ChemPass

Your Pass to Chemistry

digital drug discovery

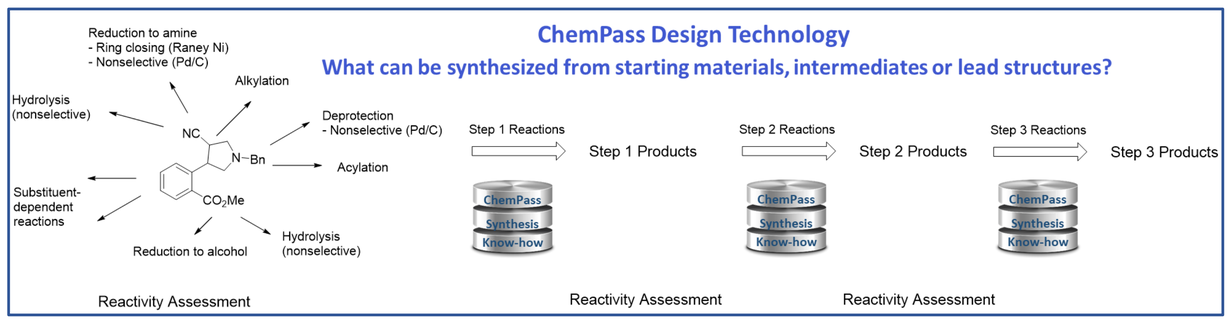
An Artificial Intelligence Technology for the Generation of Synthetically-enabled Scaffold and Lead Analog Space for Medicinal Chemistry and AI-driven Drug Discovery

Gergely M Makara, Gabor Pocze, Laszlo Kovacs & Orsolya Demeter, ChemPass Ltd., Budapest, Hungary

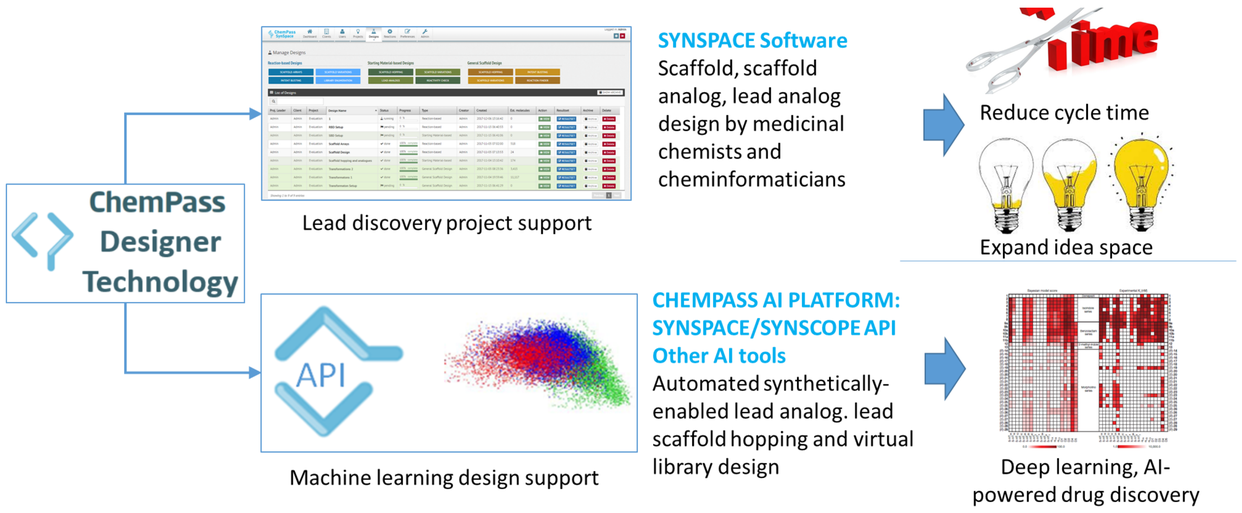
CHEMPASS' ARTIFICIAL INTELLIGENCE DESIGN TECHNOLOGY BACKGROUND

High failure rates and the increasing cost of drug discovery as well as extended research and development timelines hinder the development of medicines. Due to these challenges there has been an increasing need for substantial innovations in the pharmaceutical industry.
ChemPass has developed a rule-based artificial intelligence technology that can produce a large number of novel synthetically-enabled lead analogs and scaffold hopping designs around lead structures. Since its introduction, the cloud-based SynSpace software has been found by multiple organizations to generate more novel ideas around leads than medicinal chemist teams do to advance lead development projects.
We have also been developing an automated lead analysis toolbox and a synthesis-based library enumerator that in conjunction with SynSpace (API) can automatically carry out scaffold hopping and lead analog idea generation and thereby offer large sets of novel and project specific lead-like structures to advanced AI platforms for selection. The built-in synthetic feasibility in our methodology ensures that laboratory synthesis does not become a critical bottleneck in AI-supported drug discovery, a potentially emerging issue with computer-generated structures without thorough organic synthesis knowledge. The ChemPass platforms have the biggest impact on cycle time, number of discovery cycles, the number of compounds to be synthesized and coverage of IP space. Improvements in these factors can be converted into higher success rates and major resource savings.

CHEMPASS TECHNOLOGY: FORWARD REACTION-BASED DESIGN



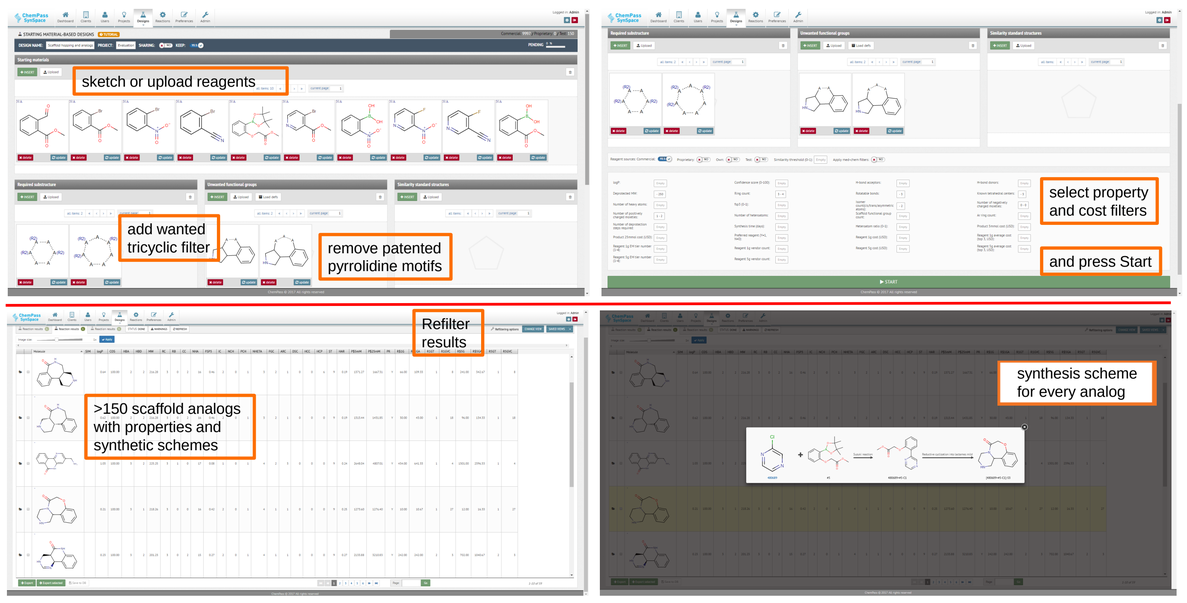
CHEMPASS DESIGN PLATFORM: SYNSPACE SOFTWARE AND ASSOCIATED TOOLS



USE CASE 1: SYNSPACE SCAFFOLD HOPPING / PATENT BUSTING

With SynSpace there is no need for any cheminformatics or computer skills for chemists to start designing!

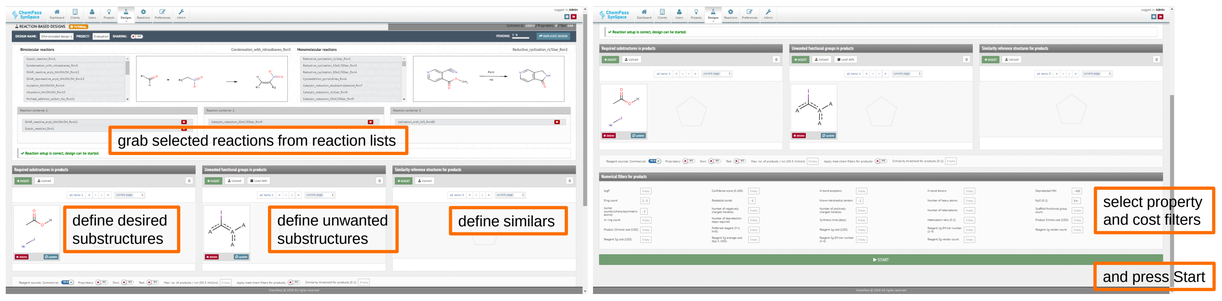
Objective: 5-HT modulator tricyclic pyrrolidine scaffold analog design using reagents that would be on the shelf in the research group working on the patented project (US 2016/0096851 A1).



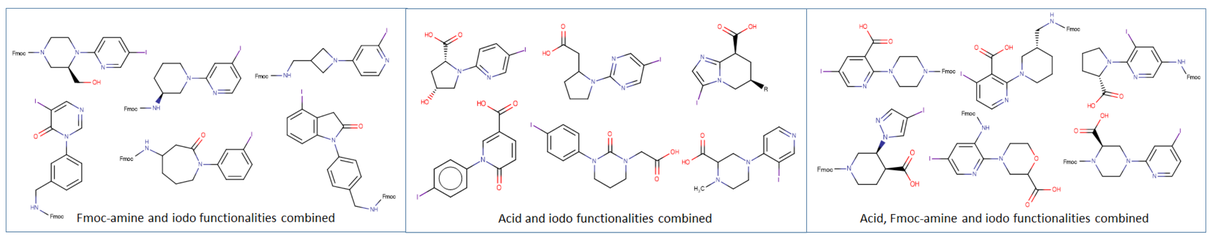
2-step and 3-step sequences provide a few hundred synthetically enabled novel scaffold ideas for evaluation by medicinal chemists to initiate scaffold hopping or to get around the patented scaffold.

USE CASE 2: SYNSPACE SCAFFOLD DESIGN FOR DEL SYNTHESIS

DNA-encoded synthesis campaigns often require diverse scaffolds with preferred protection schemes and a set of specific functional groups. SynSpace tracks functional groups and protecting groups making scaffold design easy.



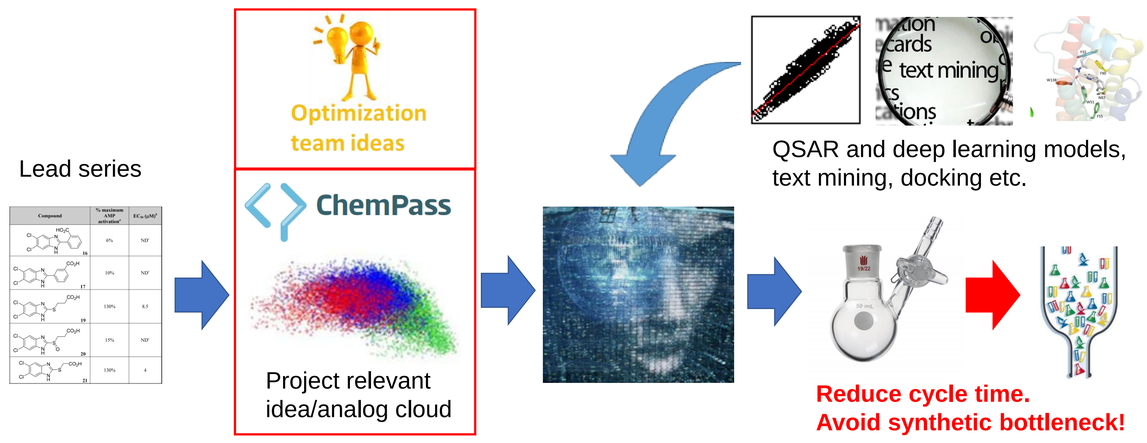
DESIGN EXAMPLES FOR COMBINATIONS OF ACIDIC, FMOC-AMINE AND IODO FUNCTIONAL GROUPS



The designed scaffolds can easily be filtered to Fmoc-protected amines by setting: Fmoc-primary-amine + Fmoc-secondary-amine fields to = 1. Other combinations are just as simple. Property and substructure filters can also be applied per user's preference. ChemPass has designed thousands of scaffolds for DEL campaigns.

AI-SUPPORTED LEAD DISCOVERY

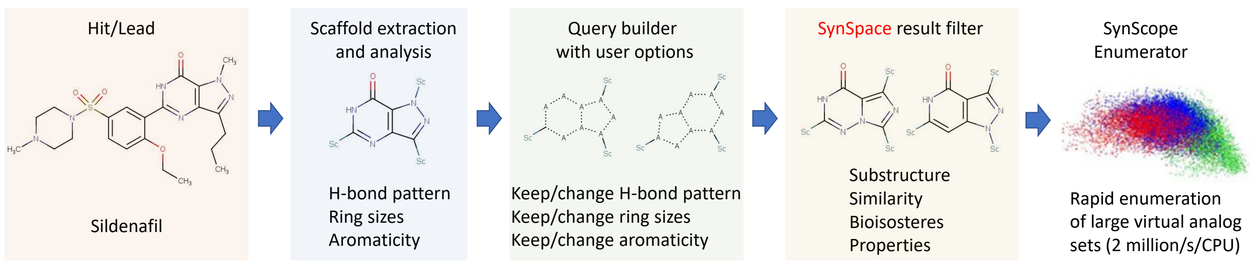
It has been shown that if the selection of the synthetic targets in lead optimization cycles is supported by QSAR or deep learning methods, the number of compounds synthesized as well as the cycle time for each iteration can be significantly reduced. However, current AI-driven drug discovery techniques mostly select from human designed molecule subsets, existing compound databases, or computer-generated structure analogues that are synthetically not vetted. In case of the latter, if synthesis is not incorporated into the design, it can be reasonably feared that laboratory synthesis time will grow and become a critical bottleneck.



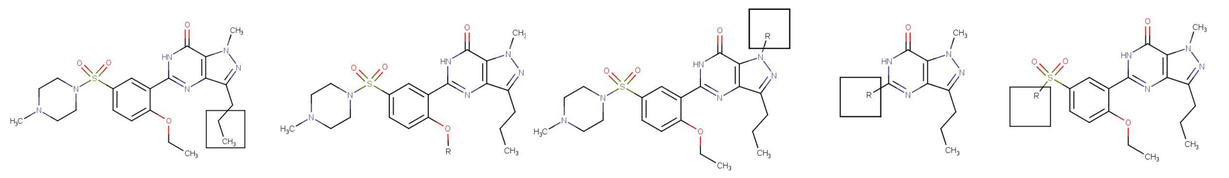
ChemPass has been developing an automated lead analysis toolbox that can *automatically* carry out lead analysis, lead analogue design and scaffold hopping thereby offering small or large sets of novel and project specific lead-like structures to advanced AI platforms for selection (to complement ideas coming from the med-chem team). Our tools eliminate synthesis concerns with computer-generated ideas because all designs are overseen by ChemPass' synthesis know-how database.

CHEMPASS' AI TOOLBOX: Two approaches in combination offer a complete solution

1. Scaffold analoging and scaffold hopping tools are composed of 5 elements built into a unified workflow: Scaffold extraction and analysis, variable query builder, design engine (SynSpace), result filter, and a library enumerator

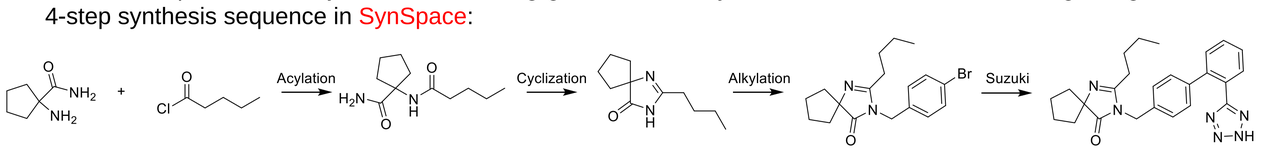


2. Lead decomposition and synthesizable analog generation via synthetic routes

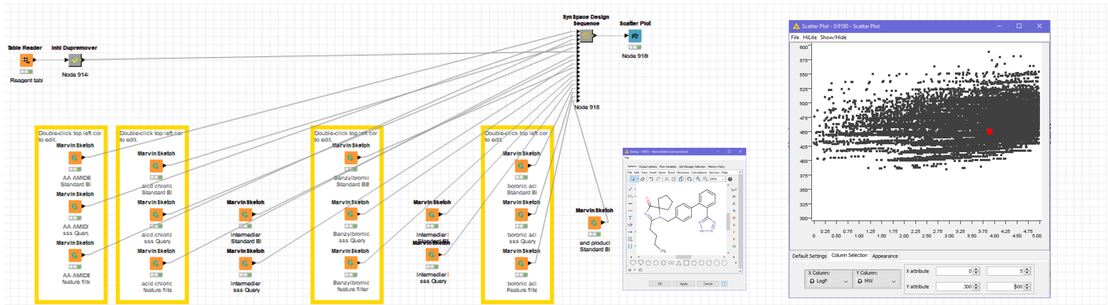


CHEMPASS' AI TOOLBOX EXAMPLES

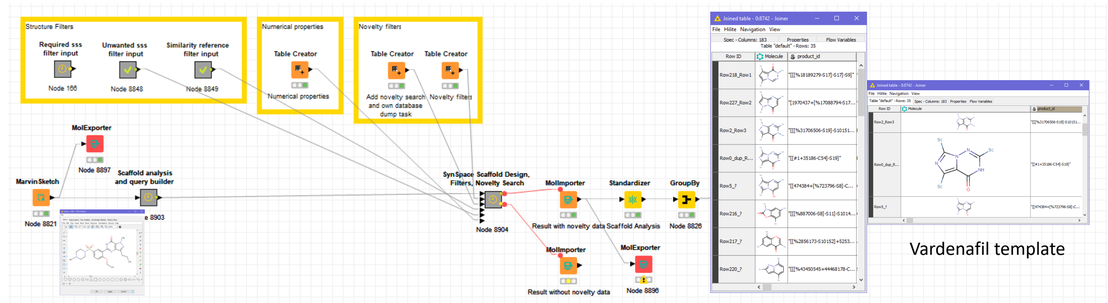
1. Lead decomposition and synthesizable analog generation via synthetic routes: Ibersartan analog design via a 4-step synthesis sequence in SynSpace:



Analog selection by multiple similarity methods, bioisosteres and substructures: >90K analogs generated before property filtration



2. Scaffold analoging and scaffold hopping design using Sildenafil: >10 reasonable scaffold analogs design including the framework of Vardenafil and a few scaffolds with IP freedom (not shown).



SUMMARY

SynSpace: ChemPass has developed a revolutionary new cloud-based software, SynSpace to assist in idea generation for organic and medicinal chemists in scaffold design, scaffold variation design, patent busting, hit or lead analog design and any other design tasks. All designs are generated based on organic synthesis know-how and thus all suggestions come with proposed synthetic routes.

AI-supported lead discovery: ChemPass' emerging toolkit along with SynSpace provides automatic idea generation for lead series inclusive of synthetically-enabled lead analog libraries and scaffold analog libraries that feed advanced AI selection algorithms that are based on QSAR, deep learning models and other modelling results. Along with our AI Partner, we are currently seeking collaborators for validation projects and datasets.

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Contact: gergely.makara@chempassltd.com

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