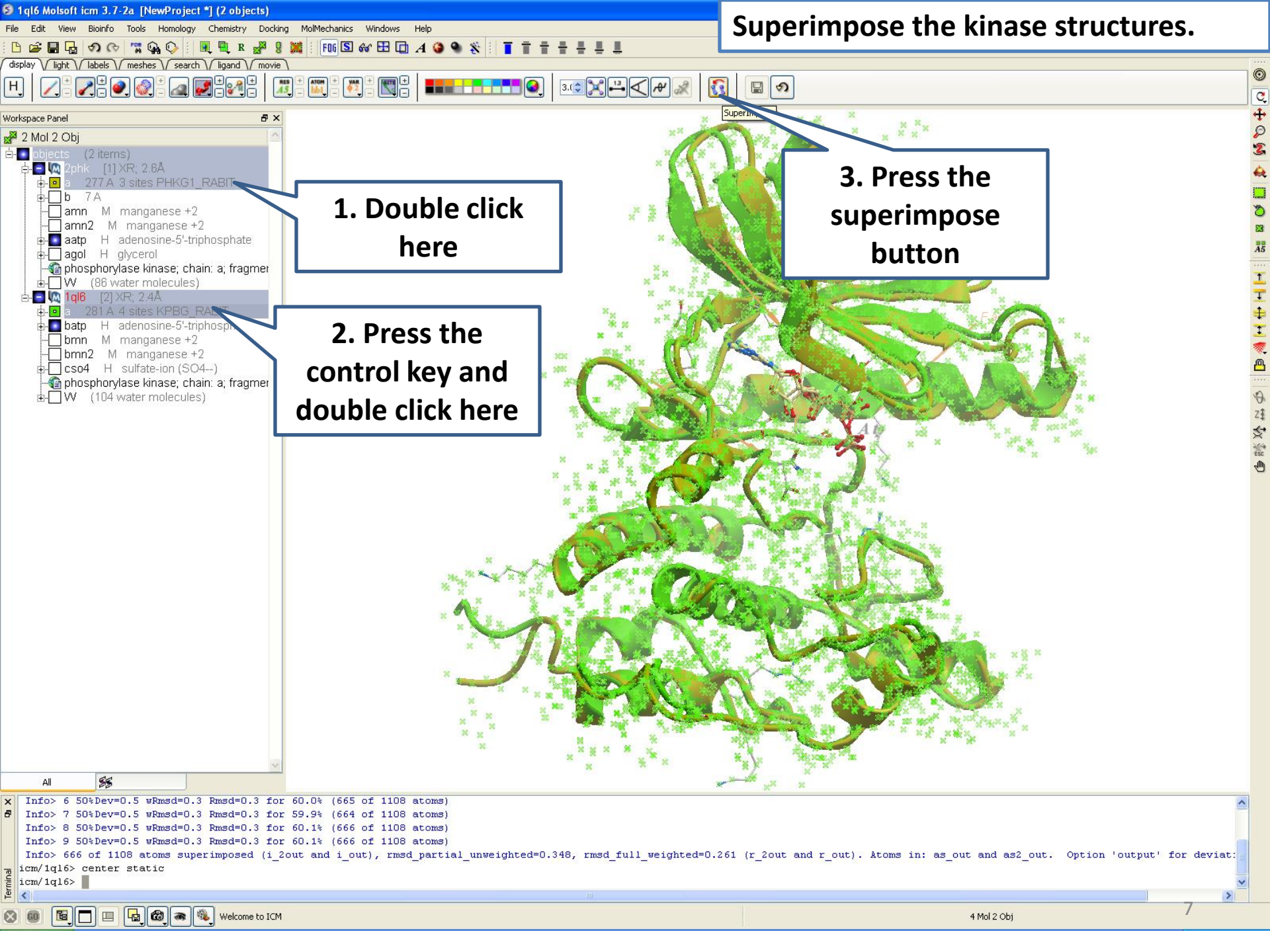
Load another kinase structure from the PDB.




1ql6 Molsoft icm 3.7-2a [NewProject *] (2 objects)
File Edit View Bioinfo Tools Homology Chemistry Docking MolMechanics Windows Help
display light labels meshes search ligand movie
Workspace Panel
no selection
objects (2 items)
2phk [1] XR; 2.6Å
a 277 A 3 sites PHKG1_RABIT
1ql6
Display both kinase structures.
1. Display the first subunit of each structure and the ligand. Click on blue box to display/undisplay
3. Right click here to change background color to white
2. Click on the center button
icm/1ql6> undisplay store a_1ql6.bmn
icm/1ql6> undisplay store a_1ql6.bmn2
icm/1ql6> undisplay store a_1ql6.cso4
icm/1ql6> cool a_2phk.a
icm/1ql6> cool a_2phk.aatp
icm/1ql6> center static
icm/1ql6> color background rgb=(255,255,255)
icm/1ql6>
Terminal
Welcome to ICM
4 Mol 2 Obj

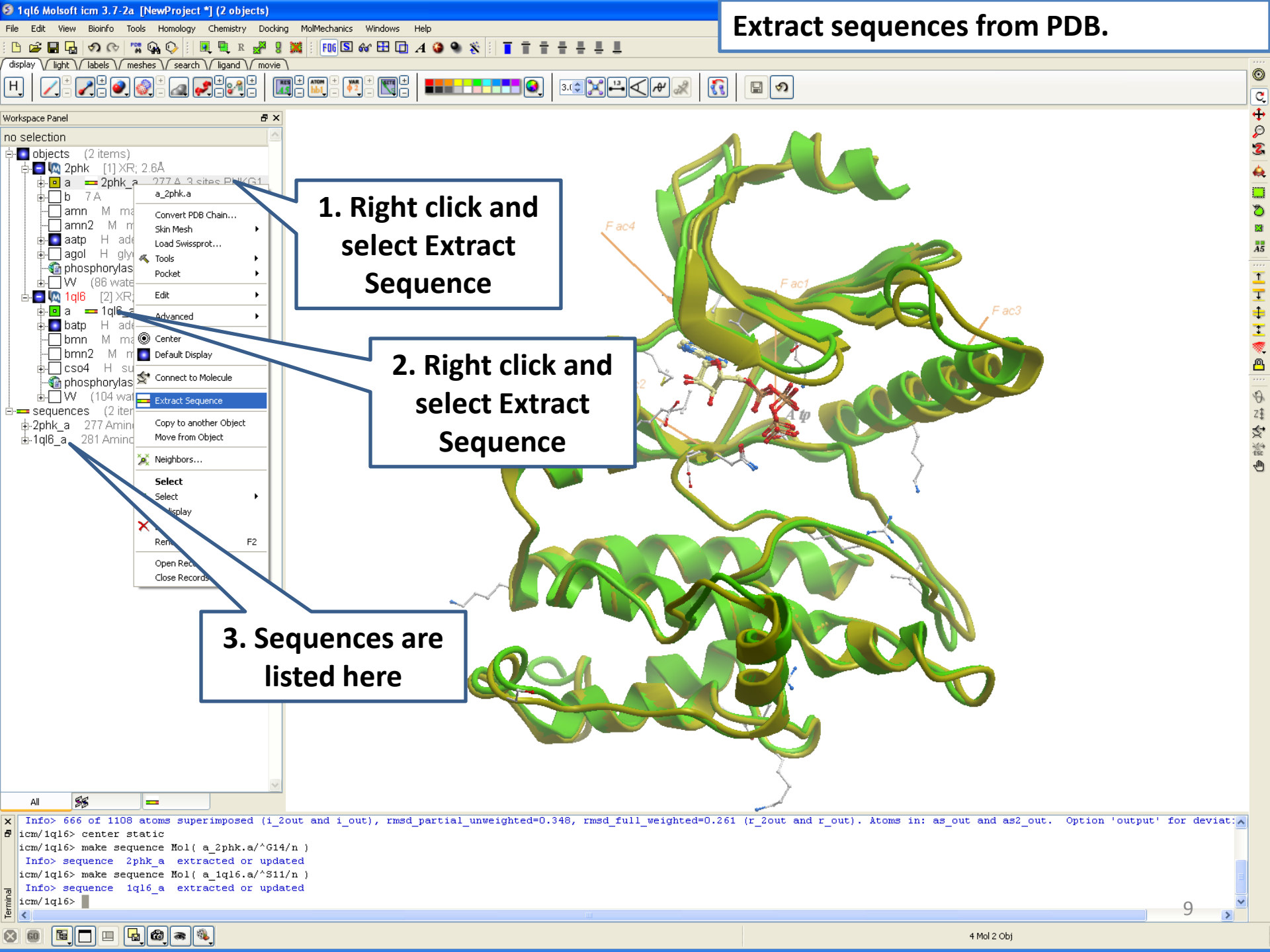

1. Click and hold
Color each kinase structure ribbon a different color.
color..
..by ->
Unlink Color from Alignment
Link Color to Alignment
assign sec. structure
ribbon
smooth ribbon
wide ribbon
wide smooth ribbon
cylinders
protein worm
DNA worm
Display Chain Breaks
Display Chain Break Labels
undisplay other representations
display complete residues
select
transparent
secondary structure
secondary structure segment
residue
molecule
object
bfactor
occupancy
residue order
accessibility
hydrophobicity
polarity
NtoC
user field
alignment
2. Color by Object
icm/1ql6> undisplay store a_1ql6.bmn2
icm/1ql6> undisplay store a_1ql6.cso4
icm/1ql6> cool a_2phk.a
icm/1ql6> cool a_2phk.aatp
icm/1ql6> center static
icm/1ql6> color background rgb=(255,255,255)
icm/1ql6> color Res(a_*.//DD) object ribbon
icm/1ql6>
Welcome to ICM
4 Mol 2 Obj

Superimpose the kinase structures.



EXTRACT SEQUENCES FROM PDB STRUCTURES AND LOAD NEW SEQUENCES FROM SWISSPROT

Extract sequences from PDB.

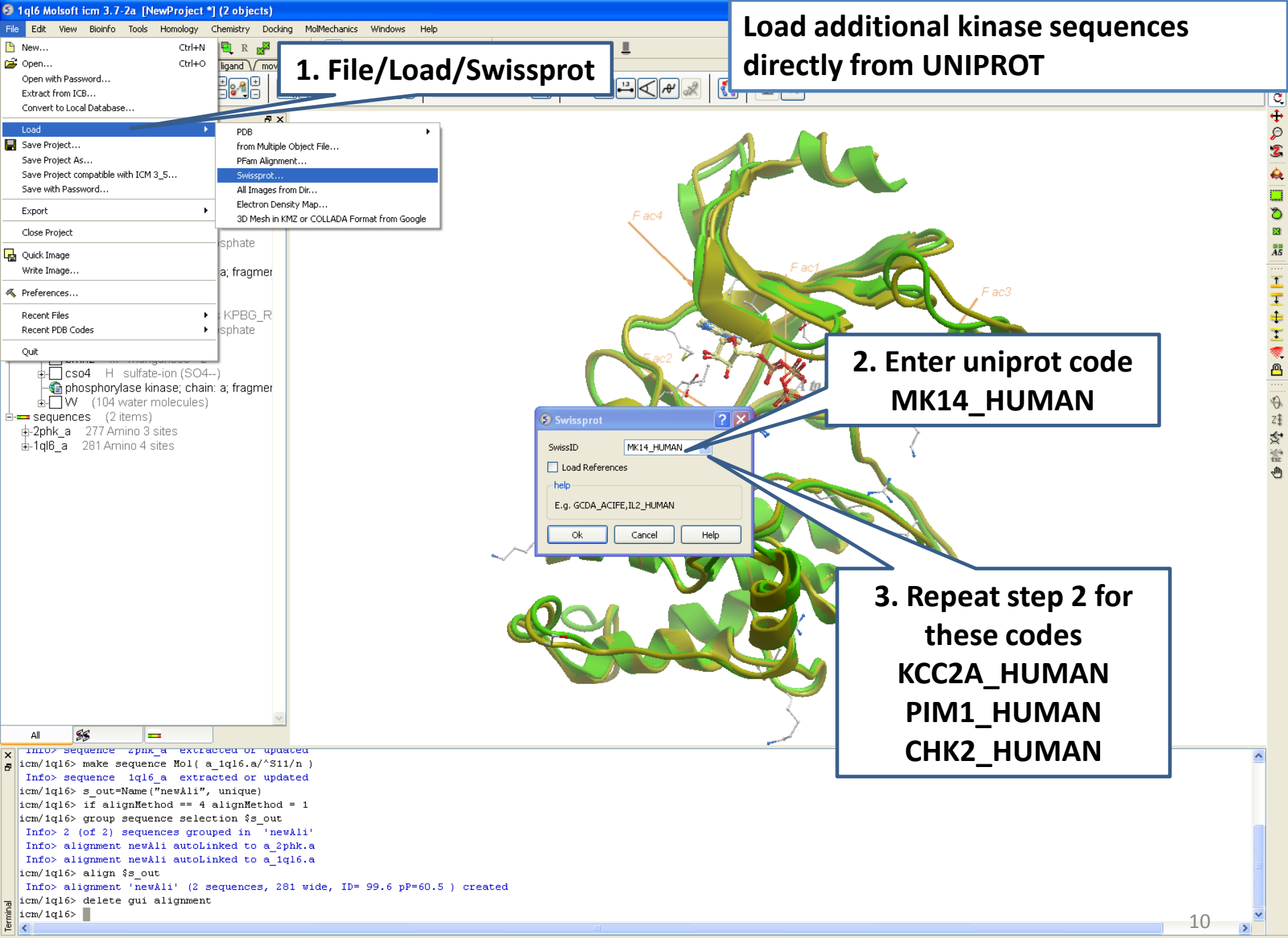


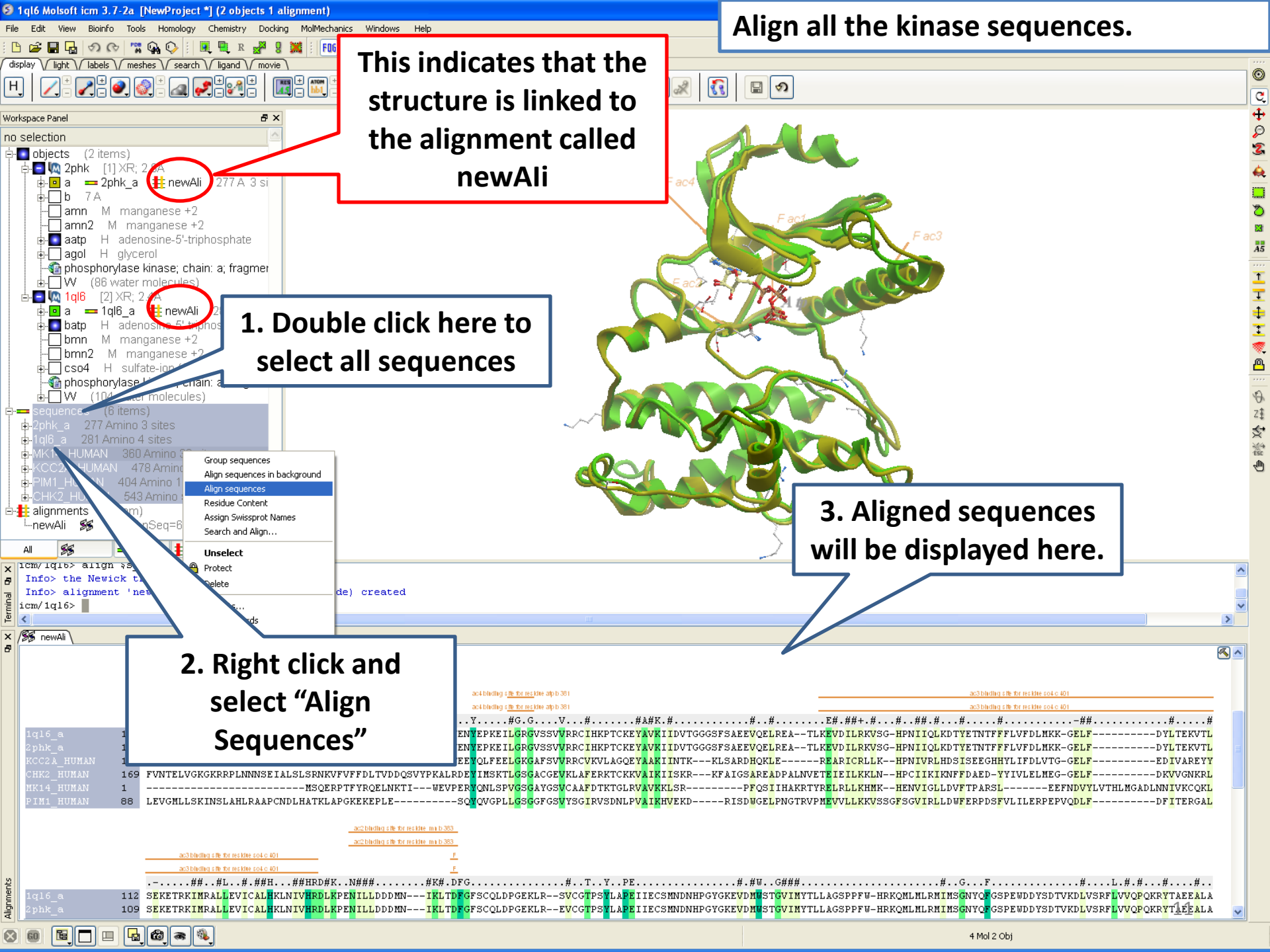
Load additional kinase sequences directly from UNIPROT

1. File/Load/Swissprot

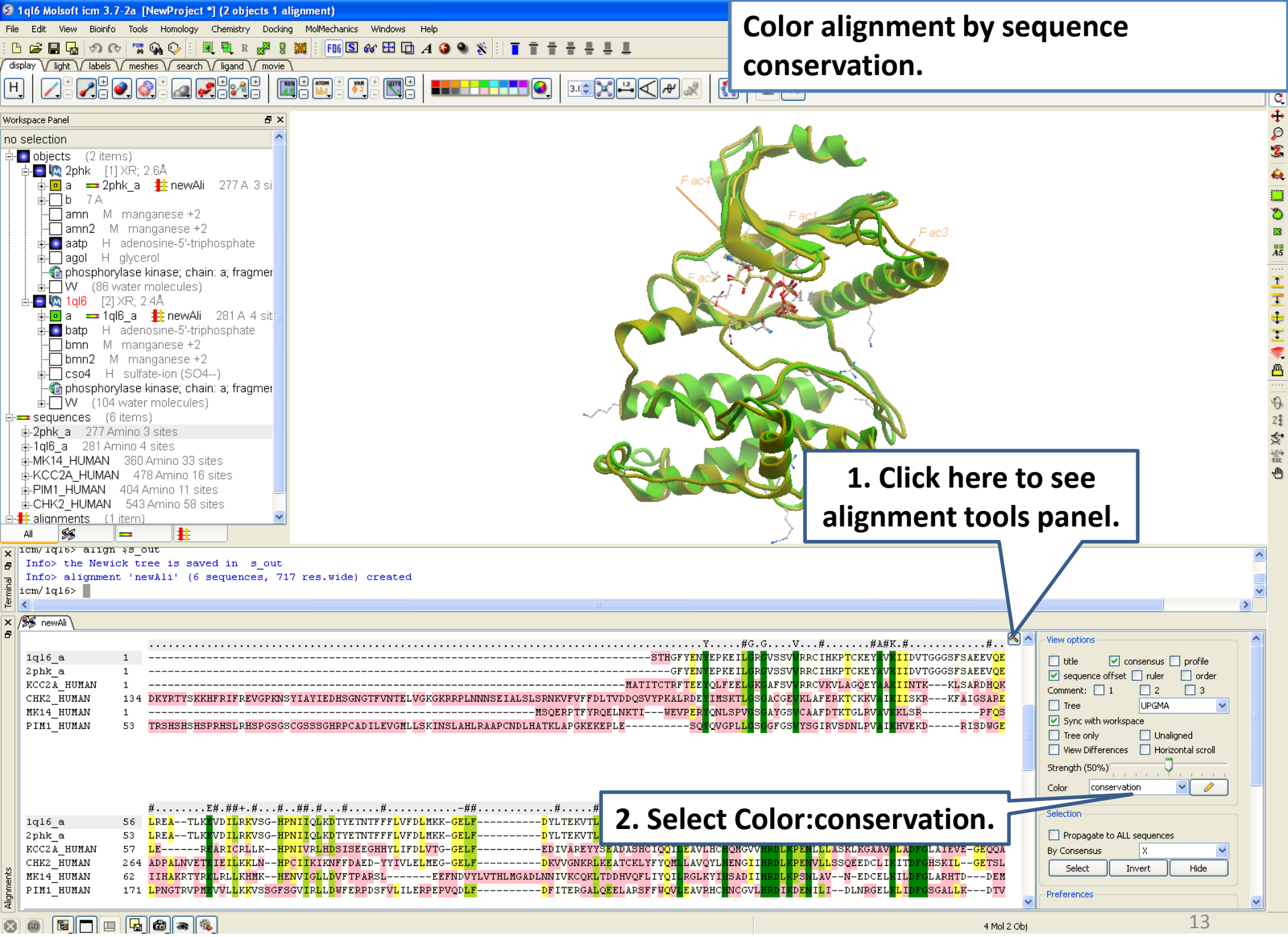
2. Enter uniprot code
MK14_HUMAN

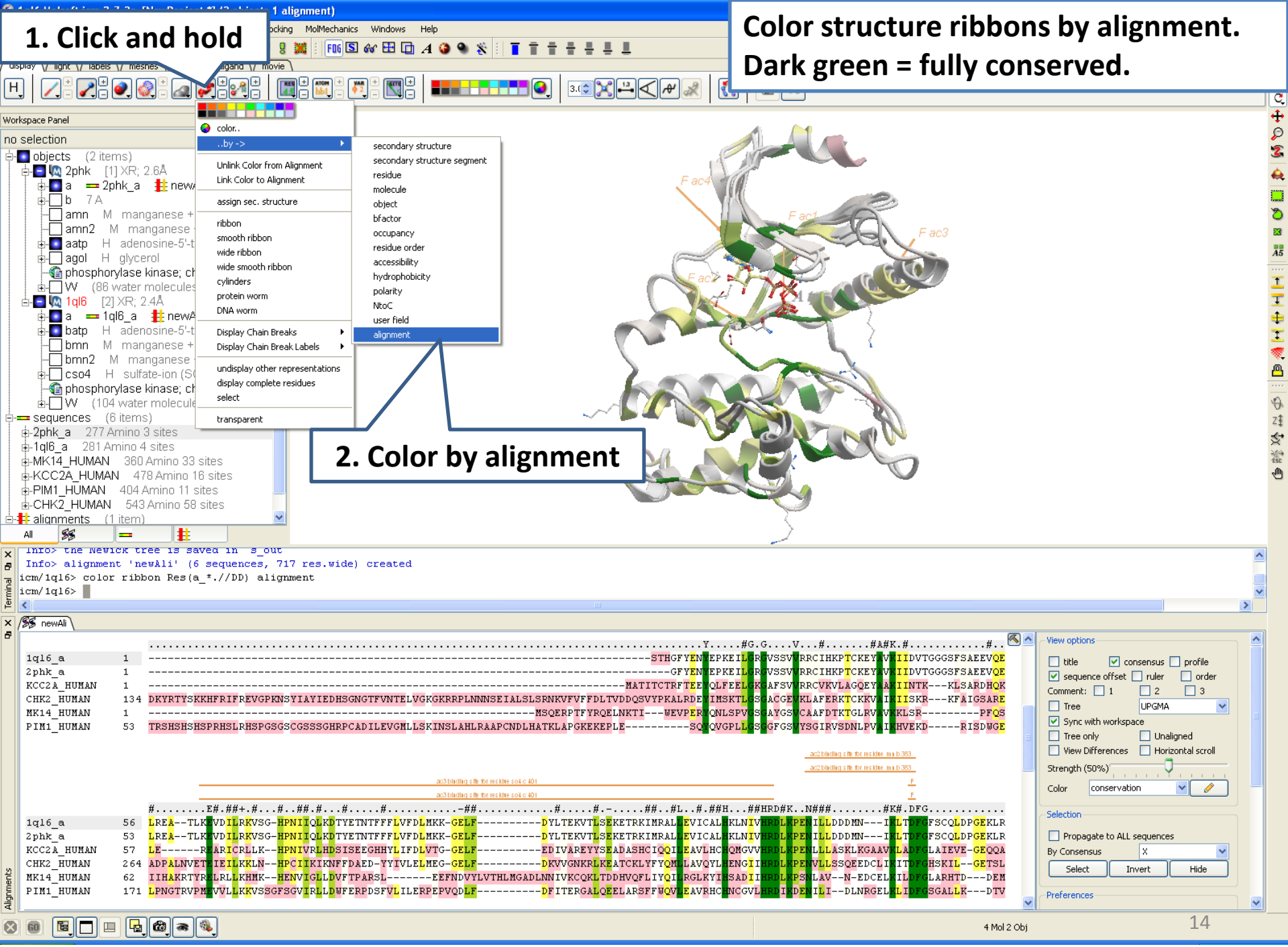
3. Repeat step 2 for these codes
KCC2A_HUMAN
PIM1_HUMAN
CHK2_HUMAN




1ql6 Molsoft icm 3.7-2a [NewProject *] (2 objects 1 alignment)
File Edit View Bioinfo Tools Homology Chemistry Docking MolMechanics Windows Help
Align all the kinase sequences.
This indicates that the structure is linked to the alignment called newAli
1. Double click here to select all sequences
2. Right click and select “Align Sequences”
3. Aligned sequences will be displayed here.
Workspace Panel
no selection
objects (2 items)
2phk [1] XR; 2.0A
a 2phk_a newAli 277 A 3 si
b 7 A
amn M manganese +2
amn2 M manganese +2
aatp H adenosine-5'-triphosphate
agol H glycerol
phosphorylase kinase; chain: a; fragmer
W (86 water molecules)
1ql6 [2] XR; 2.0A
a 1ql6_a newAli
batp H
bmn M manganese +2
bmn2 M manganese +2
cso4 H sulfate-ion
phosphorylase
W
sequences (6 items)
2phk_a 277 Amino 3 sites
1ql6_a 281 Amino 4 sites
MK1 HUMAN 360 Amino
KCC2A HUMAN 478 Amino
PIM1 HUMAN 404 Amino 1
CHK2 HUMAN 543 Amino
alignments
newAli
Group sequences
Align sequences in background
Align sequences
Residue Content
Assign Swissprot Names
Search and Align...
Unselect
Protect
Delete
icm/1ql6> align
Info> the Newick t
Info> alignment 'ne
de) created
icm/1ql6>
newAli
1ql6_a
2phk_a
KCC2A_HUMAN
CHK2_HUMAN
MK14_HUMAN
PIM1_HUMAN
4 Mol 2 Obj

LINKING SEQUENCE ALIGNMENT TO STRUCTURE

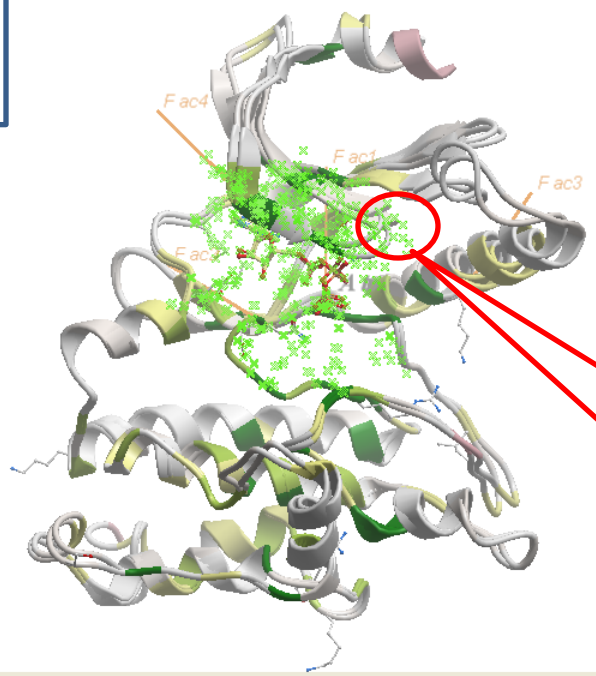

1ql6 Molsoft icm 3.7-2a [NewProject *] (2 objects 1 alignment)
Color alignment by sequence conservation.
1. Click here to see alignment tools panel.
2. Select Color:conservation.
Workspace Panel
no selection
objects (2 items)
2phk [1] XR; 2.6Å
1ql6 [2] XR; 2.4Å
sequences (6 items)
alignments (1 item)
icm/1ql6> align $s_out
Info> the Newick tree is saved in s_out
Info> alignment 'newAli' (6 sequences, 717 res.wide) created
icm/1ql6>
newAli
1ql6_a
2phk_a
KCC2A_HUMAN
CHK2_HUMAN
MK14_HUMAN
PIM1_HUMAN
View options
Color
conservation
Selection
Preferences


1. Click and hold
Color structure ribbons by alignment.
Dark green = fully conserved.
color..
..by ->
Unlink Color from Alignment
Link Color to Alignment
assign sec. structure
ribbon
smooth ribbon
wide ribbon
wide smooth ribbon
cylinders
protein worm
DNA worm
Display Chain Breaks
Display Chain Break Labels
undisplay other representations
display complete residues
select
transparent
secondary structure
secondary structure segment
residue
molecule
object
bfactor
occupancy
residue order
accessibility
hydrophobicity
polarity
NtoC
user field
alignment
2. Color by alignment
Info> alignment 'newAli' (6 sequences, 717 res.wide) created
icm/1ql6> color ribbon Res(a_*.//DD) alignment
icm/1ql6>
1ql6_a
2phk_a
KCC2A_HUMAN
CHK2_HUMAN
MK14_HUMAN
PIM1_HUMAN
View options
Selection
Preferences

IDENTIFY SEQUENCE CONSERVATION IN LIGAND BINDING POCKET

Select residues surrounding ligand binding pocket.

1. Right click on ATP ligand in the first object

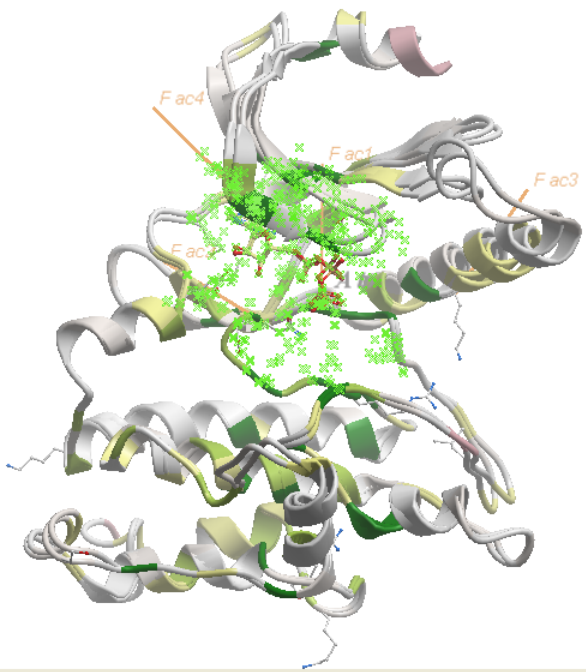


Green crosses = graphical selection

2. Select/Neighbors

Notice selection is returned to alignment – highlighted in blue

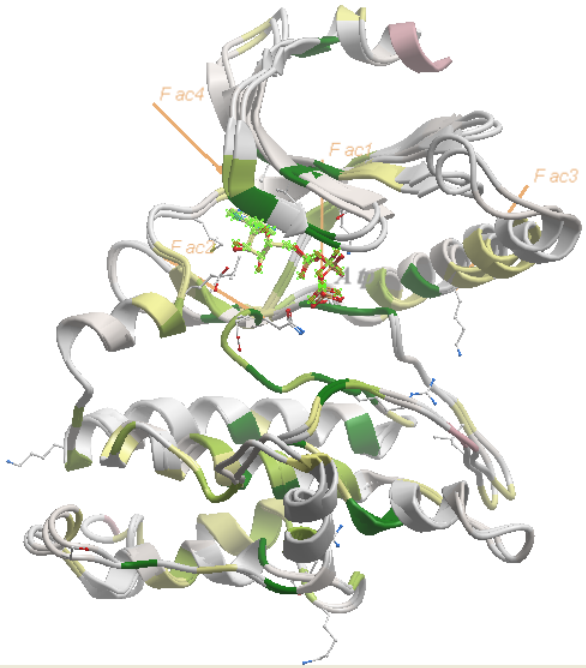
Propagate selection to all sequences in alignment.



1. Propagate to all sequences

Notice selection is propagated to all sequences in the alignment – highlighted in blue

Display only the residues in the ligand binding pocket.

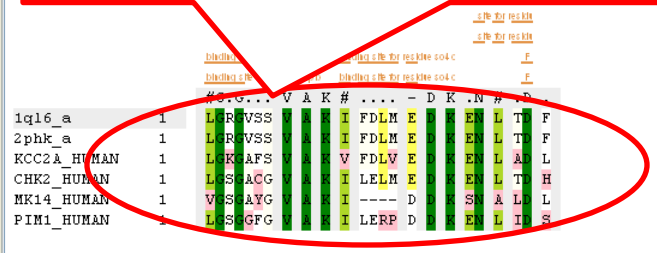


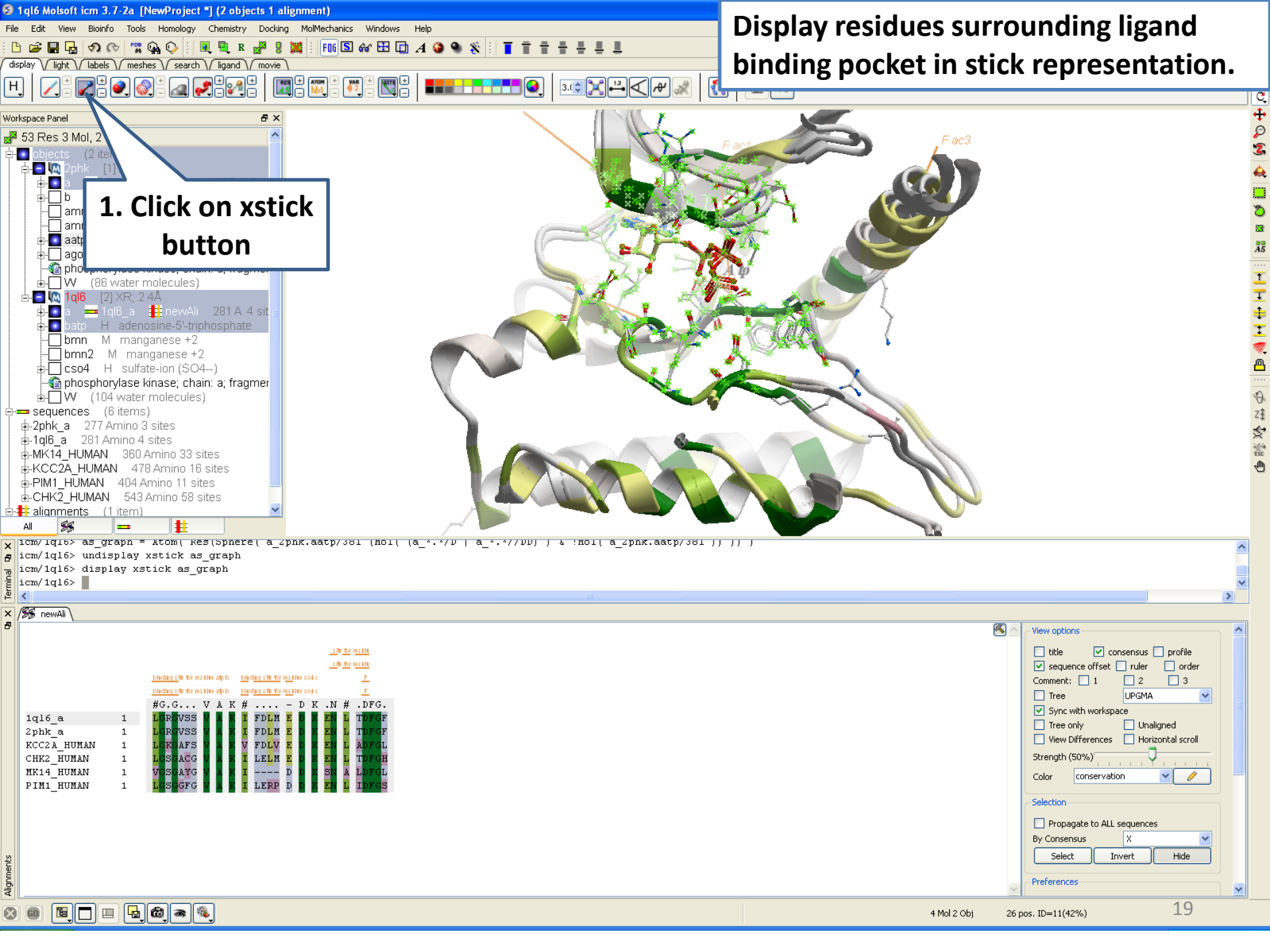
3. Click again to restore view

2. Hide selection

1. Invert selection

Residue conservation in the ligand binding pocket




1ql6 Molsoft icm 3.7-2a [NewProject *] (2 objects 1 alignment)
File Edit View Bioinfo Tools Homology Chemistry Docking MolMechanics Windows Help
display light labels meshes search ligand movie
Display residues surrounding ligand binding pocket in stick representation.
1. Click on xstick button
Workspace Panel
53 Res 3 Mol, 2
objects (2 items)
2phk [1]
1ql6 [2] XR; 2.4Å
1ql6_a newAli 281 A 4 sit
batp H adenosine-5'-triphosphate
bmn M manganese +2
bmn2 M manganese +2
cso4 H sulfate-ion (SO4--)
phosphorylase kinase; chain: a; fragmer
W (104 water molecules)
sequences (6 items)
2phk_a 277 Amino 3 sites
1ql6_a 281 Amino 4 sites
MK14_HUMAN 360 Amino 33 sites
KCC2A_HUMAN 478 Amino 16 sites
PIM1_HUMAN 404 Amino 11 sites
CHK2_HUMAN 543 Amino 58 sites
alignments (1 item)
F ac1
F ac3
A tp
icm/1ql6> undisplay xstick as_graph
icm/1ql6> display xstick as_graph
icm/1ql6>
Terminal
newAli
1ql6_a 1
2phk_a 1
KCC2A_HUMAN 1
CHK2_HUMAN 1
MK14_HUMAN 1
PIM1_HUMAN 1
View options
title consensus profile
sequence offset ruler order
Comment: 1 2 3
Tree UPGMA
Sync with workspace
Tree only Unaligned
View Differences Horizontal scroll
Strength (50%)
Color conservation
Selection
Propagate to ALL sequences
By Consensus X
Select Invert Hide
Preferences
Alignments
4 Mol 2 Obj
26 pos. ID=11(42%)

Color stick by alignment.