# EuroHPC Summit Week 2022

## Using Supercomputers for Accelerating Drug Design

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From **22** to **24 March 2022** | **Paris**, France

#EHPCSW #PRACEdays

# The problem with drug design…

Billion dollar investment in bringing to market

Low success rate – typically only 12% that enter clinical development are approved *

Lead development time ~10 yrs

Uneven coverage – few new antivirals and antibiotics

* https://engitix.com/technology/

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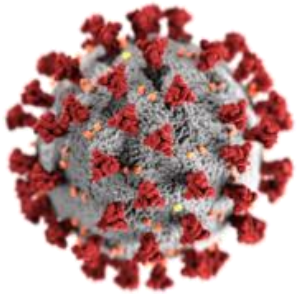
# COVID-19

- Rapid vaccine development for COVID-19 is a remarkable success story.
- Much harder to find successful drug therapies.
- Supercomputers around the world were asked to help with drug design



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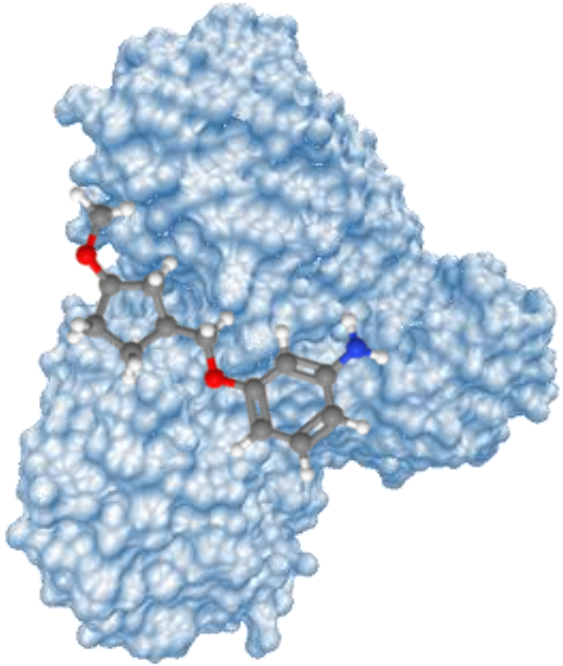
# Computational Drug design - background

- Drugs are often small molecules which bind to specific proteins.
- The effect of binding may inhibit the usual activity of the protein.
- For example, binding a molecule to a viral enzyme may stop viral infection



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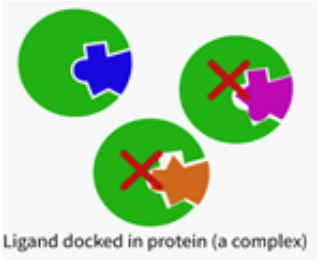
# Virtual Screening

- In virtual screening databases of *ligands* are screened against the target protein.
- At the simplest level, we just look for the right shape.
- Higher levels also consider specific interactions, protein flexibility, etc.
- The docked ligand is assigned a *score*. Highest scoring ligands are studied further.


⇩ *Docking*

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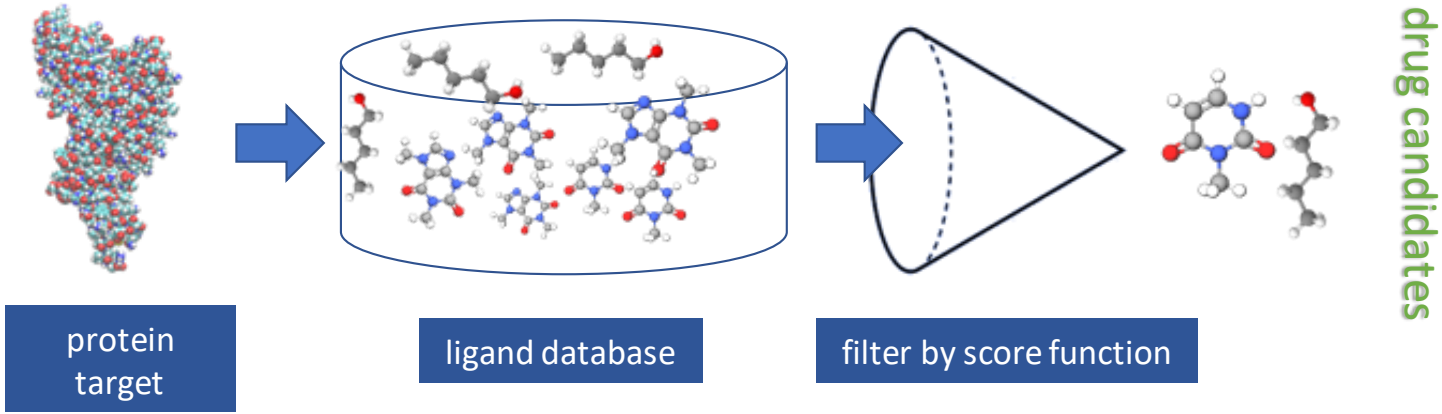
# High Throughput Virtual Screening




With massively parallel computers we can rapidly filter extremely large molecule databases (e.g. billions of molecules).

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EXSCALATE 4COV

LIGATE

| | |
|---|---|
| Urgent Computing H2020 to find anti-covid19 agents. | EuroHPC JU grant for integrated drug-design solution |
| Jan 2020-June 2021 | Jan 2021-Dec 2023 |
| Multi discpl. approach – bioinformatics, HPC, laboratory, clinical, big data. | Long term focus on integrated platform for drug design. |
| Coordinator: Dompé farmaceutici SpA | |

LIGEN High Throughput Docking system*

* Dompe' proprietary software, co-developed with Cineca and others.

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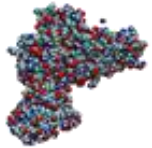
# Exscalate4Cov computational pipeline


= CINECA M100, ENI HPC5

*Molecule database*


3D protein structures


**LIGEN**
High-Throughput Virtual Screening

In-silico drug molecule candidates

Laboratory in-vitro tests, animal studies

Clinical trials

EXSCALATE 4COV

Raw 3D protein structures from experiments or models


**GROMACS**
10 µs molecular dynamics

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# Exscalate4Cov impact

- Initial strategy of *drug repurposing** to rapidly find new drugs.
- Key achievement: **identification of the osteoporosis drug Raloxifene as possibly active against COVID-19.**
- Registered and generic with known safety characteristics (e.g., dosage and side effects).
- In clinical trials (France and Italy), also for vaccinated people.

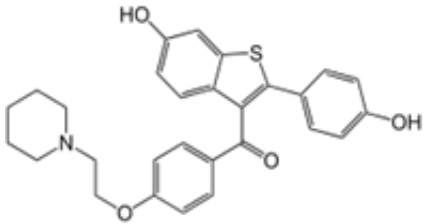
**400k** molecules tested in-silico

**7k** molecule candidates

**100** molecules deemed interesting from in-vitro tests

**40** molecules effective in limiting virus replication

approved drugs or safe in humans




raloxifene

* re-using existing drugs for different conditions.

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# The Big Run

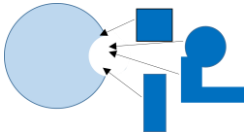
12 viral proteins

70+ billion ligands

60 hours run time
(~ 3M ligands /second per protein)

2 supercomputers (Cineca M100+ Eni HPC5)

15 binding sites for each protein



>1 trillion evaluations

81 Pflops total performance

7.3Tb archive data

http://arxiv.org/abs/2110.11644

Data still being analysed…

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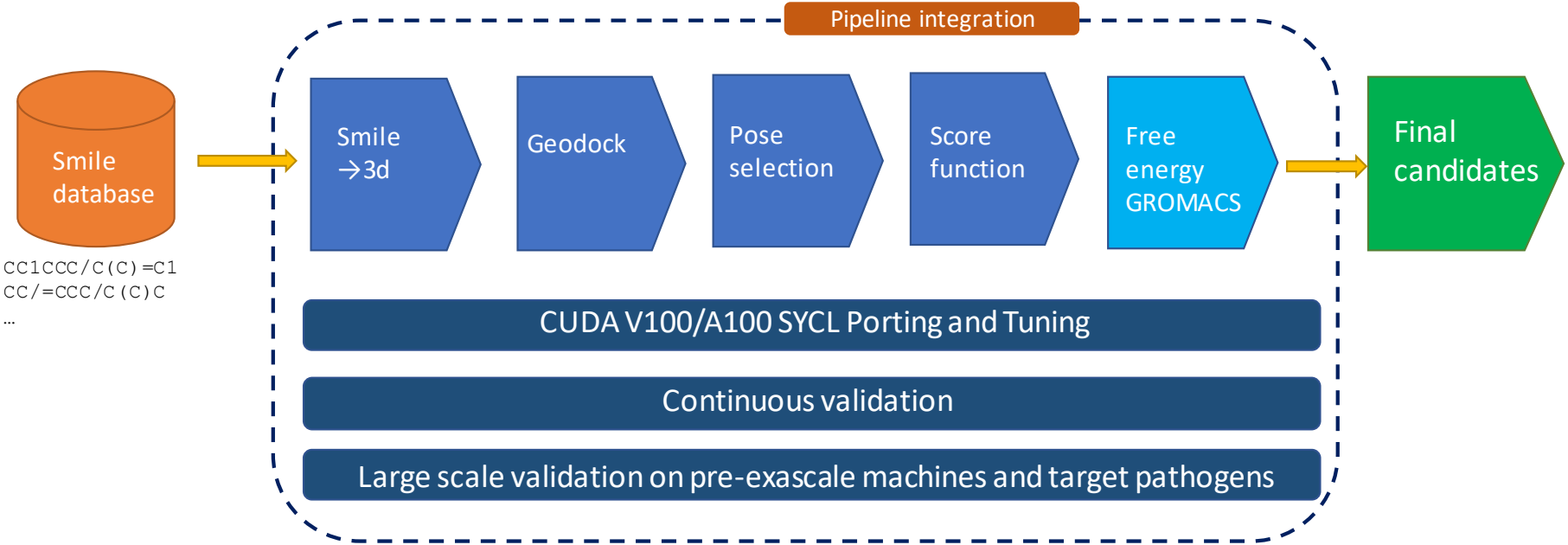
# Ligate Pipeline

LIGATE

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# Ligate Components

software

- LIGEN docking system
- GROMACS free energy estimation
- HyperQueue scheduling

libraries

- SYCL
- Celerity

cross validation

- Tof Computer Vision Simulation Use Case

Partners

- 11 partners across Europe

HPC resources

- -Two supercomputers
- -GPU servers

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# Acknowledgements

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**Ligate**

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# Thank you for your attention

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