PLEXUS DESIGN TO FACILITATE STRUCTURE-BASED DRUG DESIGN

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BETTER MOLECULES – FASTER

A key challenge in preclinical drug discovery
SPRINT BIOSCIENCE

Treat cancer

Select target

Find hits

Medicinal chemistry

Reduce tumor growth
DRIVING MEDICINAL CHEMISTRY PLANS

Make

Better molecules faster

Test

Design

Analyze
IDEA TO DESIGN TO TARGET MOLECULE

Hypothesis

What question to be answered?
What properties to improve?

Populate

What structures to look at?
How many structures to assess?

Evaluate

What models to use?
What molecules to actually make?
HOW TO MAKE BETTER IDEAS – FASTER?

Access to Chemical Space for everyone

Ease of use and increase diversity

Improve workflow when sharing, documenting and evaluating ideas
Virtual Chemical Space

Design

- Filter
- Search
- Similarity search
- Register
- Brainstorm
Scaffold enumeration

R1: 
R2: 

Annual Meeting 2016
Reaction enumeration
MISSION: LEAD FROM FRAGMENT

Fragment → Lead Compound

How?
SOLUTION: LEAD FROM FRAGMENT

PDB: 3LS8 Crystal structure of human PIK3C3 in complex with 3-{4-(4-Morpholinyl)thieno[3,2-d]pyrimidin-2-yl}-phenol

4 x ~100,000 Virtual cmpds:
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MISSION: LEAD FROM FRAGMENT

Fragment

How?

Expand!

PDB: 3LS8 Crystal structure of human PIK3C3 in complex with 3-[4-(4-Morpholinyl)thieno[3,2-d]pyrimidin-2-yl]-phenol
PLEXUS DESIGN CASE 1

“I have an idea. Let’s do something like this.”

Synthetic route? No idea!

Reagents? No idea!

Create diverse structures!

- Few – draw R-sets
- Many – R-sets as files

Scaffold-based enumeration:

✅ Very easy to use
✅ Increased diversity
✅ Results in sd-format
PLEXUS DESIGN CASE 2

“Let’s expand in selectivity pocket!”

Synthetic route?
Suzuki

Reagents?
Boronic acids/esters

• Large set
  • Commercial
  • Virtual

• Focused
  • Commercial
  • Available

Reaction-based enumeration:

- Easy to use large R-sets from databases
- Pre-defined reactions available
- Results in sd-format
GOOD & ENHANCEMENTS

• Easy to use for all
  • Increase number & diversity of structures being evaluated
  • Better workflows
    • Myself
    • Communicate with colleagues

• Filter on the fly
  • Improve spreadsheet functions
  • Strip salts from reagents
  • Naming of products
ML + PD: COMBINE BRAIN AND COMPUTER POWER

Brain Power + Computer Power = Better & Faster

Only bad ideas? I can't help you!

Treat cancer
Plexus Design

- Large virtual libraries
  - Multiparameter Optimization
  - Virtual Screening
  - Registration to Virtual Database
  - And many more ...
THANK YOU!

QUESTIONS?

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