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Biomacromolecular structure analysis - channels

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CEITEC, Masaryk University

EUROPEAN UNION
EUROPEAN REGIONAL DEVELOPMENT FUND
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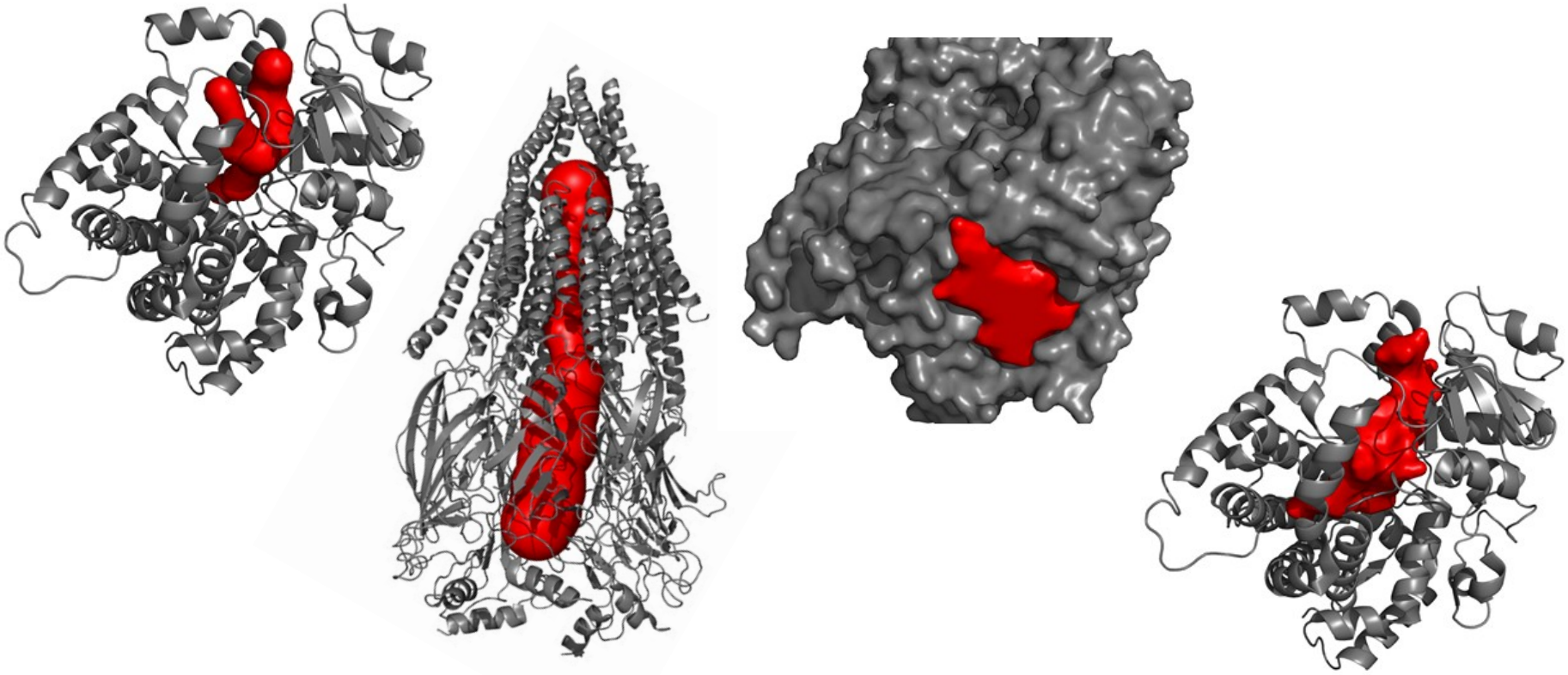
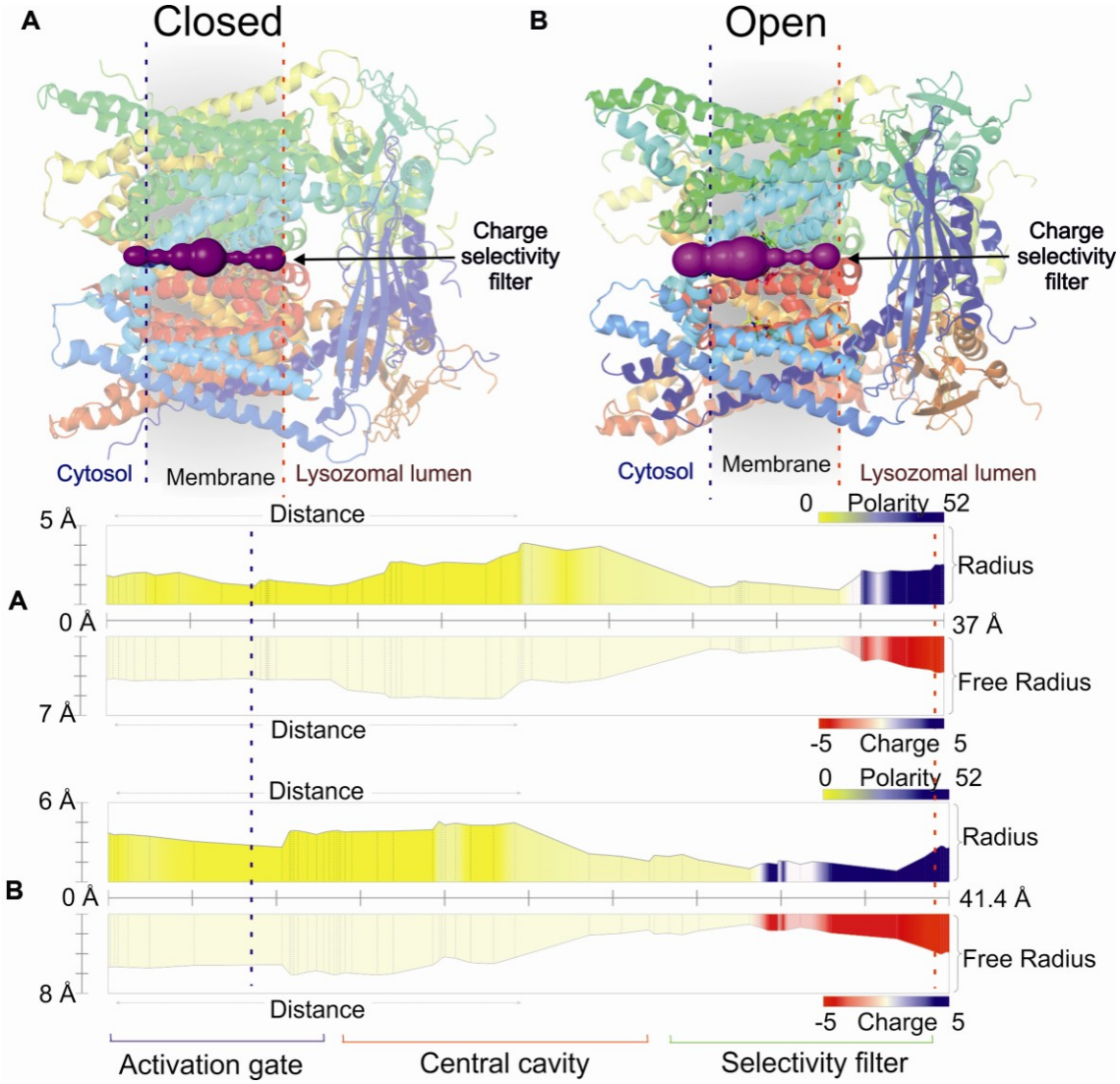
2007–13
OP Research and Development for Innovation

Tunnels, pores, pockets, cavities: Locations of key biochemical processes



MOLEonline

Use case: Transient receptor potential mucolipin 1



(A) The channel (closed conformation) of TRPML1 (PDB ID: 5WJ5). The blue and red dashed lines delimit the membrane region. The profiles depict polarity and charge along the pore.

(B) The channel in open conformation (PDB ID: 5WJ9). The pore is divided into three main parts: Activation gate; Central cavity and Selectivity filter. The figure was generated using Pymol software.

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MOLEonline

MOLEonline: Web application for detection of channels and pores and calculation of their geometrical and physico-chemical properties

New features:

- Automatic detection of transmembrane pores
- Visualization of properties on the channel's profile
- Interconnection with other bioinformatics tools (PDBe, CSA, ChannelsDB, OPM, UniProt) and data transfer from them
- Integration of LiteMol suite

- Pravda L., Sehnal D., Toušek D., Navrátilová V., Bazgier V., Berka K., ... & **Koča J.**, Otyepka M. (2018). *MOLEonline: a web-based tool for analyzing channels, tunnels and pores (2018 update)*. **Nucleic acids research.**

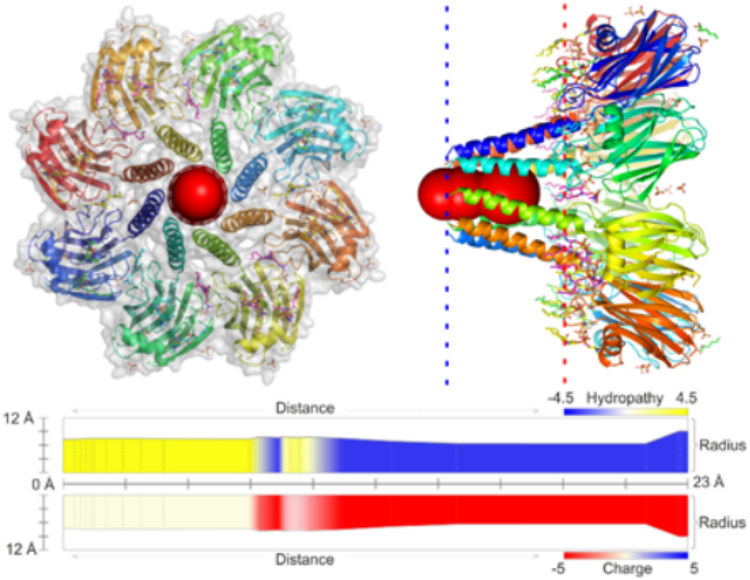
MOLEonline - Initialization

MOLE*online*

Home | Online | Documentation | About

MOLE*online* web interface provides a direct access to MOLE functionality and enables on-line and easy-to-use interactive channel analysis.

MOLE 2.5 is an universal toolkit for rapid and fully automated location and characterization of channels, tunnels and pores in (bio)macromolecular structures, e.g., proteins, RNA, DNA and biomacromolecular assemblies.



MOLE*online* features

- Quickest channel calculation on the market
- Automatic transmembrane pore identification
- Layered channel profile - geometry, length and radius
- List of residues lining channels (distinguishing sidechain/mainchain contact with the channel)
- Layered or channel-wise physico-chemical properties (several types of channel radius, length, charge, polarity, hydropathy, hydrophobicity, mutability, etc.)

Quick start

PDBID | File | Last session

PDB ID: 1tqn

Assembly ID (optional):

Use biological unit: ☑

Next

News

Attention 8. 6. 2019

Update to Chrome 75 disables WebGL functionalities important for MOLEonline LiteMol visualization. We are working on fix on this issue. Meanwhile use other browsers for accessing MOLEonline.

Server room maintenance 17. 12. 2018

We would like to announce that MOLEonline will not be available on Monday (December 17th) due to web server room maintenance. Sorry for the inconvenience.

MOLEonline update 2018 was published 1. 5. 2018

Our paper, which describes the new features of MOLEonline, is accepted for publication in Web issue of Nucleic Acids Research.

New features and updates 2. 4. 2018

New features in MOLEonline:

- new Help button will allow to send us your troubled session so we can help you more thoroughly,
- multiple layers can be selected/deselected to show average properties

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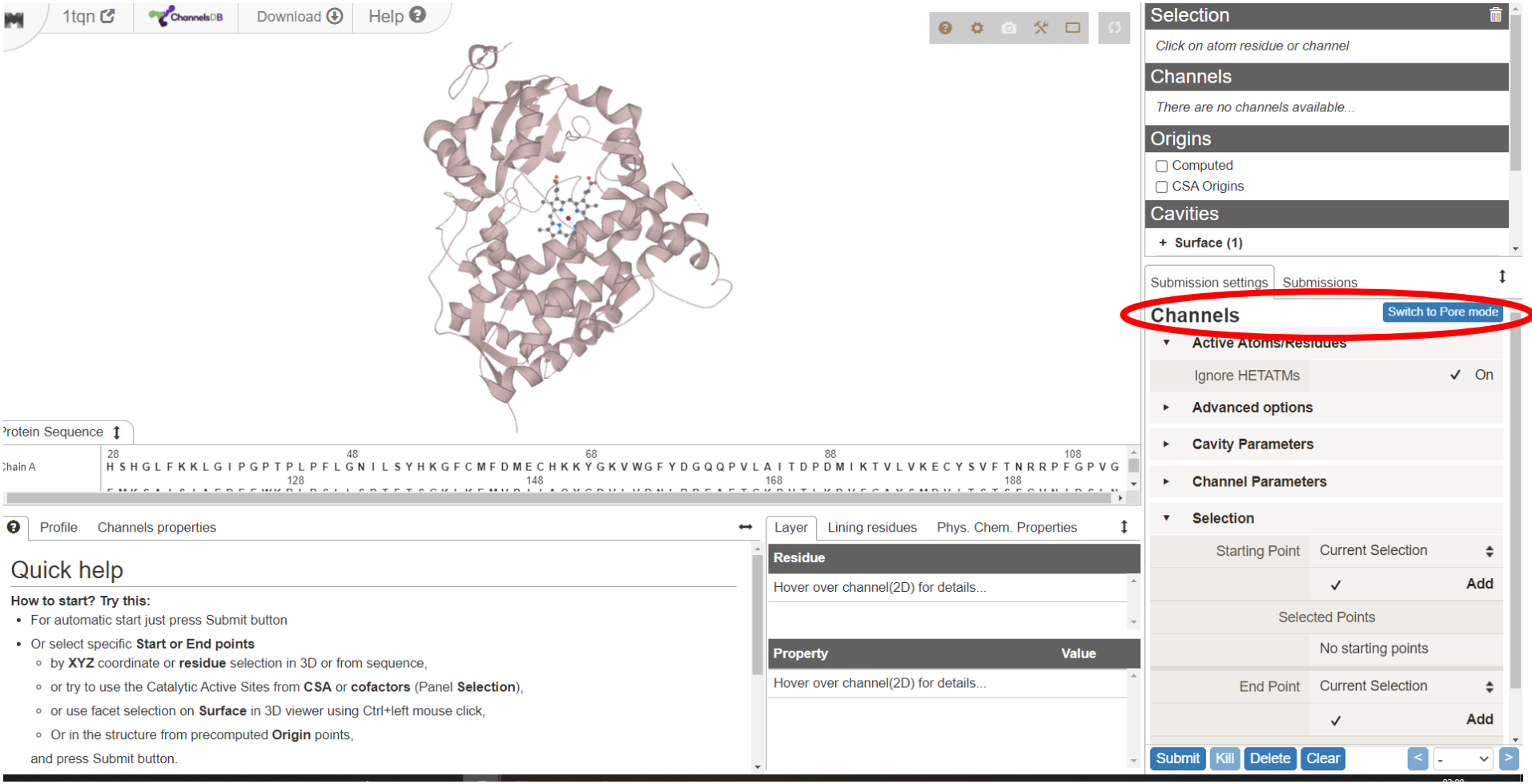

1tqn
ChannelsDB
Download
Help
Selection
Click on atom residue or channel
Channels
There are no channels available...
Origins
Computed
CSA Origins
Cavities
+ Surface (1)
Submission settings
Submissions
Channels
Switch to Pore mode
Active Atoms/Residues
Ignore HETATMs
On
Advanced options
Cavity Parameters
Channel Parameters
Selection
Starting Point
Current Selection
Add
Selected Points
No starting points
End Point
Current Selection
Add
Submit
Kill
Delete
Clear
Protein Sequence
Chain A
Profile
Channels properties
Layer
Lining residues
Phys. Chem. Properties
Residue
Hover over channel(2D) for details...
Property
Value
Hover over channel(2D) for details...
Quick help
How to start? Try this:
For automatic start just press Submit button
Or select specific Start or End points
by XYZ coordinate or residue selection in 3D or from sequence,
or try to use the Catalytic Active Sites from CSA or cofactors (Panel Selection),
or use facet selection on Surface in 3D viewer using Ctrl+left mouse click,
Or in the structure from precomputed Origin points,
and press Submit button.

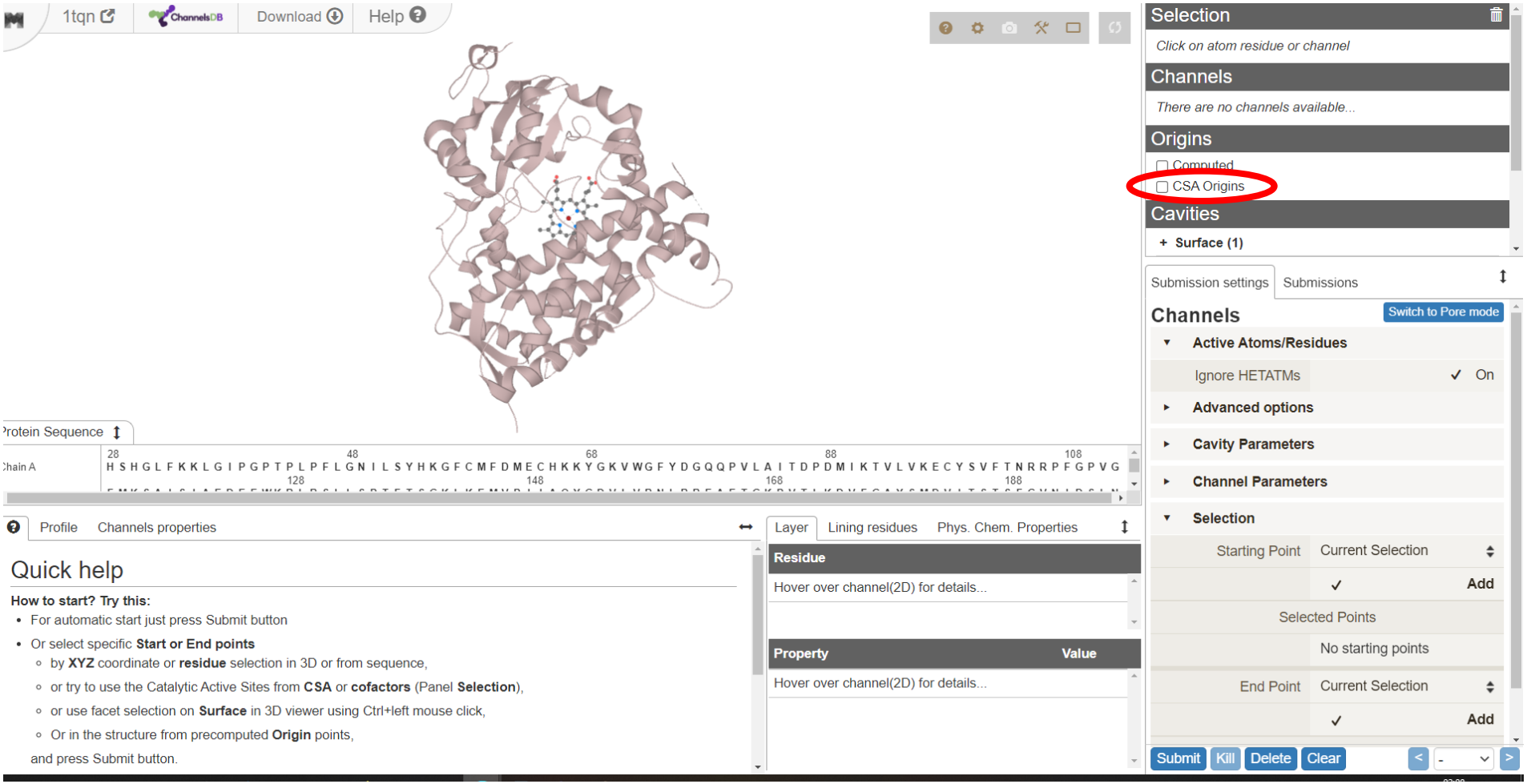
Channels mode

- Identification of channels and other types of pores

Origins of channels:

- **Origins -** Automatic Start points definition in the deepest points within cavities
- **CSA origins** - Catalytic site residues from Catalytic Site Atlas
- Start and end points user definition
  - List of residues (selectable from sequence or 3D stucture)
  - Cofactors
  - XYZ coordinates

MOLEonline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Selection
Click on atom residue or channel
Channels
There are no channels available...
Origins
Computed
CSA Origins
Cavities
+ Surface (1)
Protein Sequence
Chain A
Submission settings
Submissions
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No starting points
End Point
Current Selection
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Clear
Profile
Channels properties
Layer
Lining residues
Phys. Chem. Properties
Residue
Hover over channel(2D) for details...
Property
Value
Hover over channel(2D) for details...
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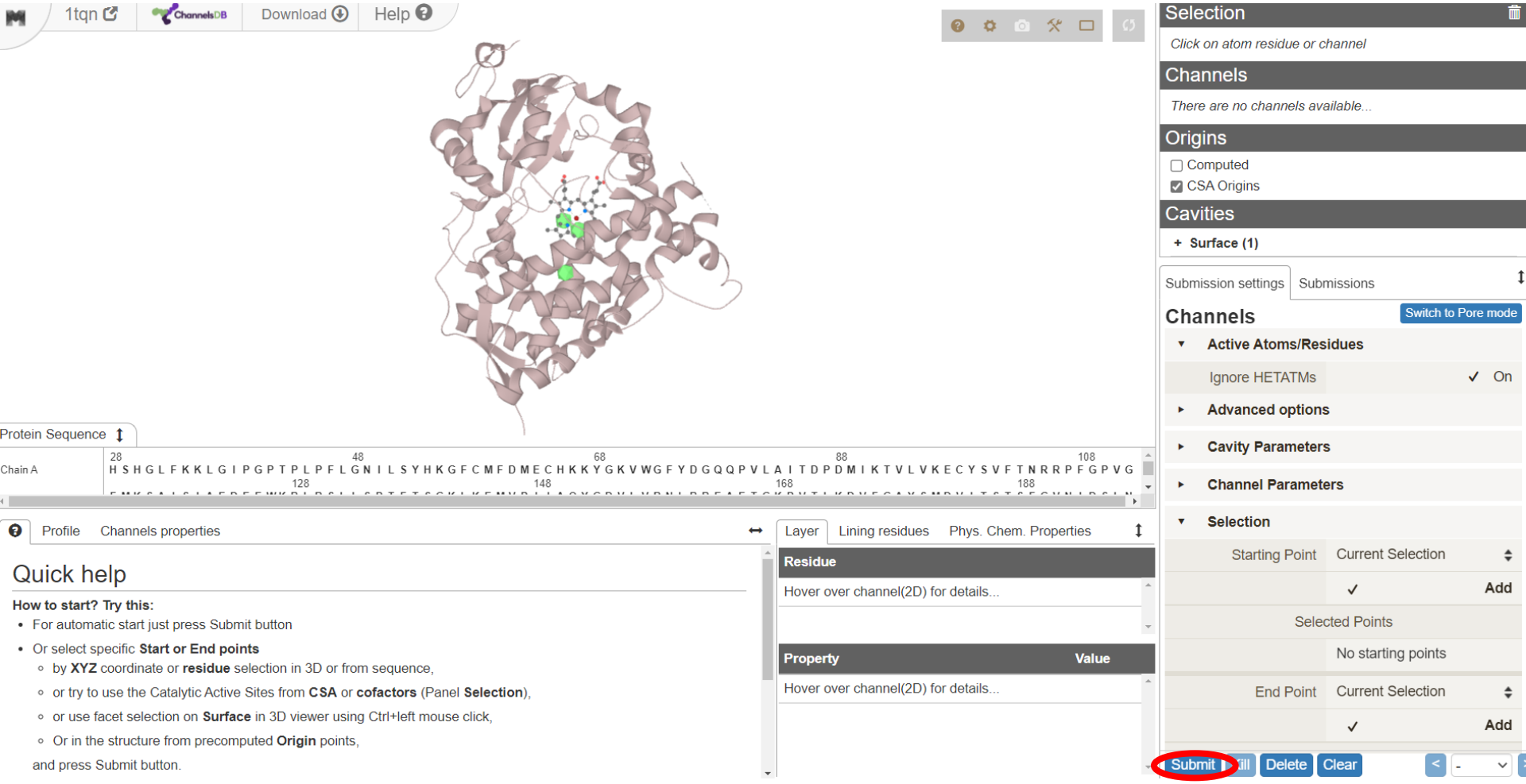
MOLEonline


1tqn
ChannelsDB
Download
Help
Selection
Click on atom residue or channel
Channels
There are no channels available...
Origins
Computed
CSA Origins
Cavities
+ Surface (1)
Submission settings
Submissions
Channels
Switch to Pore mode
Active Atoms/Residues
Ignore HETATMs
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Advanced options
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Channel Parameters
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No starting points
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Protein Sequence
Chain A
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Lining residues
Phys. Chem. Properties
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Property
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Hover over channel(2D) for details...
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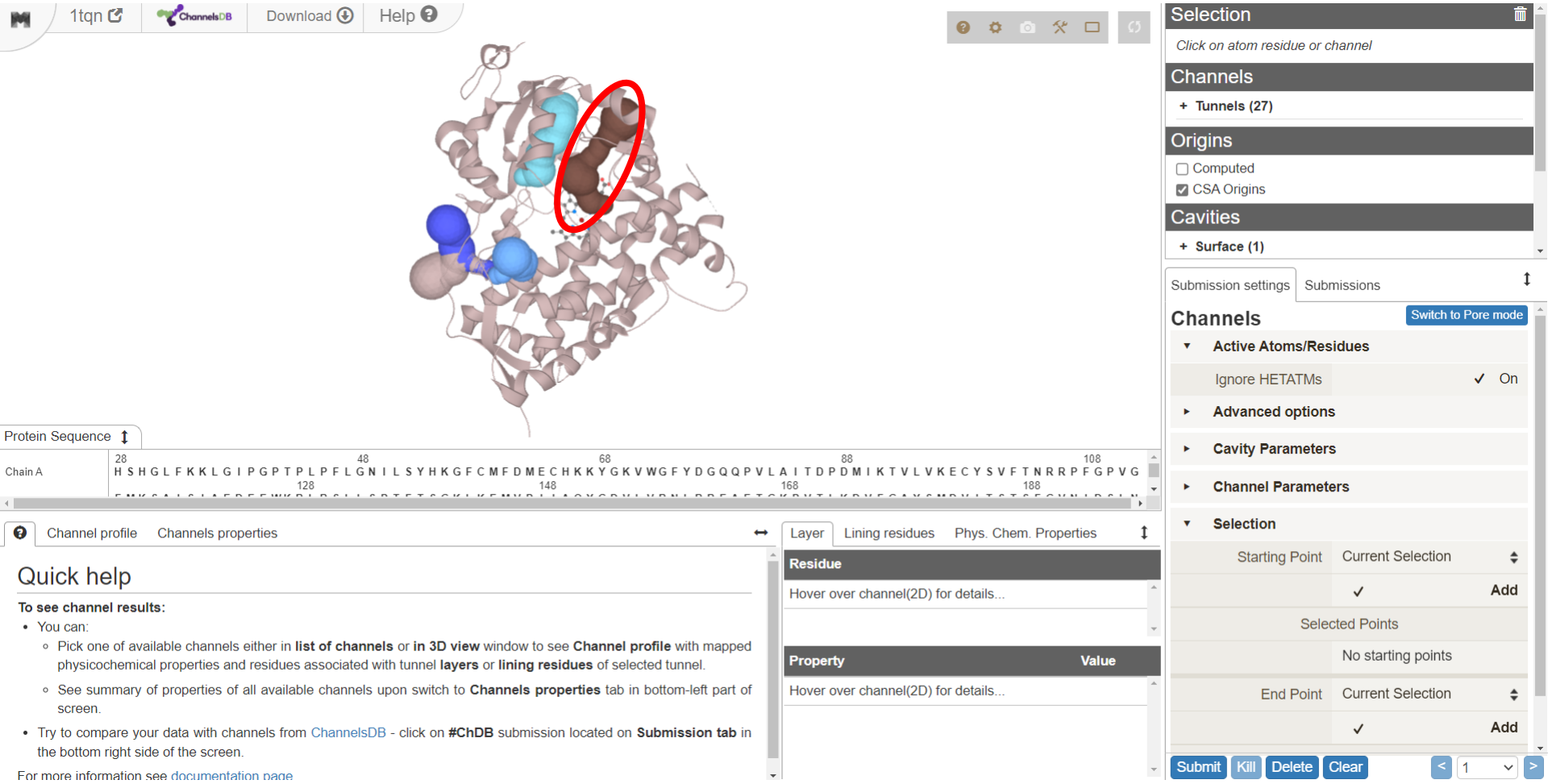
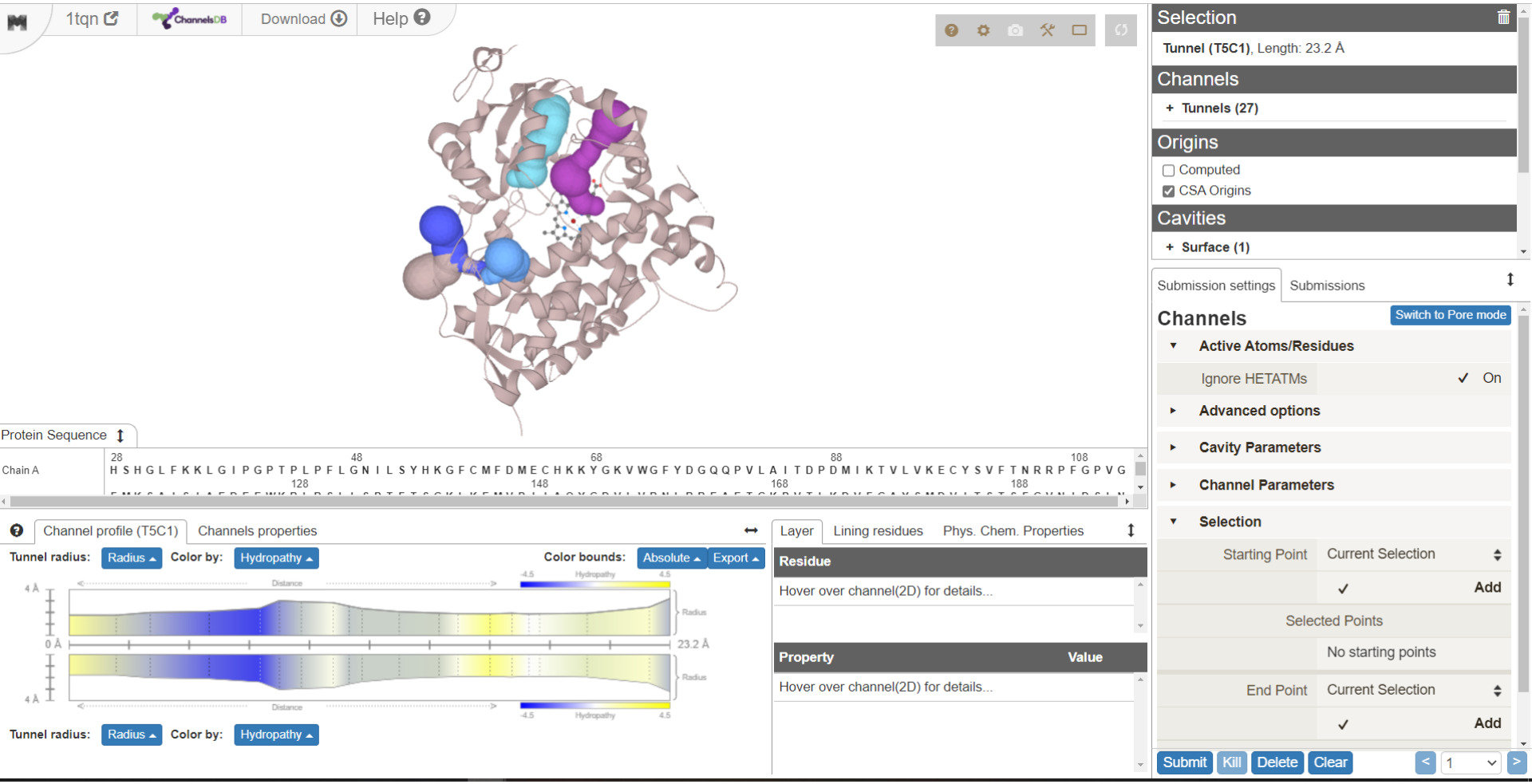
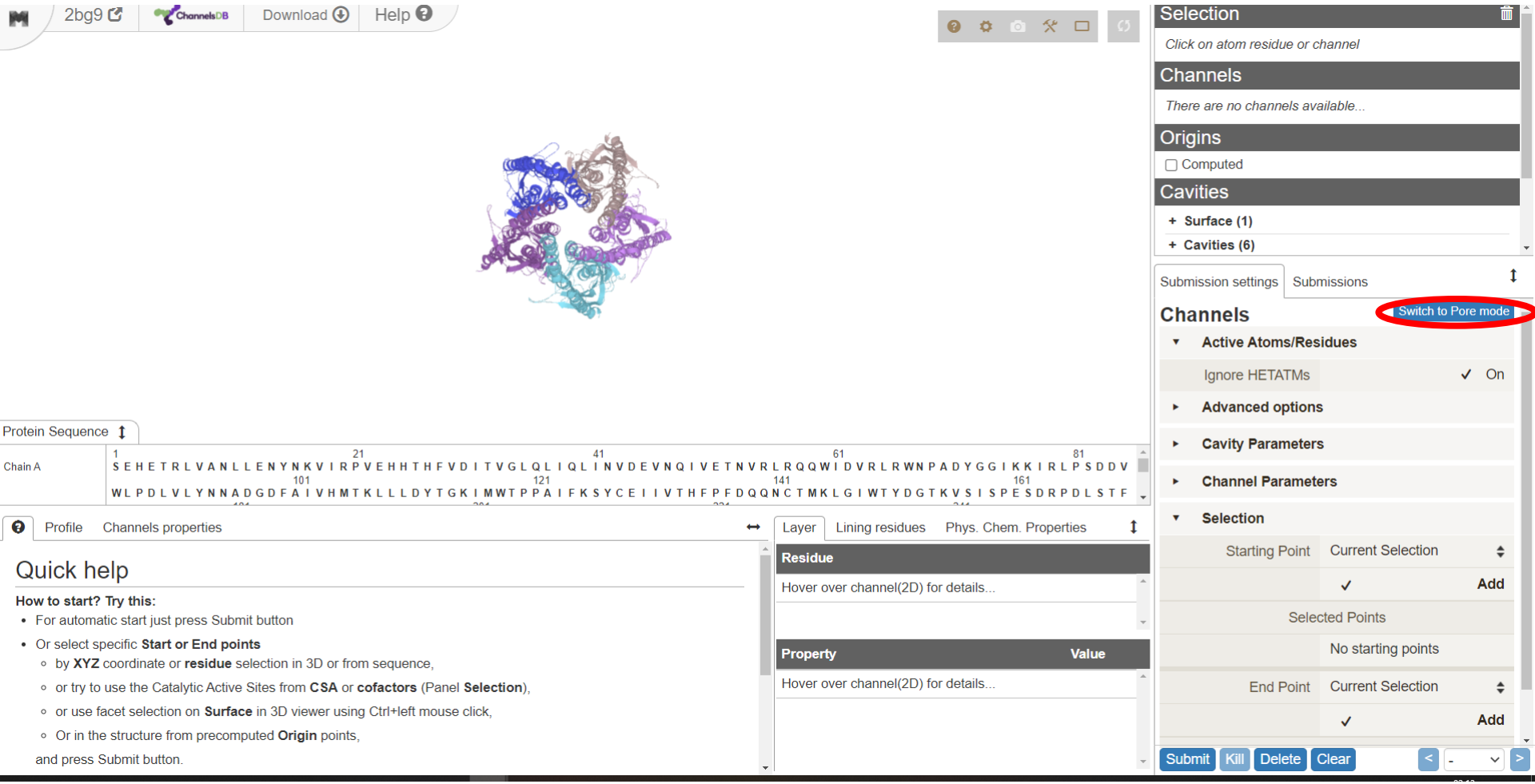

1tqn
ChannelsDB
Download
Help
Selection
Click on atom residue or channel
Channels
+ Tunnels (27)
Origins
Computed
CSA Origins
Cavities
+ Surface (1)
Protein Sequence
Chain A
Submission settings
Submissions
Channels
Switch to Pore mode
Active Atoms/Residues
Ignore HETATMs
On
Advanced options
Cavity Parameters
Channel Parameters
Selection
Starting Point
Current Selection
Add
Selected Points
No starting points
End Point
Current Selection
Add
Submit
Kill
Delete
Clear
Channel profile
Channels properties
Layer
Lining residues
Phys. Chem. Properties
Residue
Hover over channel(2D) for details...
Property
Value
Hover over channel(2D) for details...
Quick help
To see channel results:
You can:
Pick one of available channels either in list of channels or in 3D view window to see Channel profile with mapped physicochemical properties and residues associated with tunnel layers or lining residues of selected tunnel.
See summary of properties of all available channels upon switch to Channels properties tab in bottom-left part of screen.
Try to compare your data with channels from ChannelsDB - click on #ChDB submission located on Submission tab in the bottom right side of the screen.
For more information see documentation page

MOLEonline


1tqn
ChannelsDB
Download
Help
Selection
Tunnel (T5C1), Length: 23.2 Å
Channels
+ Tunnels (27)
Origins
Computed
CSA Origins
Cavities
+ Surface (1)
Protein Sequence
Chain A
Submission settings
Submissions
Channels
Switch to Pore mode
Active Atoms/Residues
Ignore HETATMs
On
Advanced options
Cavity Parameters
Channel Parameters
Selection
Starting Point
Current Selection
Add
Selected Points
No starting points
End Point
Current Selection
Add
Channel profile (T5C1)
Channels properties
Tunnel radius:
Radius
Color by:
Hydropathy
Color bounds:
Absolute
Export
Distance
Hydropathy
Radius
23.2 Å
Layer
Lining residues
Phys. Chem. Properties
Residue
Hover over channel(2D) for details...
Property
Value
Hover over channel(2D) for details...
Submit
Kill
Delete
Clear

MOLEonline


2bg9
ChannelsDB
Download
Help
Selection
Click on atom residue or channel
Channels
There are no channels available...
Origins
Computed
Cavities
+ Surface (1)
+ Cavities (6)
Protein Sequence
Chain A
Submission settings
Submissions
Channels
Switch to Pore mode
Active Atoms/Residues
Ignore HETATMs
On
Advanced options
Cavity Parameters
Channel Parameters
Selection
Starting Point
Current Selection
Add
Selected Points
No starting points
End Point
Current Selection
Add
Submit
Kill
Delete
Clear
Profile
Channels properties
Layer
Lining residues
Phys. Chem. Properties
Residue
Hover over channel(2D) for details...
Property
Value
Hover over channel(2D) for details...
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and press Submit button.

Pore mode

- transmembrane pores
- membrane position from Orientations of Proteins in Membranes (OPM) database or calculated with MEMEMBED program.
- *Membrane region parameter* - calculate pore in transmembrane region only
- *Beta structure parameter* is recommended for transmembrane regions formed by β-barrel structure

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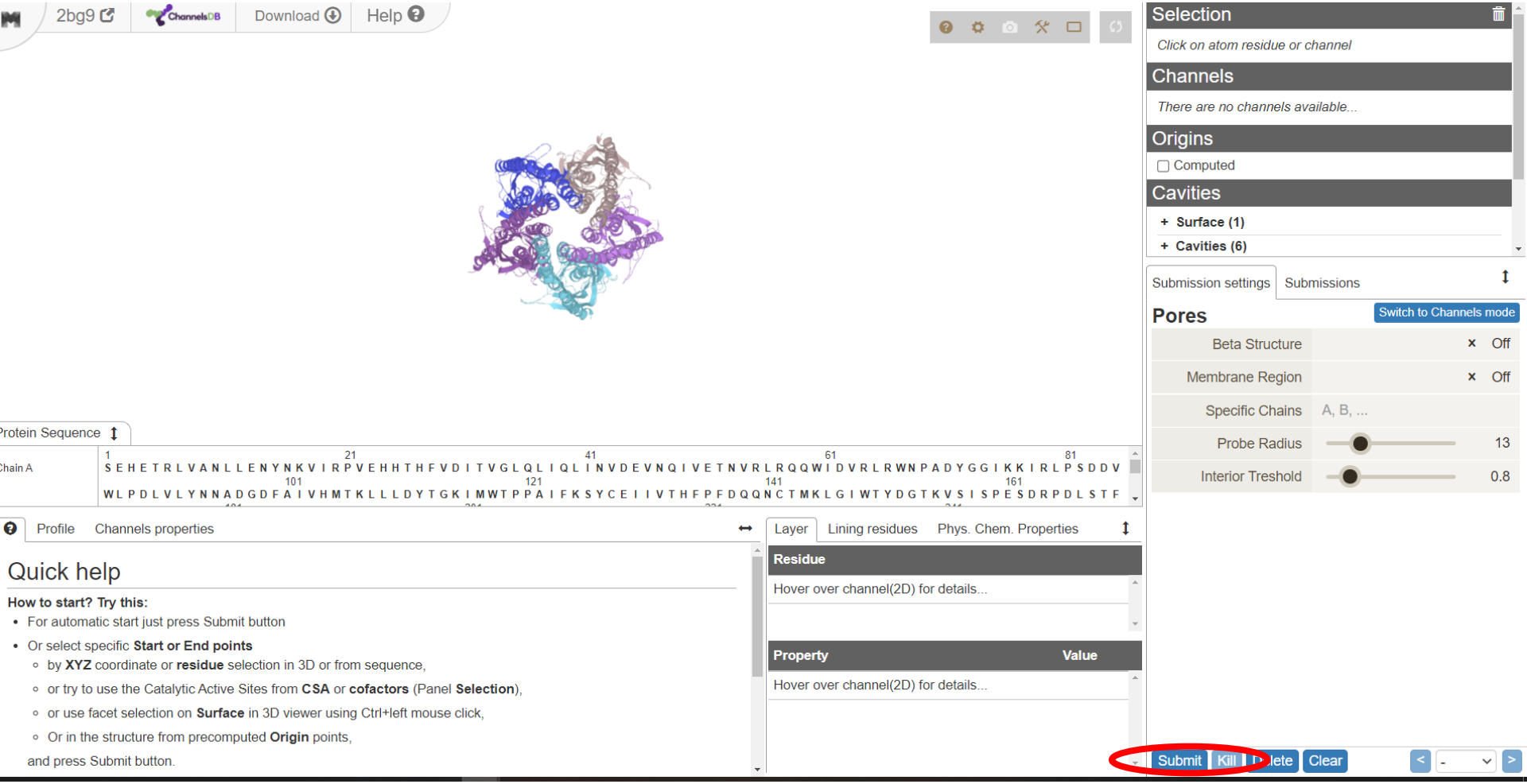

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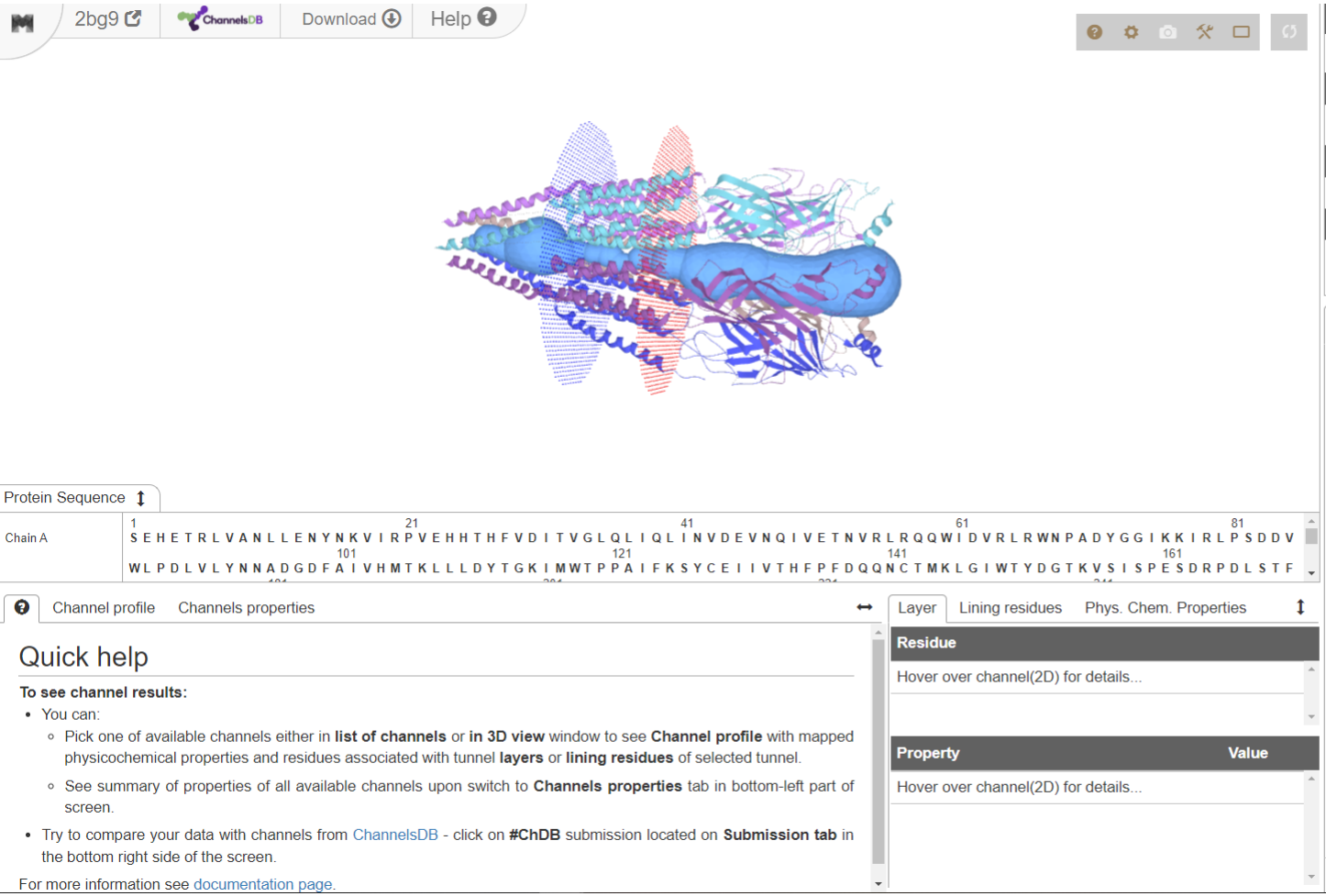
MOLEonline


2bg9
ChannelsDB
Download
Help
Selection
Click on atom residue or channel
Channels
+ Paths (1)
Origins
Computed
Cavities
+ Surface (1)
+ Cavities (1)
Protein Sequence
Chain A
Submission settings
Submissions
Pores
Switch to Channels mode
Beta Structure
Off
Membrane Region
Off
Specific Chains
A, B, ...
Probe Radius
13
Interior Treshold
0.8
Channel profile
Channels properties
Quick help
To see channel results:
You can:
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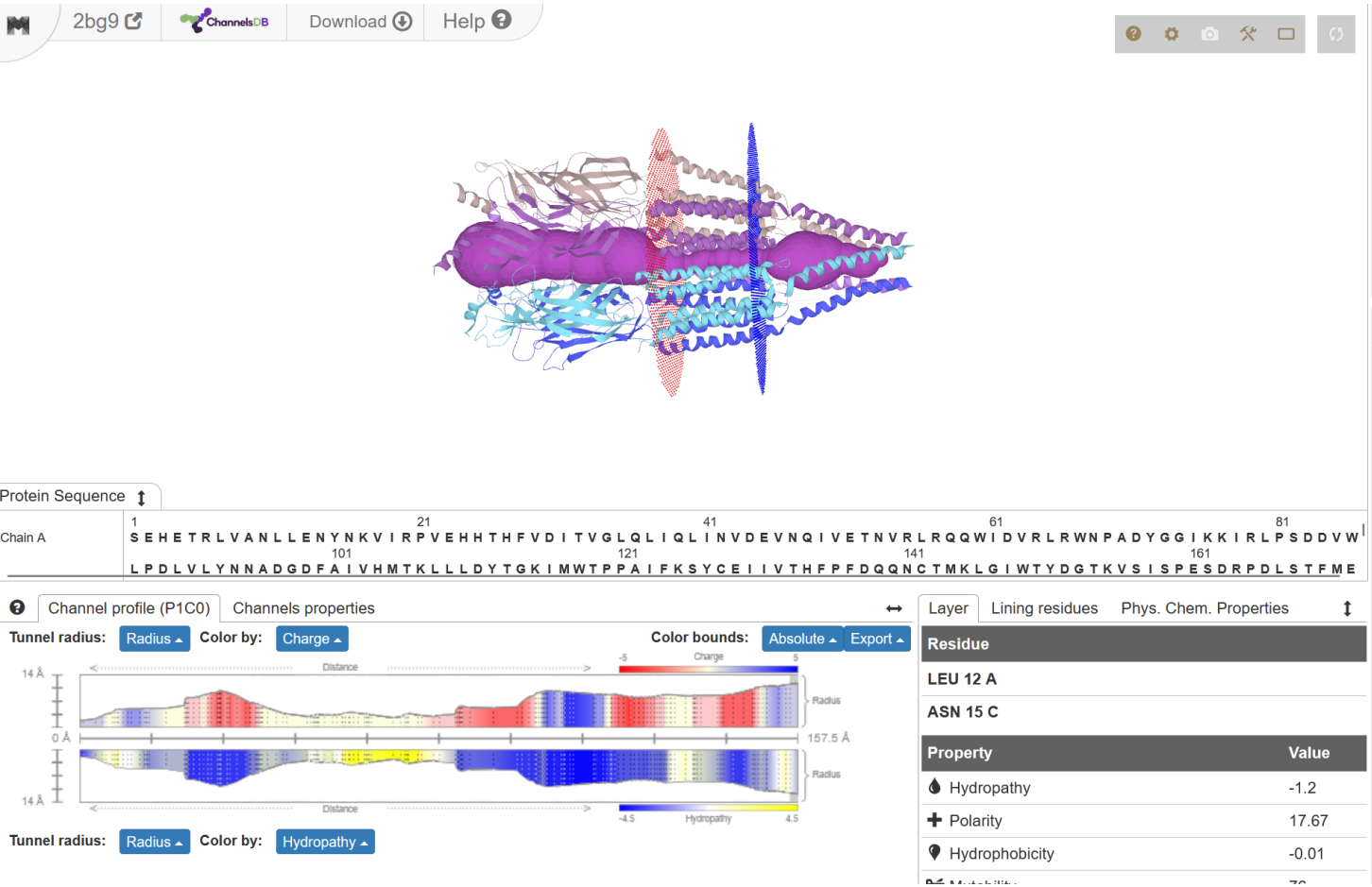
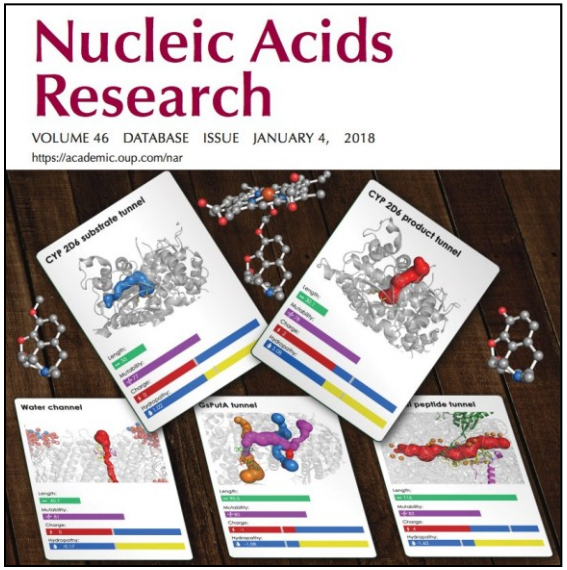
Try to compare your data with channels from ChannelsDB - click on #ChDB submission located on Submission tab in the bottom right side of the screen.
For more information see documentation page.
Layer
Lining residues
Phys. Chem. Properties
Residue
Hover over channel(2D) for details...
Property
Value
Hover over channel(2D) for details...
Submit
Kill
Delete
Clear

MOLEonline


2bg9
ChannelsDB
Download
Help
Selection
Path (P1C0), Length: 157.5 Å
Channels
+ Paths (1)
Origins
Computed
Cavities
+ Surface (1)
+ Cavities (1)
Submission settings
Submissions
Pores
Switch to Channels mode
Beta Structure
× Off
Membrane Region
× Off
Specific Chains
A, B, ...
Probe Radius
13
Interior Treshold
0.8
Protein Sequence
Chain A
1 21 41 61 81
S E H E T R L V A N L L E N Y N K V I R P V E H H T H F V D I T V G L Q L I Q L I N V D E V N Q I V E T N V R L R Q Q W I D V R L R W N P A D Y G G I K K I R L P S D D V W
101 121 141 161
L P D L V L Y N N A D G D F A I V H M T K L L L D Y T G K I M W T P P A I F K S Y C E I I V T H F P F D Q Q N C T M K L G I W T Y D G T K V S I S P E S D R P D L S T F M E
Channel profile (P1C0)
Channels properties
Tunnel radius:
Radius
Color by:
Charge
Color bounds:
Absolute
Export
Distance
Charge
-5
5
14 Å
0 Å
157.5 Å
Radius
Hydropathy
-4.5
4.5
Tunnel radius:
Radius
Color by:
Hydropathy
Layer
Lining residues
Phys. Chem. Properties
Residue
LEU 12 A
ASN 15 C
Property
Value
Hydropathy
-1.2
Polarity
17.67
Hydrophobicity
-0.01
Submit
Kill
Delete
Clear
1

ChannelsDB

- **ChannelDB** – interactive database of channels with expected and annotated biological relevancy.
- Pathways were calculated using an algorithms CAVER and MOLE
- Channel visualisation via LiteMol



Pravda L., Sehnal D., Svobodová R., Navrátilová V., Toušek D., Berka K., ... & Koča J. (2017). *ChannelsDB: database of biomacromolecular tunnels and pores*. **Nucleic acids research**, 46(D1), D399-D405.

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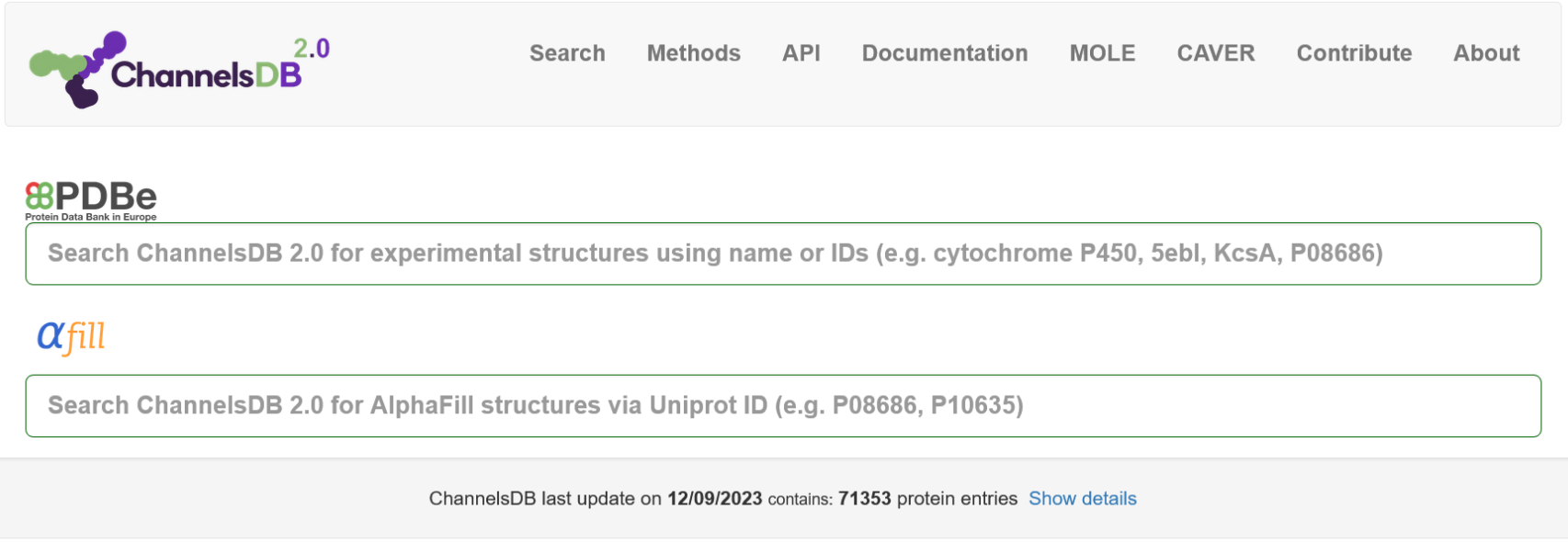
ChannelsDB – Search



ChannelsDB

ChannelsDB 2.0 | Search | Methods | API | Documentation | MOLE | CAVER | Contribute | About

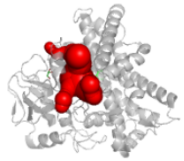
PDBe Protein Data Bank in Europe

cytochrome P450

αfill

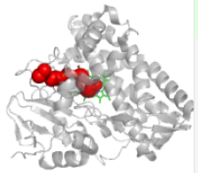
Search ChannelsDB 2.0 for AlphaFill structures via Uniprot ID (e.g. P08686, P10635)

Search: cytochrome P450 (1584; 1083 with channels)



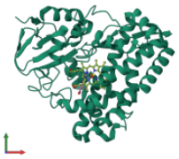
5y5g Structure of cytochrome P450nor in NO-

Experiment Method: X-ray diffraction | 1.36 Å
Organism: *Fusarium oxysporum*
5 channels; CofactorTunnels MOLE (4), CofactorTunnels Caver (1)



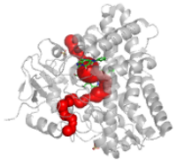
5uvb The crystal structure of 4-

Experiment Method: X-ray diffraction | 1.54 Å
Organism: *Rhodopseudomonas palustris*
4 channels; CofactorTunnels MOLE (1), CofactorTunnels Caver (3)



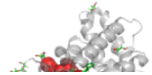
6u31 The crystal structure of 4-(1H-imidazol-1-

Experiment Method: X-ray diffraction | 1.578 Å
Organism: *Rhodopseudomonas palustris HaA2*
14 channels; ProcognateTunnels MOLE (2), ProcognateTunnels Caver (12)



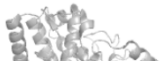
6geo Crystal structure of Mycobacterium

Experiment Method: X-ray diffraction | 1.5 Å
Organism: *Mycobacterium tuberculosis CDC1551*
6 channels; CofactorTunnels MOLE (3), CofactorTunnels Caver (3)



6tet The structure of CYP121 in complex with

Experiment Method: X-ray diffraction | 1.4998689 Å



6rq8 CYP121 in complex with 3-iodo

Experiment Method: X-ray diffraction | 1.41 Å

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ChannelsDB

4nm9 - Proline utilization A protein (PutA)

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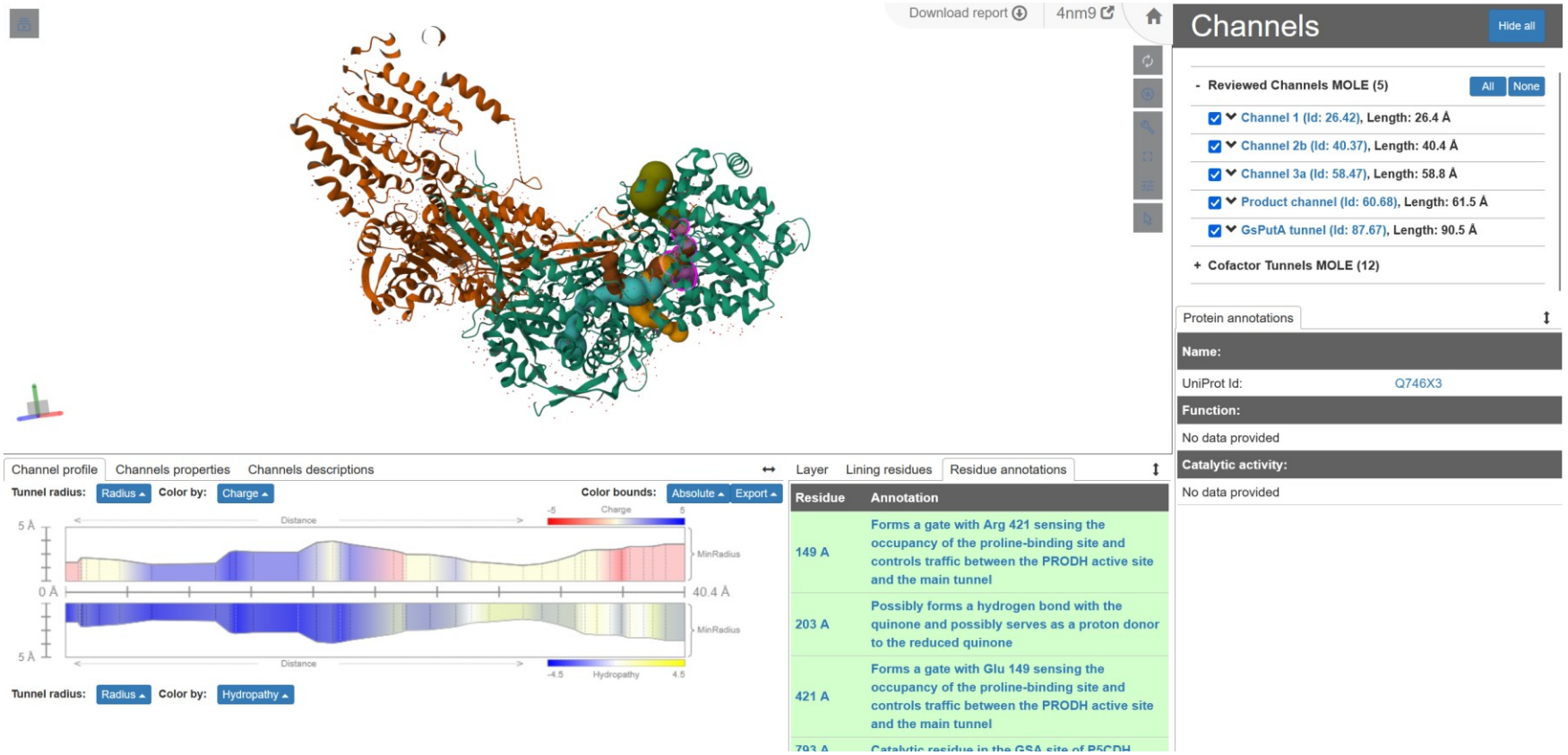
Download report
4nm9
Channels
Hide all
- Reviewed Channels MOLE (5)
All
None
Channel 1 (Id: 26.42), Length: 26.4 Å
Channel 2b (Id: 40.37), Length: 40.4 Å
Channel 3a (Id: 58.47), Length: 58.8 Å
Product channel (Id: 60.68), Length: 61.5 Å
GsPutA tunnel (Id: 87.67), Length: 90.5 Å
+ Cofactor Tunnels MOLE (12)
Protein annotations
Name:
UniProt Id: Q746X3
Function:
No data provided
Catalytic activity:
No data provided
Channel profile
Channels properties
Channels descriptions
Tunnel radius: Radius
Color by: Charge
Color bounds: Absolute
Export
5 Å
0 Å
5 Å
Distance
Charge
-5
5
MinRadius
40.4 Å
-4.5
Hydropathy
4.5
Tunnel radius: Radius
Color by: Hydropathy
Layer
Lining residues
Residue annotations
Residue
Annotation
149 A
Forms a gate with Arg 421 sensing the occupancy of the proline-binding site and controls traffic between the PRODH active site and the main tunnel
203 A
Possibly forms a hydrogen bond with the quinone and possibly serves as a proton donor to the reduced quinone
421 A
Forms a gate with Glu 149 sensing the occupancy of the proline-binding site and controls traffic between the PRODH active site and the main tunnel

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Středoevropský technologický institut

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Thank you for your attention!

EVROPSKÁ UNIE
EVROPSKÝ FOND PRO REGIONÁLNÍ ROZVOJ
INVESTICE DO VAŠÍ BUDOUCNOSTI

2007–13
OP Výzkum a vývoj pro inovace