SUCCESS STORY

From Data to Discovery: AI-Driven Drug Target Identification Through International Collaboration

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Title: Application of machine learning and virtual screening to the modelling and design of SIRT2/VEGFR2 dual inhibitors with in vitro experimental validation on cancer cell lines

A Short-Term Scientific Mission (STSM) funded under the COST Action programme PRECISION MEDICINE IN BILIARY TRACT CANCER [CA22125] has yielded promising advances in computational drug discovery. By harnessing the power of machine learning and virtual screening, the collaborative research team has successfully identified a shortlist of novel inhibitor candidates now ready for experimental validation — a critical step toward developing new therapeutic agents.

The Challenge

Identifying effective drug candidates is one of the most resource-intensive challenges in modern biomedical research. Traditional experimental screening of large compound libraries is costly and time-consuming. To address this bottleneck, researchers are increasingly turning to computational approaches — but integrating multiple in silico methodologies into a coherent, reliable pipeline requires both specialized expertise and strong cross-disciplinary collaboration.

The Collaborative STSM Activities

This STSM brought together researchers from complementary backgrounds to build an integrated computational pipeline targeting a key biological pathway. The collaborative activities spanned four interconnected areas:

- Analysis of ML-QSAR Models — Machine learning-based Quantitative Structure-Activity Relationship (ML-QSAR) models were rigorously analysed to understand and predict the biological activity of candidate compounds, enabling data-driven prioritisation of the chemical space.
- Integration of Virtual Screening and Molecular Docking — State-of-the-art virtual screening methods were combined with molecular docking simulations to evaluate how candidate molecules interact with the target protein at the atomic level. This dual approach significantly improved the reliability of hit identification.

- Shortlisting of Promising Inhibitors for Experimental Validation — From an initial pool of thousands of compounds, the team applied a multi-criteria filtering process to produce a focused shortlist of the most promising inhibitor candidates. These compounds exhibit favourable predicted binding affinity, drug-like properties, and selectivity profiles.
- Initiation of Cell-Based Assays to Evaluate Biological Activity — Bridging the gap between computation and experiment, the team-initiated cell-based assays to begin evaluating the shortlisted compounds under biologically relevant conditions, translating computational predictions into measurable experimental outcomes.

Key Outcomes and Impact

The STSM has delivered significant and tangible results that advance both the research coordination and capacity-building objectives of the COST Action:

- A validated computational pipeline integrating ML-QSAR modelling, virtual screening, and molecular docking that can serve as a replicable framework for future drug discovery campaigns within the network.
- A curated shortlist of novel inhibitor candidates with strong in silico evidence of biological activity, now proceeding to experimental testing.
- The initiation of cell-based assays, marking the transition from purely computational research to experimental science — a milestone that significantly strengthens the translational potential of the findings.
- Enhanced cross-institutional knowledge transfer and skills development, supporting the next generation of researchers in computational and experimental drug discovery.
