Drug Design Teaching

Answers to questions of Session4 (Target Prediction)

- With that results let's try to answer the following questions about compound CHEMBL461792:

  - *How many protein targets are predicted in total (select* Show "**All**" entries *on the menu above the table). What is the proportion of kinases (click on "**All**" left to the pie-chart)?*
    100 protein targets were predicted for compound CHEMBL461792 ; 95 are kinases.

  - *What is the most probable protein target for this compound? Can we consider this result as an actual prediction? Why?*
    The epidermal growth factor receptor (EGFR, also called erbB1) is at rank #1; this the most probable target.
    The probability for this protein to be an actual target of CHEMBL461792 is 100%, because the compound itself is among the known actives on EGFR that were screened (you can visualized the "known actives in 2D" to see that indeed CHEMBL461792 is displayed with a similarity of 1.000). As seen at the beginning of this session, this compound is recorded in the ChEMBL database as experimentally active in vitro at 10.8 nM on EGFR. Therefore, this result cannot be considered as a prediction but as the retrieval of an experimental data (which is already useful as one cannot know all bioactivity data by heart).

  - *Looking at the ranking, what is the most probable non-kinase target?*
    Fructose-1,6-bisphosphatase, at rank #4

  - *How many known actives of this non-kinase protein are similar to molecule CHEMBL461792 based on 2D chemical structure similarity? Same question for 3D shape similarity?*
    16 compounds, experimentally active on FBP1 in vitro, are similar in 2D (chemically) to CHEMBL461792.
    44 compounds, experimentally active on FBP1 in vitro, are similar in 3D (in shape) to CHEMBL461792.

  - *Are the actives most similar in 2D and in 3D to CHEMBL461792 the same compound?*
    No, CHEMBL64950 is known active on FBP1 most similar in 2D to CHEMBL461792.
    CHEMBL63906 is known active on FBP1 most similar in 3D to CHEMBL461792.
    None are the input molecule itself. Fructose-1,6-bisphosphatase as a possible target of CHEMBL461792 is an actual prediction.
    This, together with the other actives, give a valuable diverse structural information for designing new molecules, potentially active on the protein target of interest.