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Introduction

Commercial libraries, with mostly synthetic compounds, access only a small fraction of the possible chemical diversity¹

This could potentially undermine screening productivity and therefore drug discovery

Natural products, in contrast, possess a vast structural diversity and have been proven to be an outstanding source of new drugs

Methodology

A collaborative effort between research groups

Unique set of 223 natural products derived from fungi

CCF and Fsp³: Mean complexity

Properties: HBD, HBA, LogP, TPSA, MW and RB

Drug-like chemical space

Scaffold diversity

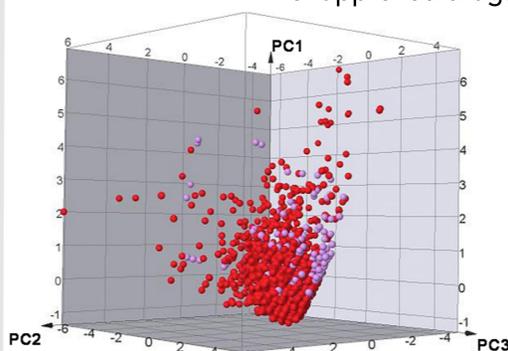
Properties diversity

MACCS keys fingerprint diversity

Consensus Diversity Plot

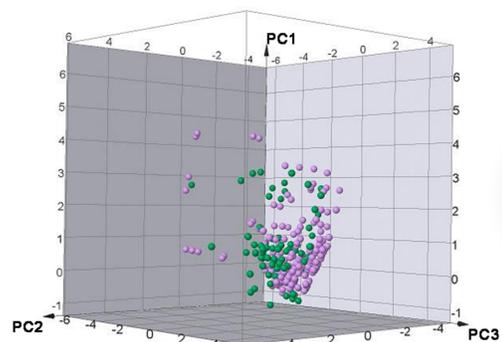
Results

Occupy similar and different areas of the chemical space of approved drugs



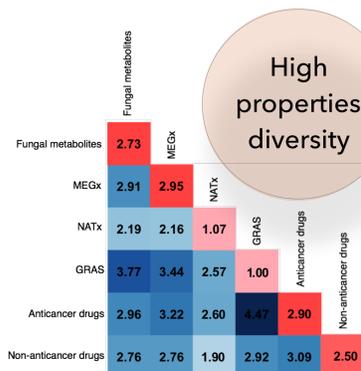
● Approved drugs
 ● Approved anticancer drugs
 ● Fungal metabolites

1st PC = HBA and HBD
 2nd PC = LogP
 3rd PC = RB



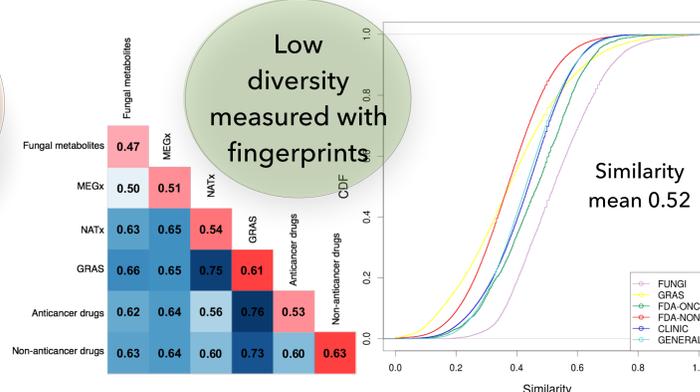
Are drug-like and fulfill Lipinski's and Veber's rules

6 properties. Euclidean intra-library distance



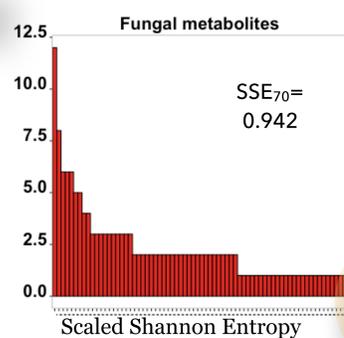
High properties diversity

Finger prints. Soergel intra-library distance and CDF

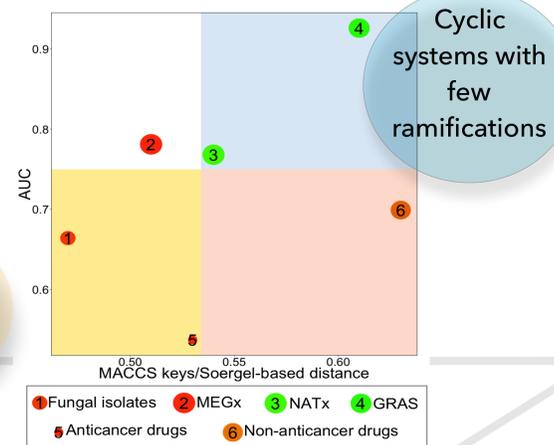


Low diversity measured with fingerprints

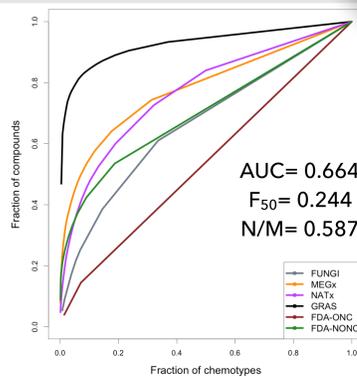
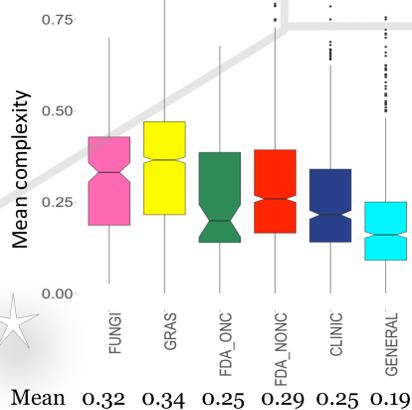
Similarity mean 0.52



High scaffold diversity³



Greater mean complexity than approved drugs and commercial libraries²



Conclusions

Fungal metabolites:

- Higher molecular complexity and possibly increased selectivity.
- High content of unique scaffolds.
- More diverse than commercial libraries with more compounds.
- Are drug-like and fulfill Lipinski and Veber's rules.
- Share areas of the chemical space of approved drugs.
- Occupy different areas of the chemical space of approved drugs.
- Can improve commercial libraries for High Throughput Screening and a good source of novel leads.

Perspectives

- ADME/Tox predictions
- Chemical space with fingerprints
- Target fishing with epigenetic and other oncology-related targets
- Similarity searching

Acknowledgments

UNAM: PAPIPE PE200116; PAIP 5000-9163

References

- [1] Cragg GM. et al. *Biochim Biophys Acta*. 2013, 1830, 3670-3695. [2] González-Medina M. et al. *Future Med Chem*. 2016, 8, 1399-1412. [3] González-Medina M. et al. *Molec Divers*. 2017, submitted.