Detecting pharmaceuticals and their transformation products with SIRIUS

Pharmaceutical contamination can disrupt ecosystems, harm aquatic life, and affect biodiversity. Yet traditional annotation methods often miss transformation products—drug breakdown compounds that may be even more persistent, bioaccumulative, and even more harmful than the original drug. We need to expand analytical strategies to include transformation products.

From **precursor drug screening** in structure databases and spectral libraries to **transformation product screening** using a custom-generated database

Pharmaceuticals in Luxembourgish Rivers

- 92 surface water samples from 13 different locations (routine monitoring 2019-2020)
- solid-phase extraction and liquid chromatography coupled to high-resolution mass spectrometer
  https://doi.org/10.1021/acsenvironau.1c00008
- 15,819 valid features after preprocessing

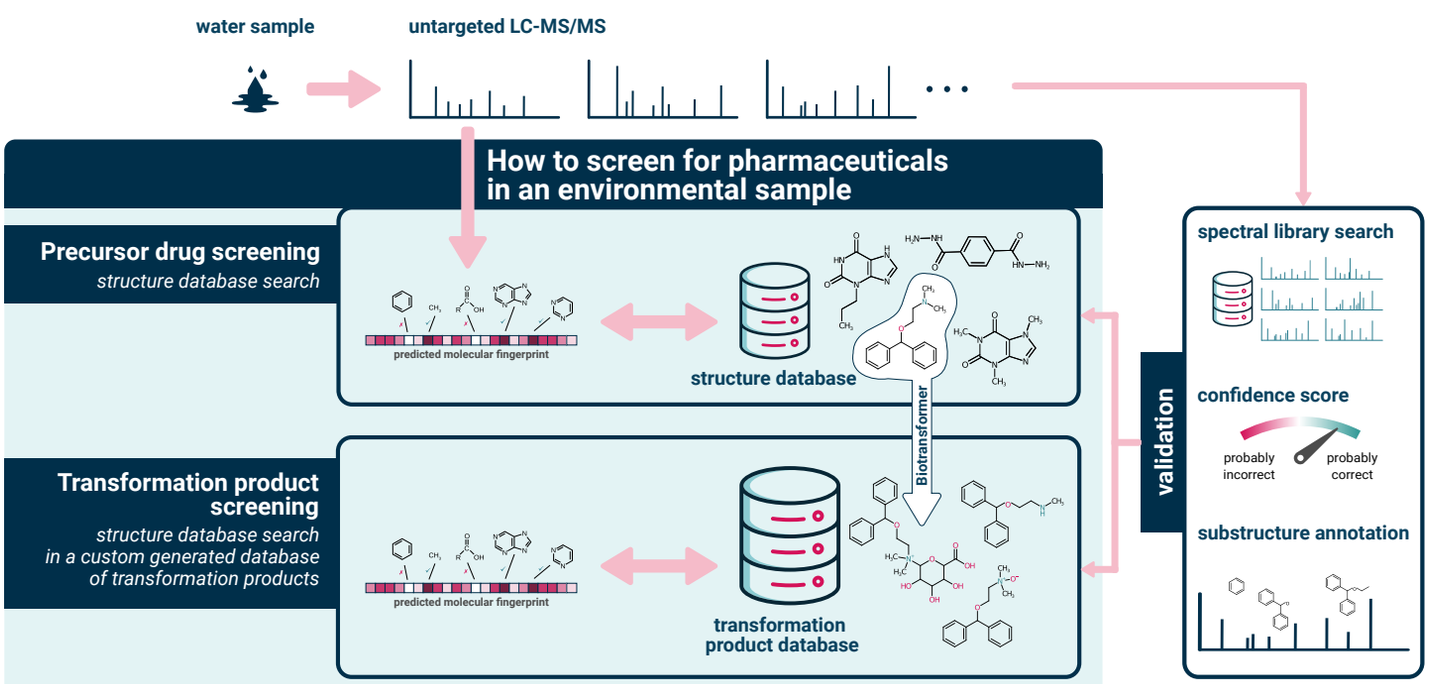
Data Resources

Drug list
816 approved pharmaceuticals

Spectral libraries
MassBank & MoNA (400 drug spectra)

Precursor drug structure database
772 structures of the pharmaceuticals from the drug list

Transformation product structure database
483 203 unique transformation product structures generated with **BioTransformer**
https://doi.org/10.1093/nar/gkac313

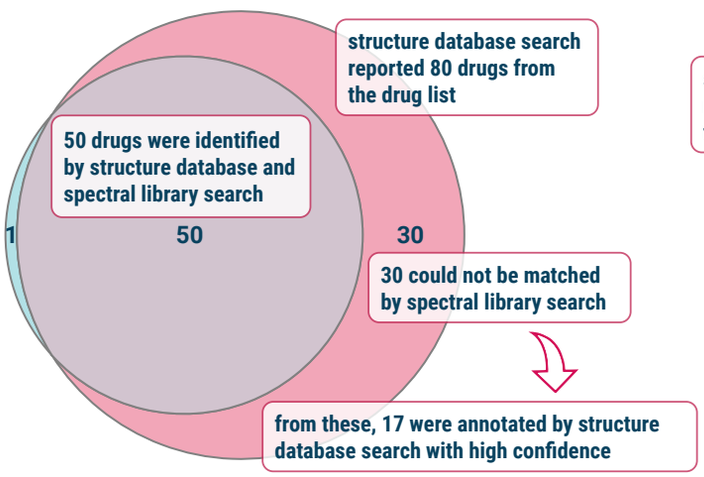


BRIGHT GIANT

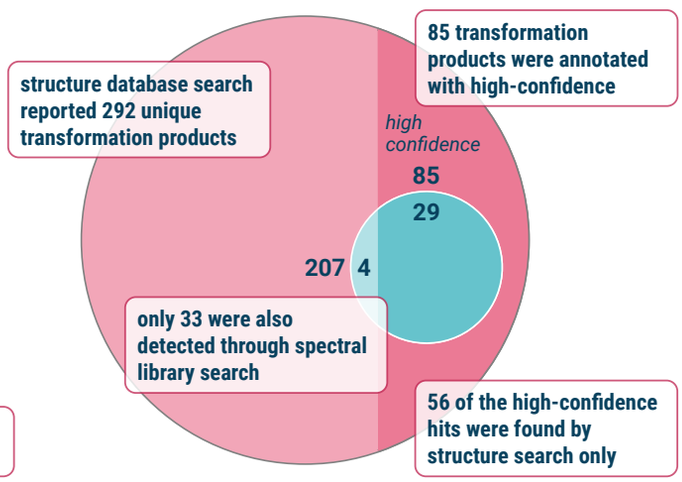
bright-giant.com
bright-giant.com/request-demo/
bright-giant.com/sirius-release-latest

SIRIUS

precursor drug screening



transformation product screening



With SIRIUS you can identify both, precursor drugs and transformation products, simultaneously.

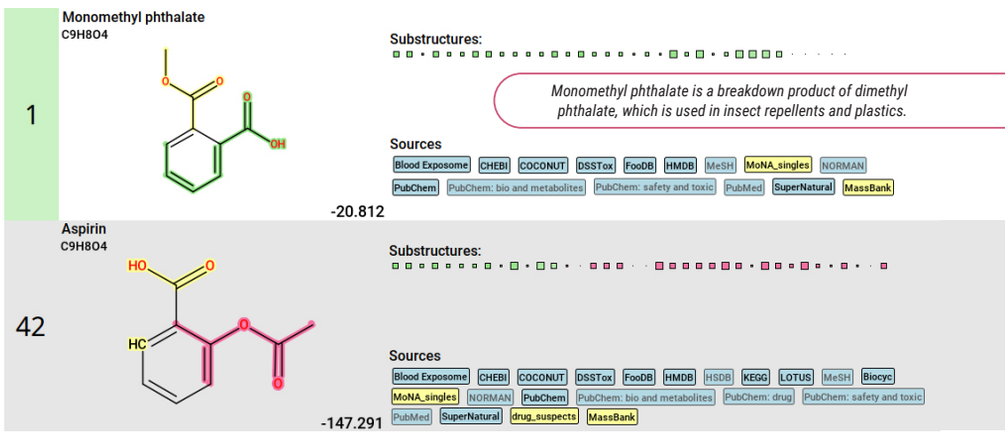
SIRIUS detects compounds that would have been missed by spectral library search while still integrating the power of (analog) spectral library hits for validation.

Preventing Suspect Blindness

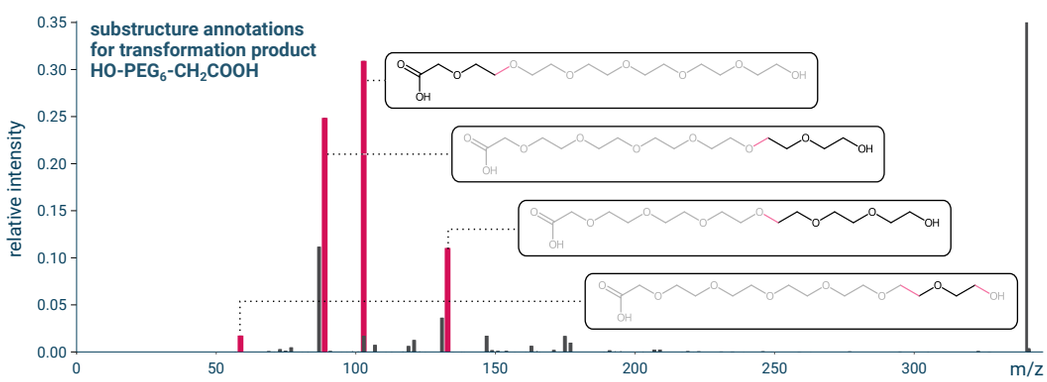
One drug was putatively identified as Aspirin through spectral library search and as monomethyl phthalate by structure database search. Both candidates had an equally high spectral library search score.

As molecular structure annotation in SIRIUS is based on molecular fingerprinting, structural explanations can be explored within SIRIUS.

The advantage of using SIRIUS lies in its ability to present both possibilities preventing "suspect-blindness" and showing that the annotation of Aspirin is not unambiguous.



Validating Results



SIRIUS provides different levels of validation to investigate results: confidence scoring, fingerprint-based substructure highlighting, spectral library matching, and substructure annotations. Substructure annotations visualize the direct connection between the input MS/MS spectrum and structure candidates. Providing substructure annotations also for analog spectral library matches offers a powerful method for validation.

As no experimental validation was performed, all identifications should be considered putative.

BRIGHT GIANT

bright-giant.com

bright-giant.com/request-demo/

bright-giant.com/sirius-release-latest