



Enalos Cloud Platform: Prediction of MNPs Uptake in PaCa2 Cancer Cells

A brief tutorial

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Overview

Online toxicity predictions for coated iron oxide manufactured nanoparticles (MNPs) are made available through *Prediction of MNPs Uptake in PaCa2 Cancer Cells* web service of Enalos Cloud Platform.

Enalos Cloud Platform hosts a fully validated predictive model, developed by NovaMechanics Ltd, for the prediction of the cellular uptake of NPs in pancreatic cancer cells. Full documentation on the model development can be found in:

G. Melagraki and A. Afantitis, "Enalos InSilicoNano platform: an online decision support tool for the design and virtual screening of nanoparticles", RSC Advances, vol. 4, pp. 50713-25, 2014.

Prediction of MNPs Uptake in PaCa2 Cancer Cells web service is accessible through the following url:

http://enalos.insilicotox.com/QNAR_PaCa2/

The platform can be easily accessed, there is no need for authorization and the user can directly use the provided service. Without prior computational skills, the user can insert one or several structures of compounds (small molecules that modified NP coating) and get a predicted cellular uptake value for PaCa2 cancer cells along with an indication of its reliability based on the model's domain of applicability limits.

The web service provides the functionality to virtually screen a set of compounds of interest based on the validated model, and thus yielding a preliminary *in silico* testing. Along with other Enalos Cloud web-services, the present platform will facilitate the computer aided nanoparticles design as it can serve as a source of activity prediction for novel nano-structures.

Instructions

Required input

To initiate a prediction, the user must provide a structure (or a set of structures) for one (or more compounds). For this purpose, the platform provides three different options for inserting the required input to the model (Figure 1, areas 1-2-3):



Prediction of MNPs Uptake in PaCa2 Cancer Cells

Design a molecule

Enter SMILES separated by newlines

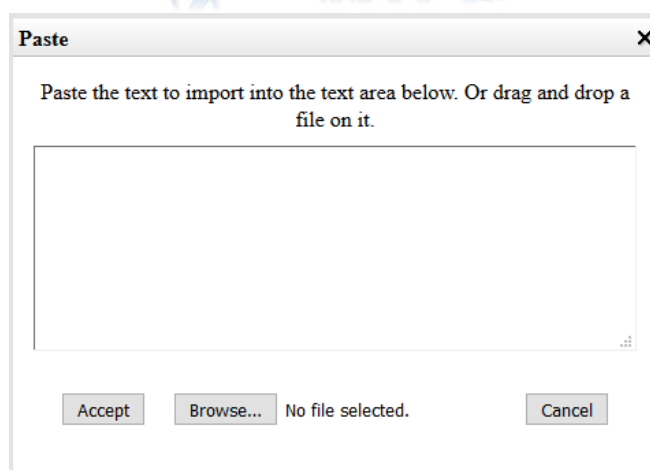
Name	Description
QNaR_PaCa2	QNaR model correlating chemical descriptors and MNP cellular uptakes (similar nanoparticle core with different surface modifiers)

Figure 1: Prediction of MNPs Uptake in PaCa2 Cancer Cells input page. (1) At the left-handed side the molecular drawing tool is found. (2) At the top right-handed the SMILES input form can be seen followed by (3) the option of importing a .sdf file.

1. The user can draw the chemical structure of interest using the drawing tool [Figure 1 (1) and Figure 2 (A) and (B)].

When using the drawing tool, only one structure can be submitted at a time. The user can easily select from the different panels specific atoms, bonds or substructures and then design the molecule. The JSME sketcher also enables the user to open, save and convert files with a variety of chemical formats such as, SMILES, IUPAC Chemical Identifier, MDL MOL file using the drop down menu of the online sketcher or with a mouse right click (Figure 2 A, see red circle). The name of the compound can be seen at the bottom ribbon of the drawing tool (Figure 2A, see blue arrow). It is also possible to search via InChIKey identification, information about the chemical structure of interest (Figure 2A, see green arrow). By clicking on "Paste any chemical text repr." a new window opens and the user can either manually enter or upload structures in several formats (Figure 2B).

(A)



(B)

Figure 2: Molecular drawing tool. (A) The user can design the structure of a compound using the different substructures at the top and left ribbons. At the bottom the name of the structure can be seen. With the right mouse click or by clicking on the drop down menu, the user can copy the structure in different formats (useful for the generation of several structures). (B) By clicking on "Paste any chemical text repr." a new window opens and the user can either manually enter or upload structures in several formats.

2. The user can enter the SMILES notation of one or several structures separated by newlines [Figure 1 (3)].

If the SMILES notation is known, the user can directly submit it in the SMILES notation area. If the SMILES notation is not initially known, the chemical sketcher included gives the users the opportunity to draw the chemical structure and then copy the structure as SMILES with a right mouse click or by using the drop down menu (Figure 2A, see yellow arrow). This facilitates the generation of several structures, by allowing a multitude of modifications to be performed using the sketcher and then coping all structures as SMILES and pasting in the appropriate field (Figure 3), so that a prediction for the whole set of produced structures is obtained. Thus, the modifications can be visualized and multiple predictions can be realized at once.

Enter SMILES separated by newlines

```
OC2CCCc1ccccc12
C=C18CC(O)c2cscccc12
C1CC2CCC3CCCC4CCC(C1)C2C34
C#10CCC(C19CCCC8CCC6CC5CCCC4CC2CCCC1C2C(C3CCCCC3)
(C45)C6(C7CCCCC7)C89)CC#10
c1cc2CCc3ccccc4ccc(c1)c2c34
```

Select a workflow

Figure 3: Inserting structures in SMILES identification format. Each SMILE must be separated by newline.

3. The user can select and import a .sdf file with several structures, by clicking the "Browse" button found under "Import an SDF file" (Figure 1, see green arrow).



This type of files contains chemical structure records, used as a standard exchange format for chemicals information. The compounds' structure in .sdf format can be extracted from PubChem database or other repositories.

When structures are uploaded in either way, a prediction is generated (usually within seconds) by clicking the "Submit" button (Figure 1, see blue arrows) of the corresponding field.

Predictions - Output

As described above, when compounds are uploaded, a prediction is generated by submitting the input structures, the predictive workflow is then applied and the output is generated (Figure 4). The output is presented in a new .html page.

Your smiles are: c2ccc1CCCCC1c2and we have to run QNAR_PaCa2 my report is Executed successfully 812
The results are
[QNAR_PaCa2.html](#)

Figure 4: Generated output page. The user must click on the link in order to display the results in .html format.

The results include the predicted cellular uptake value in $\log_{10}[\text{NP}]$ (pM)/cell for each structure entered, and an indication of whether this prediction could be considered reliable based on the domain of applicability of the model (Figure 5). Two options are available: The "reliable" option which indicates a prediction within the domain of applicability limits of the model and the "unreliable" option which is a warning for a prediction out of the domain of applicability of the predictive model.

If more NPs need to be submitted, the user can return to the initial page and by clicking on the "Reset" button (next to "Submit" button of each field) the form is cleared and new input data can be submitted (Figure 1, see yellow arrows).

Prediction of MNPs Uptake in PaCa2 Cancer Cells

Knime report powered by Birt

"PaCa2 cellular uptake (log10 [nanoparticles]/cell pM)"	"Domain of Applicability Prediction"
3.009	reliable
3.009	reliable
3.857	reliable
3.752	reliable
3.737	reliable

Date: Jan 27, 2017 2:16 PM
www.knime.org

Author: NovaMechanics Ltd

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Figure 5: Results table. The first column contains the prediction for each input sample and the second column contains the reliability of each prediction according to the domain of applicability.

A demonstration video is available at:
<https://www.youtube.com/watch?v=SKenRzr1FbI>