A NEW LANDSCAPE FOR DRUG REPUROSING

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ABSTRACT

Drug repurposing (DRP) aims to find new indications for old drugs. To facilitate this process, we have developed a classification scheme to catalogue chemical structures according to market-availability and protection rights: off-patent (OFP; on-market drugs with expired patent and/or exclusivity), on-patent (ONP; on-market drugs with ongoing patent and/or exclusivity) and off-market (OFM; discontinued drugs). Further, we mapped these groups into a self-organizing map (SOM) model generated based on chemical properties, bioactivity, and clinical profiles of 959 drugs. The resulted map validates known drug classes and offers unexpected drug groups with potentially new indications.

MOTIVATION

Currently, pharmaceutical research and development (PR&D) efforts to bring a new drug to market take, on average, at least a decade, and cost, on average, 985.3 million USD, although the cost can reach more than 2.77 billion USD (on average) for antineoplastic and immunomodulating agents. Pharmaceutical patents play an essential role in motivating investment in PR&D, and those investments yield tremendous social gains through the resulting introduction of new drugs. PR&D investments are compensated by property rights (patents) granted to the applicants by the government of the country in which the patent is issued; and by exclusivity rights (statutorily provided periods of protection from competition), granted by regulatory agencies such as the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA), in the countries where the drugs have received marketing authorization.

Understanding the fundamentals of patents and exclusivity are key to the scientific and project decision making components of all drug repositioning studies, which is a frequently chosen route to reuse 'old' drugs to treat diseases outside their approved indication.6 Effectively, these projects make use of de-risked compounds, which in principle are more accessible due to reduced overall costs (bypassing research and development components up to phase II/III clinical trials) and shorter development timelines.

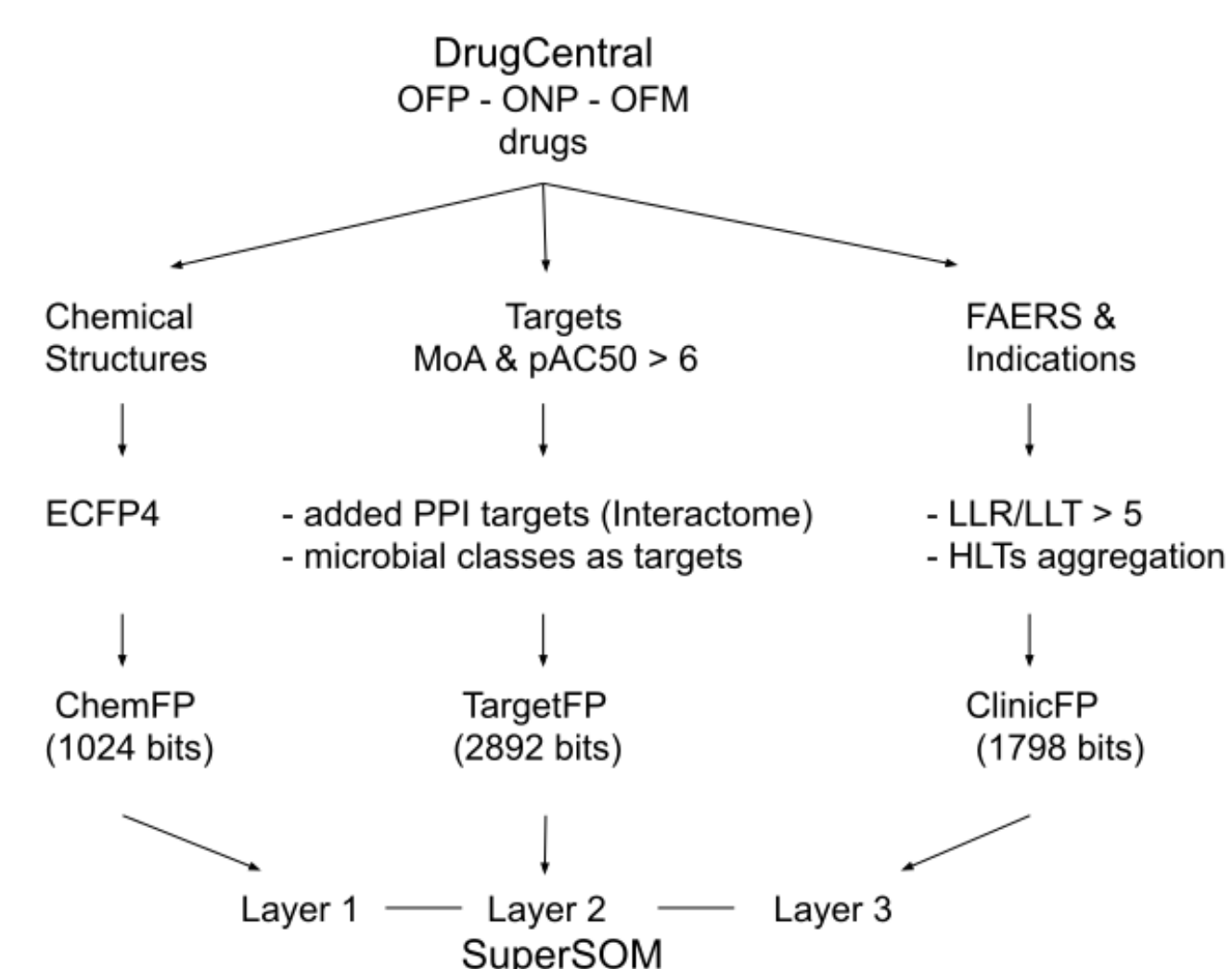## AIM

BUILD NEW TECHNOLOGIES TO DRIVE-FORWARD DRUG REPURPOSING.

WORKFLOW

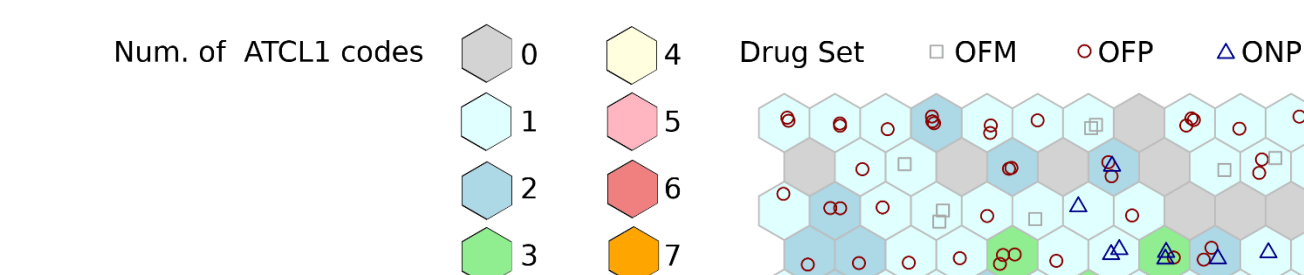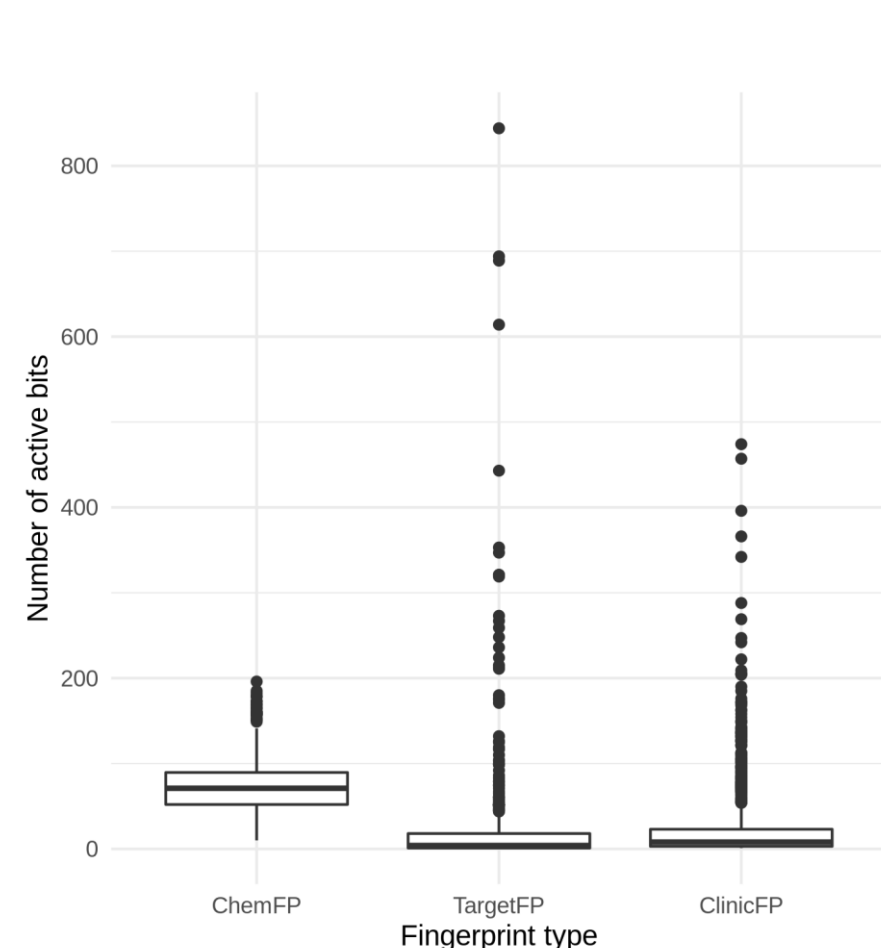**Simlarity principle: similar drugs have similar applications.**

Use data from DrugCentral and DRP categories to build a Super Self-Organizing Map (**SuperSOM**) model based on chemical, bioactivity and clinical encodings.
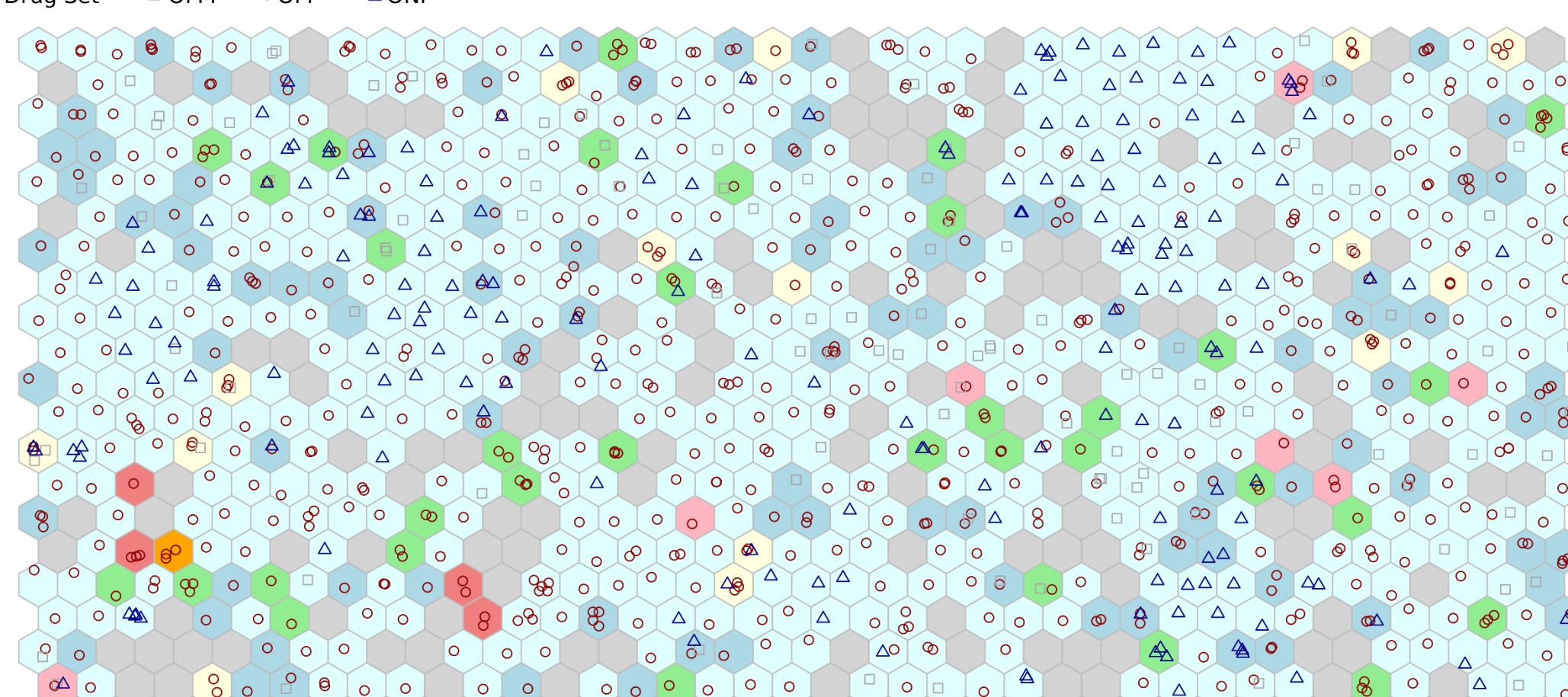

RESULTS

40x20 SuperSOM shows a landscape for drug repurposing of 959 drugs
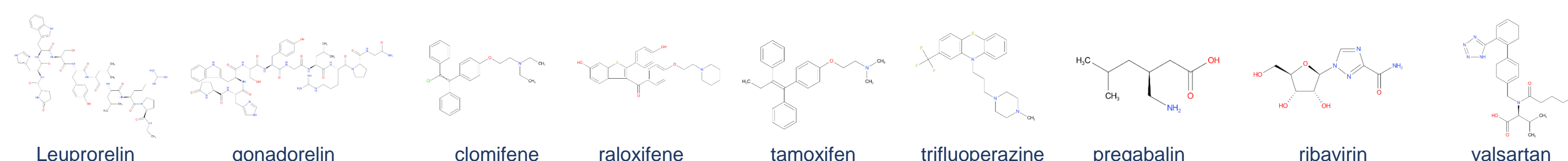

Currently in analysis:
- 101 units with ≥ 2 drugs and ≥ 2 ATC L1 are
- Contributions of ChemFP, TargetFP and ClinFP
- Potential of OFP/OFM to be reused

Unit ID	ChemFP	TargetFP	ClinFP	Set	L1	DrugNames	Indications/*Off-label uses
147	167	1	0	OFP	L	leuprorelin	Endometriosis, Precocious puberty, Advanced Prostatic Carcinoma, Anemia due to Bleeding Uterine Leiomyoma, Malignant tumor of ovary*
				OFM	H	gonadorelin	Amenorrhea, Diagnostic Test for Gonadotropin Deficiency
720	6	182	0	OFP	G	clomifene	Female infertility, Ovulation induction, Male infertility*
					G	raloxifene	Postmenopausal osteoporosis, Prevention of Breast Carcinoma, Prevention of Glucocorticoid-Induced Osteoporosis*
					L	tamoxifen	Infiltrating duct carcinoma of breast, Carcinoma of female breast, Prevention of Breast Carcinoma, Endometrial carcinoma*, Malignant tumor of ovary*
					N	trifluoperazine	Anxiety, Schizophrenia
253	4	0	70	OFP	N	pregabalin	Postherpetic neuralgia, Generalized anxiety disorder, Fibromyalgia, Diabetic peripheral neuropathy, Partial Epilepsy Treatment Adjunct
					J	ribavirin	Respiratory syncytial virus infection, Chronic hepatitis C
					C	valsartan	Hypertensive disorder, Chronic heart failure, Left ventricular cardiac dysfunction, Atrial fibrillation, Diabetic renal disease, Diastolic heart failure, Nondiabetic Proteinuric Nephropathy

L: ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS; H: SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS; G: GENITO URINARY SYSTEM AND SEX HORMONES; N: NERVOUS SYSTEM; J: ANTIINFECTIVES FOR SYSTEMIC USE; C: CARDIOVASCULAR SYSTEM

Leuprorelin · gonadorelin · clomifene · raloxifene · tamoxifen · trifluoperazine · pregabalin · ribavirin · valsartan

REFERENCES

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ACKNOWLEDGEMENTS