

WHERE
insights LEAD TO
answers



Computational Chemistry and QSAR

Sherif Farag, PhD - Inotiv-RTP

Quantitative Structure Activity Relationship (QSAR)

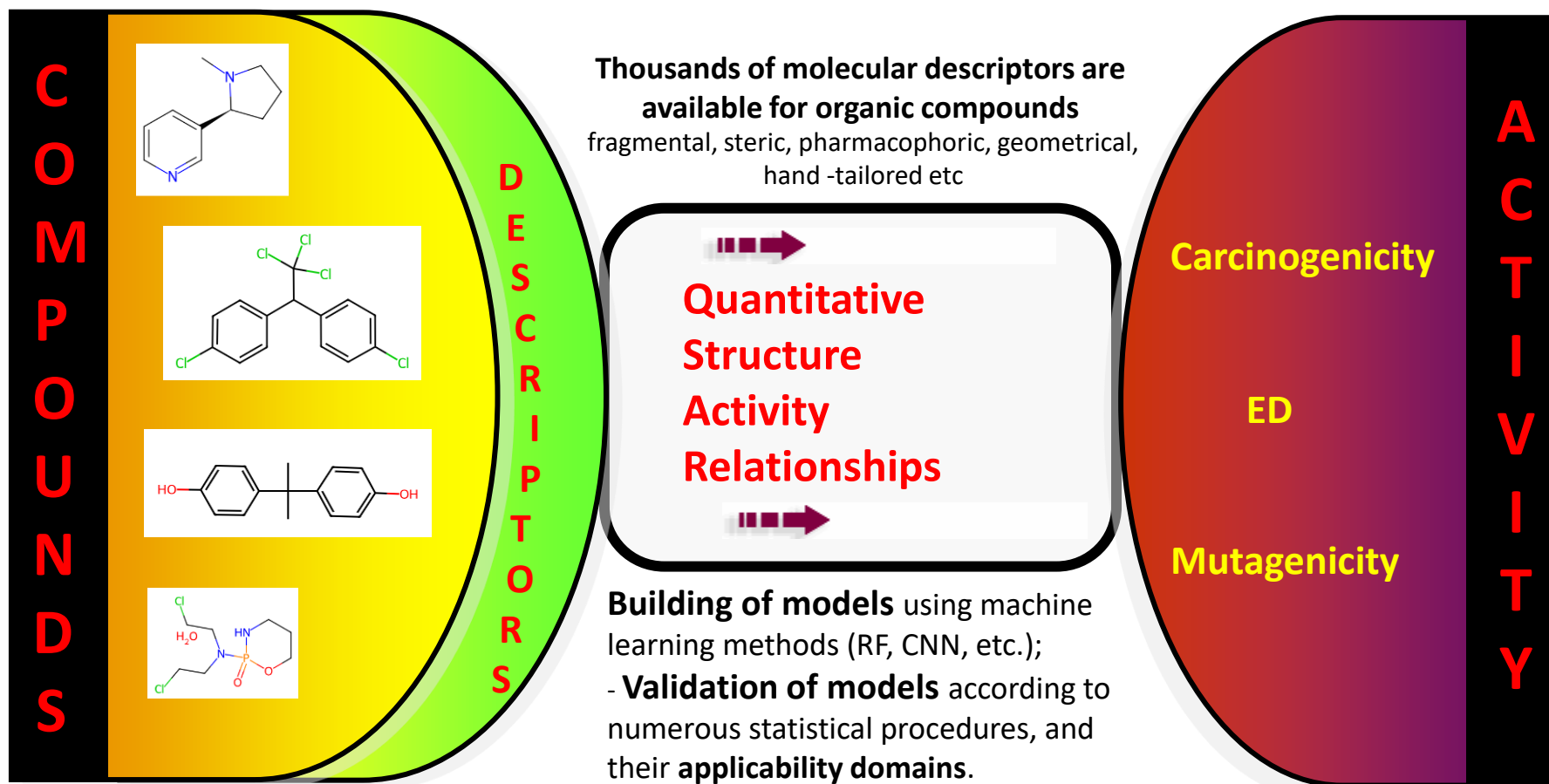
➤ Core Concept:

- Quantitative relationship between the chemical structure of a molecule and its biological activity.
- If two molecules have similar structural characteristics, then it's likely to have similar level of activity.

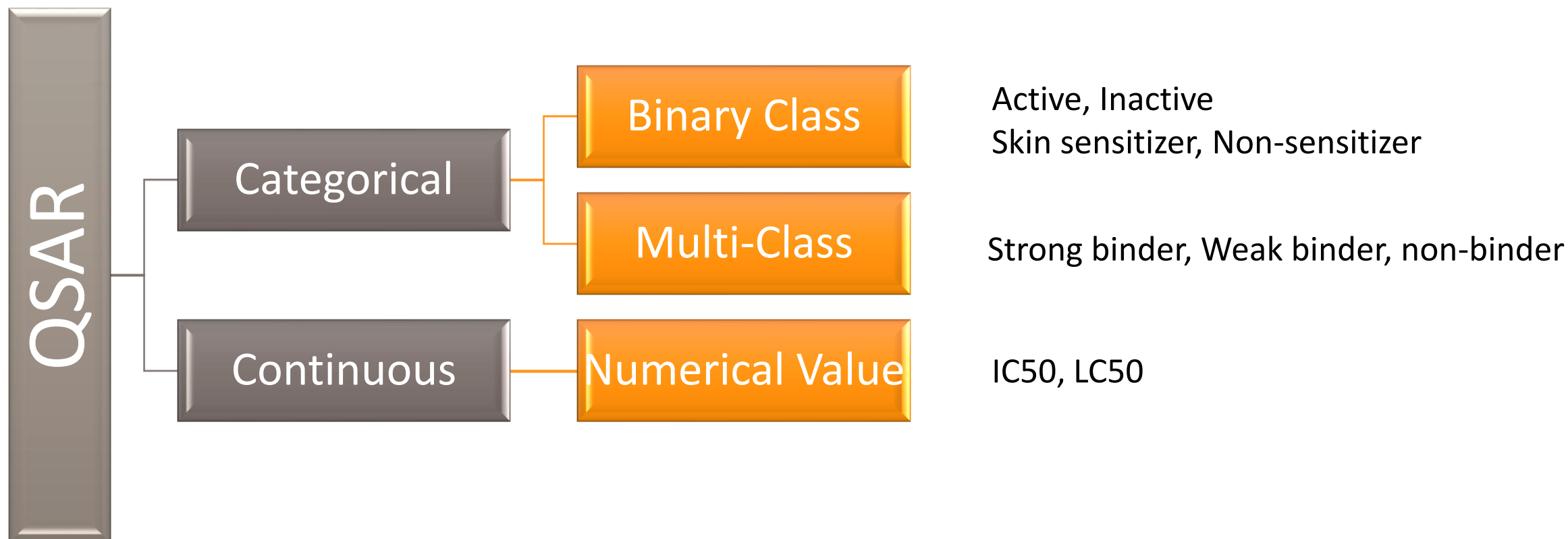
➤ Purpose:

- The goal of QSAR is to develop predictive models that can be used to estimate the activity or properties of new, untested compounds. This is valuable in various fields, particularly in drug discovery and chemical risk assessment.

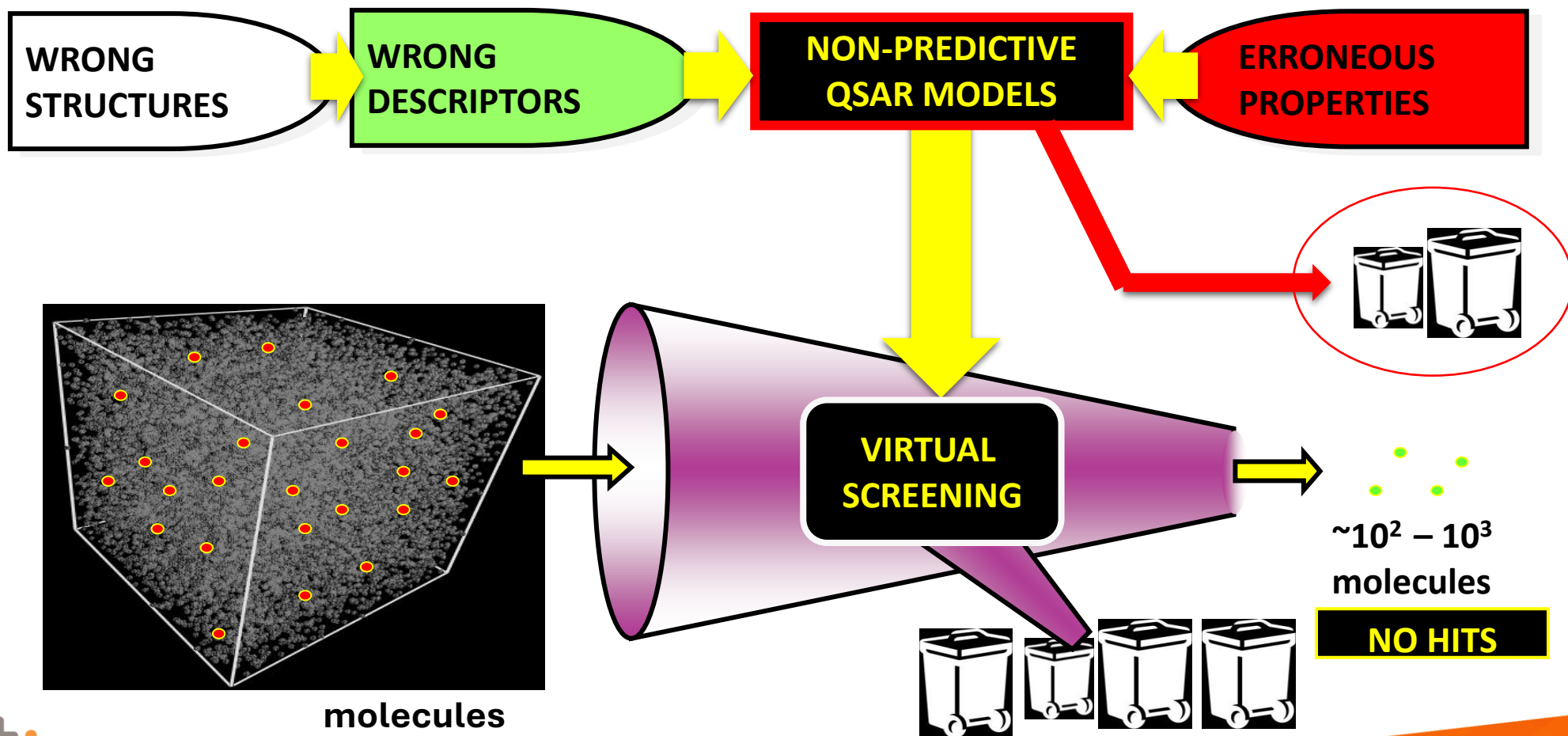
Quantitative Structure Activity Relationship (QSAR)



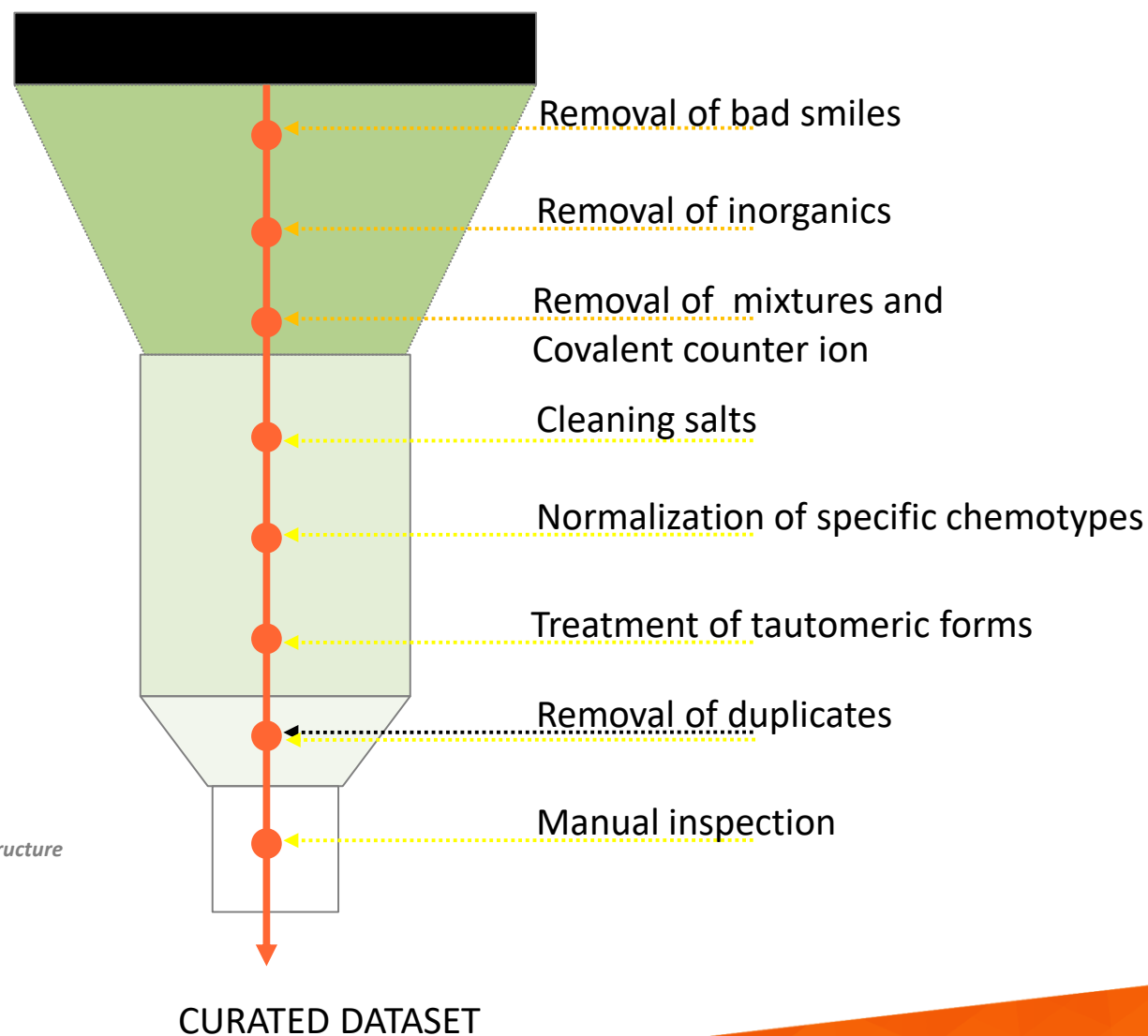
Quantitative Structure Activity Relationship (QSAR)



QSAR Modelling with non-curated datasets

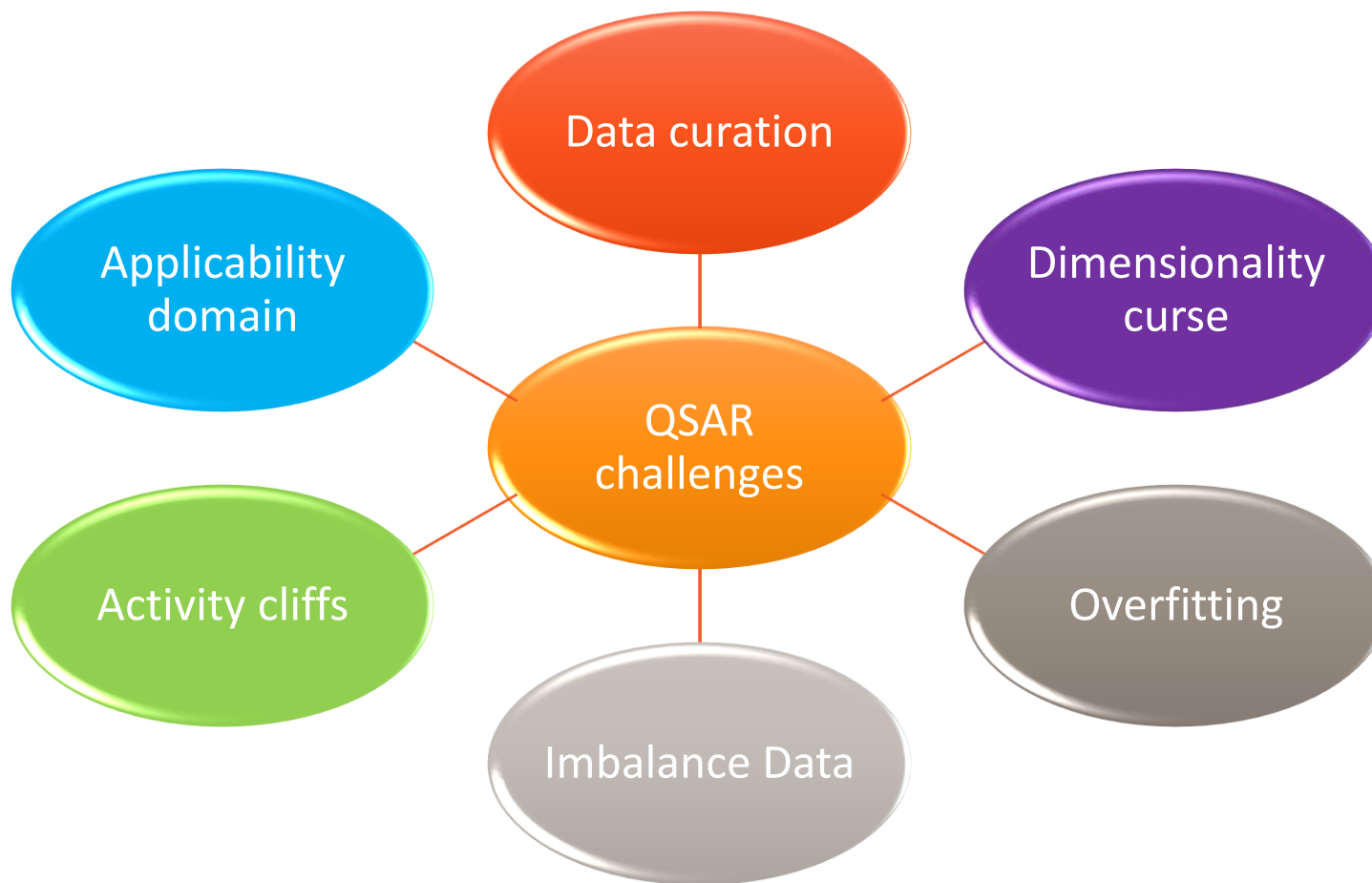


Data Curation



Denis Fourches, et al Trust, But Verify: On the Importance of Chemical Structure Curation in Cheminformatics and QSAR Modeling Research
J. Chem. Inf. Model. 2010, 50, 7, 1189–1204

QSAR Modelling Challenges



Key Advantages



COST-EFFECTIVENESS: QSAR IS SIGNIFICANTLY CHEAPER AND FASTER THAN TRADITIONAL EXPERIMENTAL TESTING.



ETHICAL CONSIDERATIONS: IT REDUCES THE USE OF ANIMALS IN TESTING.



EFFICIENCY: IT ALLOWS FOR THE RAPID SCREENING OF LARGE NUMBERS OF CHEMICALS.



VERSATILITY: MULTIPLE FUNCTIONALITIES AND APPLICATIONS

QSAR Applications

➤ **Drug Discovery and Design:**

- Identifying promising leads.
- Optimizing drug structures for improved efficacy and reduced side effects.
- Predicting ADME (absorption, distribution, metabolism, and excretion) properties.

➤ **Toxicity Prediction:**

- Evaluating the safety of new drugs.
- Assessing the environmental impact of chemicals.
- Regulatory risk assessment.

QSAR Application

➤ Chemical Property Prediction (QSPR):

- Boiling point.
- Solubility.
- Partition coefficient.

➤ Environmental Chemistry:

- Predicting the bioaccumulation of chemicals.
- Assessing the toxicity of pollutants to aquatic organisms.
- Evaluating the degradation of chemicals in the environment.

➤ Risk Assessment:

- QSAR models are used in regulatory contexts to assess the potential risks of chemicals to human health and the environment.

Cheminformatics Services

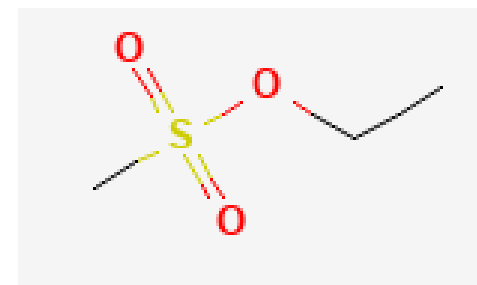
Inotiv-RTP site

Current Cheminformatics Tools and Services

- Developing and Applying Ligand and Structure Based Computational Approaches
 - QSAR Modeling
 - Virtual screening (LBVS)
 - SAR Analysis
 - Design Cheminformatics pipelines & workflows
 - Data mining, curation and visualization
- Support Prioritization of Chemical/Biological Testing and Regulatory Processes Through *In Silico* Modeling and Web Applications/Dashboard

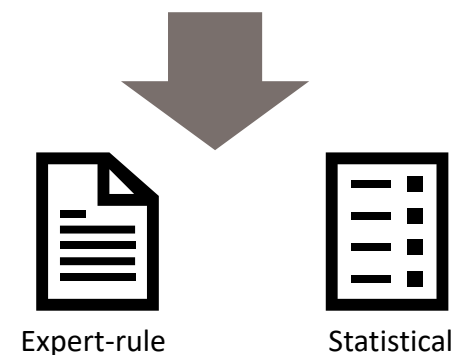
In Silico Testing for Bacterial Mutagenicity

- ICH M7 guideline
 - > Assessment and control of DNA reactive impurities in pharmaceuticals to limit potential carcinogenic risk
- CASE Ultra by MultiCASE: QSAR prediction methodologies that predict the outcome of a bacterial mutagenesis assay
 - > Expert-rule based model
 - > Statistical model



Test Compound

CCOS(=O)(=O)C



Other In silico Prediction Models that are available

- **Hepatotoxicity**

- > Models for DILI, liver function, bile duct disorders, cholestasis, gall bladder disorders

- **Cardiotoxicity**

- > Models for hERG K⁺ channel blockers and protectors

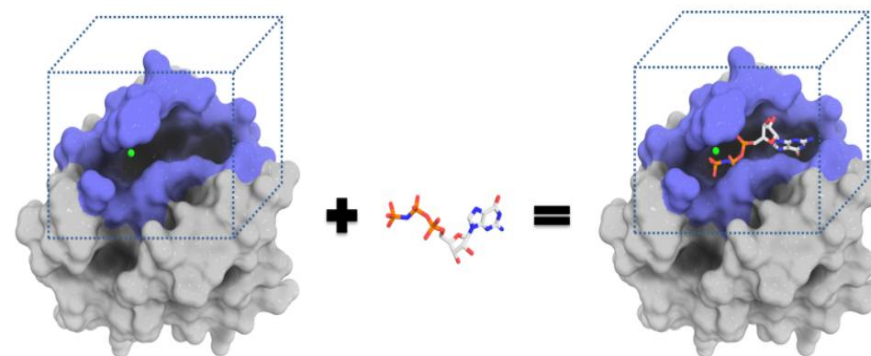
- **ADME**

- > Models for extent of metabolism, oral bioavailability, plasma protein binding, urinary excretion, volume of distribution (human)

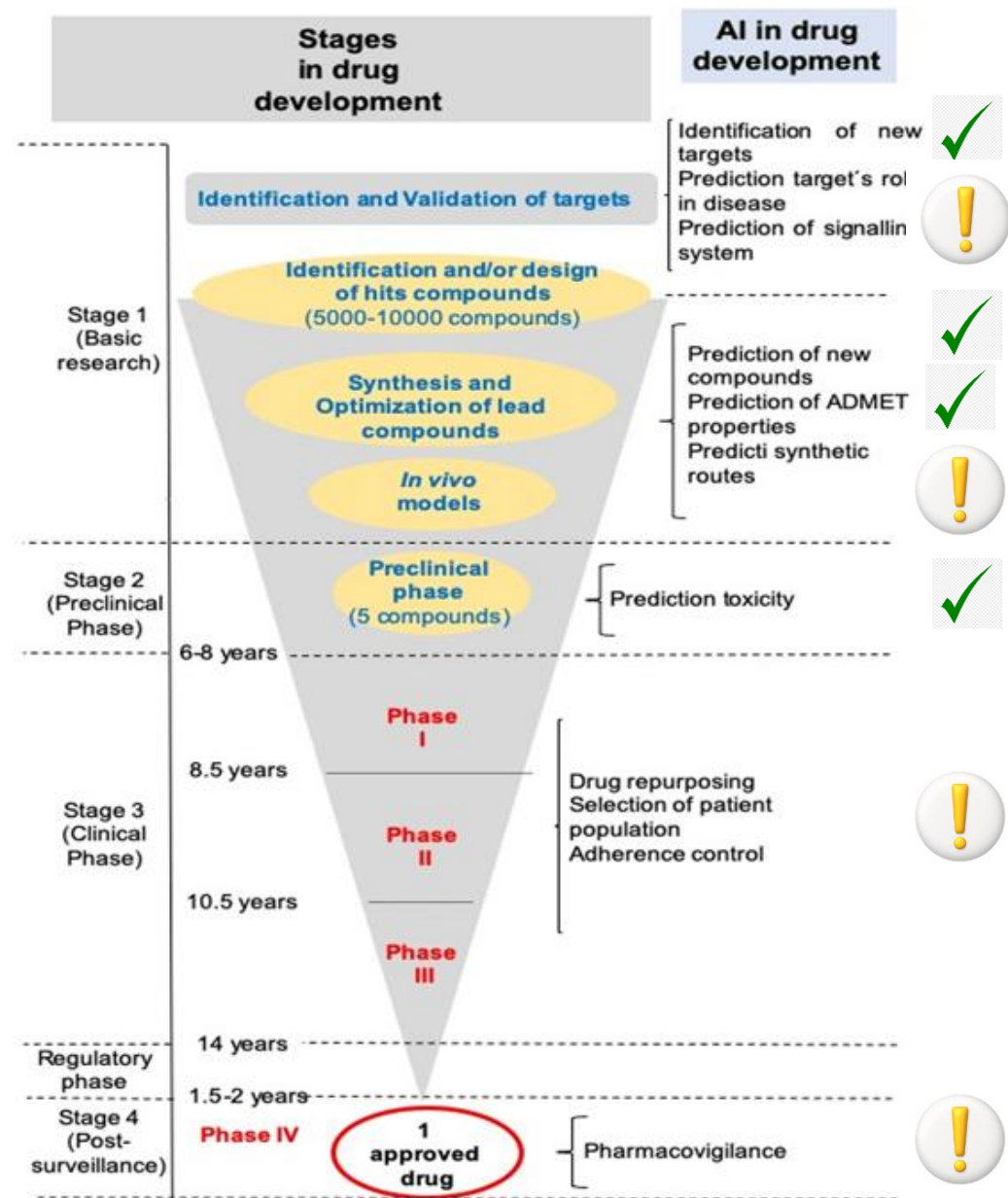
Future Cheminformatics Tools and Services

➤ Develop and Apply Ligand and Structure Based Computational Approaches

- QSAR Models
- Virtual screening (LBVS)
- SAR Analysis
- Design Cheminformatics pipelines & workflows
 - Data mining, curation and visualization
- **Docking**
- **Virtual screening (SBVS)**
- **Pharmacophore modelling**



AI in Drug Discovery



Gallego, Victor, et.al. (2021). AI in drug development: a multidisciplinary perspective. Molecular Diversity. 25. 10.1007/s11030-021-10266-8.

Explore our Genetic Toxicology Services

